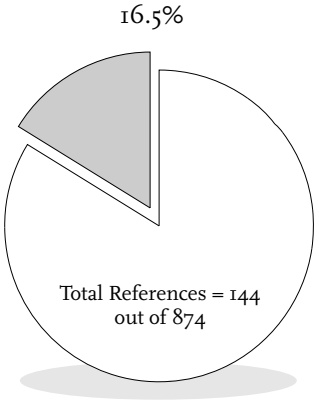
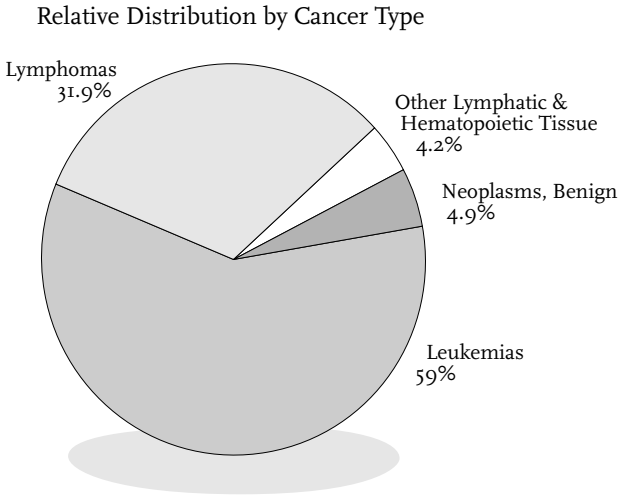
10. Remission of Neoplasms of Lymphatic and Hematopoietic Tissue

Remission of Neoplasms of Lymphatic and Hematopoietic Tissue





References in Chapter 10 = 144
References in Part One = 874

Leukemias account for 2.7% and lymphomas 5.3% of the cases of cancer reported by participating tumor registries to the SEER (Surveillance, Epidemiology, and End Results) Program between 1983 and 1987. Incidence statistics show that acute lymphocytic leukemia accounts for 0.3% of the total number of cases of leukemia reported; acute myeloid leukemia, 0.6%; chronic lymphocytic leukemia, 0.8%; chronic myeloid leukemia, 0.4%; and all other leukemias, 0.6%. Non-Hodgkin's lymphoma accounts for 3.4% of the total number of cases of lymphoma; Hodgkin's disease, 0.8%; and multiple myeloma, 1.1%. The relative five-year survival rates (1981-1986) for all types of leukemias combined is 34.9% with the survival rate for acute lymphocytic 51.8%; acute myeloid, 8.4%; chronic lymphocytic, 63.3%; chronic myeloid, 24.7%; other lymphocytic 31.8%; other myeloid, 12.9%; and other types, 25.2%. Five-year survival rates for all types of lymphoma combined is 56.4%, with the survival for Hodgkin's disease, 75.9%; non-Hodgkin's lymphoma, 50.8%; and multiple myeloma, 26.4%. Mortality data show that leukemias and lymphomas account for 13% of the mortality cases reported to the SEER Program between 1983 and 1987. Hodgkin's disease accounts for 0.5%; non-Hodgkin's lymphoma, 3.1%; multiple myeloma, 1.6%; and all leukemias combined, 3.9%. Of the leukemias, acute lymphocytic accounts for 0.3%; chronic lymphocytic, 0.7%; acute myeloid, 1.1%; chronic myeloid, 0.5%; and all others, 1.3% (Cancer Statistics Review 1973-1987).

Of the 144 references in Chapter 10, 38 are annotated with summaries. Some annotated references contain 1 or more case reports. There are 106 supplemental references provided. Full text of 32 case reports is presented. Of the 17 cases of spontaneous remission of leukemias reported there are 9 cases of chronic lymphocytic leukemia; 2 cases of acute lymphocytic leukemia; 1 case of acute myelogenous leukemia; 2 cases of adult T-cell leukemia; and 1 case of hairy cell leukemia. Of the 13 cases of lymphoma reported, there are 2 cases of follicular lymphoma; 4 cases of Burkitt lymphoma; 2 cases of lymphoblastic lymphoma; 3 cases of large cell lymphoma; and 2 cases of poorly differentiated lymphocytic lymphoma reported.

A summary of the chapter contents and a comparative analysis of cases reported in previous literature reviews are presented in Tables One and Two.

Table One: References and Case Reports in Chapter Ten †

Tumor Site	References (number)	Cases (number)	Cases (%)
Leukemia	85	17	6.6%
Lymphoma	46	13	5.0%
Other	6	0	0.0%
Benign	7	2	0.8%
Totals	144	32	12.4%

† Total number of case reports in Part One is 258.

Table Two: Comparison Between Other Major Literature Reviews of Cases of Spontaneous Remission of Hematological and Lymphatic Tissue Malignancies

Tumor Site	Rohdenburg (1918) (N =185)	Fauvet (1960) (N=192)	Boyd (1966) (N=97)	Everson* (1966) (N=182)	Challis (1990) (N=505)
Leukemia	0	0	0	0	53
Lymphoma	0	0	0	0	68
Other	0	0	0	0	2
Totals	0	0	0	0	123

* Everson and Cole did not report cases of leukemias and lymphomas.

Leukemias

Spontaneous Remission in Acute Leukemia

Report of a Case Complicated by Eclampsia

Birge RF; Jenks AL Jr; Davis SK

Journal of the American Medical Association 140: June 18 1949; 589-592

Extracted Summary

Acute leukemia in a 33-year-old woman had its onset in the seventh month of gestation. Symptoms of eclampsia developed, and she prematurely delivered a nonviable infant which showed no evidence of leukemia at autopsy. After delivery, she improved rapidly and was in good health for twenty-one months, whereafter again the clinical and hematologic picture of acute leukemia developed and the patient died.

During the remission, cytologic evidence of leukemia in the sternal marrow and in the peripheral blood disappeared. The administration of radioactive phosphorus, in an attempt to induce a second remission, was followed by reduction in the leukocyte and thrombocyte counts without clinical evidence of improvement.

The foregoing case exemplifies a unique form of acute leukemia which has been characterized by an acute febrile onset, frequent involvement of mucous membranes and less frequent splenomegaly and lymphadenopathy. Initially, severe anemia, leukopenia and thrombocytopenia are observed. There follows a remission, lasting as long as 21 months, characterized by apparent restoration of health, by disappearance of demonstrable lymphadenopathy and splenomegaly and by return of the peripheral blood and bone marrow pictures to normal or nearly normal. Suddenly, fever and other clinical manifestations of acute leukemia reappear; lymphadenopathy and splenomegaly, if previously present, return. The leukocyte count rises rapidly in most instances and evidence of acute leukemia in the peripheral blood and bone marrow is again apparent.

Ideally, remissions induced by aminopterin (4-aminopteroyl glutamic acid) or by other means should simulate the spontaneous ones described.

Selected Case Report

On September 1, 1942, a white married woman, aged 33, noticed slight edema of the feet and ankles. On the evening of September 3 she had several chills. She entered the hospital the following morning for observation, stating that she was in the seventh month of her second gestation. A right salpingectomy and ovariectomy had been performed in 1940 for ectopic pregnancy. Her maternal grandmother had profound anemia at the age of 50 and died four months later.

The temperature was 100°F. Physical examination revealed generalized slight puffiness of the skin and moderate edema of the ankles. The throat showed hyperemia. The blood pressure was 150 systolic and 84 diastolic. The abdomen was enlarged, consistent with the seventh month of pregnancy. Fetal heart tones were normal. The spleen and liver were not palpated, and enlarged lymph nodes were nowhere encountered.

Urinalysis showed albumin 1 gm/l, an acetone reaction of 4 plus and a positive diacetic acid reaction; microscopic study of a centrifuged specimen revealed 12 to 15 erythrocytes and an occasional leukocyte/high power field. The initial hemogram showed: hemoglobin 9.2 gm/100 ml, erythrocytes 2,480,000/ mm^3 and leukocytes 9,200/mm^3, with 81% stem cells, 9% neutrophils, 2% monocytes and 8% lymphocytes. Results of Kline and Kahn flocculation tests and a heterophil antibody test were negative. The icterus index was 10.7 units.

Blood smears contained many peroxidase negative stem cells. The normochromic anemia was accompanied with moderate polychromatophilia. Thrombocytes were moderately decreased.

A sternal puncture on September 7 showed a hyperplastic marrow containing a pronounced preponderance of stem cells similar to those observed in the peripheral blood.

On September 15 she had numerous convulsions. The blood pressure had risen to 180 systolic and 90 diastolic. The urine contained 20 gm/l of albumin, and the serum

protein was 4.4 gm/100 ml. The spinal fluid pressure was normal; the cell count was 1, and the protein level was 20 mg/100 ml.

Intravenously administered pentobarbital sodium (nembutal) controlled the convulsions, but the patient remained comatose through the following day. In the evening she gave birth to a nonviable infant.

At autopsy, the female infant weighed 1,240 grams; it showed slight maceration and no other grossly recognizable changes. In the placenta, numerous small fresh hemorrhagic infarcts were observed. Microscopic studies revealed no evidence of leukemic involvement of the infant's tissues or of the placenta.

After delivery, the patient remained in a comatose state for several days, but she gradually improved. Her temperature fluctuated from 100 to 105°F., but was normal after September 29. The content of albumin in the urine gradually decreased, until only a slight trace was present on October 1.

On September 24, the total leukocyte count was 5,400 with 50% stem cells. Five days later the count was 4,500 with 26% stem cells. The heterophil antibody reaction was negative. The serum protein was 4.6 gm/100 ml, and the blood uric acid was 2.9 mg/100 ml. A blood culture was negative.

During October she gradually improved. The leukocyte count dropped to 2,250 on October 7 and then gradually rose to level of 6,200 ten days later. Stem cells decreased in number until it was impossible to find them after October 12. A sternal puncture, performed on October 14, revealed a remarkably different picture from the previous one. The picture was that of an essentially normal marrow.

Interval History: The patient was placed on a highly nutritious diet, especially rich in butter. She was given yellow bone marrow, vitamin B complex, vitamin A and vitamin D. After discharge from the hospital on November 16, 1942, she gained strength and by March 1943 was doing much of her housework. By October she seemed to be entirely well doing all her housework and taking part in social activities.

For a period of almost two years, blood cell counts were taken first at weekly intervals and then at fortnightly intervals. Her erythrocyte count was always close to the lower limit of normal. The hemoglobin was normal. Slight macrocytosis was always present. The leukocyte count remained around 5,000, and no immature cells were observed in the smears.

The Recurrence: On July 15, 1944, she had an abscessed tooth treated by a dentist. Afterward she felt perfectly well, but on July 26 the hemogram showed: hemoglobin 13.9 gm/100 ml, erythrocytes 3,770,000/ mm^3 and leukocytes 4,350/mm^3, with 54% stem cells, 1 % band cells, 2 per cent neutrophils, 1% eosinophils, 3% monocytes and 39% lymphocytes.

During the middle of August she had several attacks of mild urticaria. On the morning of August 17, menstruation began. Later in the day, a mild chill occurred and the temperature was 102°F.

When she was readmitted to the hospital on August 21, physical examination revealed a few cutaneous petechiae. There was no demonstrable lymphadenopathy, splenomegaly or hepatomegaly. The blood pressure was 98 systolic and 70 diastolic.

The admission hemogram showed: hematocrit 33 vol%, hemoglobin 9.7 gm/100 ml, erythrocytes 3,010,000 /mm^3 and leukocytes 40,400/mm^3 with 88% stem cells, 1% band cells, 2% neutrophils and 9% lymphocytes. The urine was normal. The result of a Friedman test was negative. The sedimentation rate was 136 mm/hour (Westergren), blood urea nitrogen 16.3 mg/100 ml, uric acid 3.1 mg/100 ml and total protein 6.6 gm/100 ml.

The course was irregularly febrile, marked by occasional chills. Almost every transfusion was accompanied with chilling and fever. Malodorous vaginal discharge appeared, and at intervals there was passage of increasing amounts of blood and blood clots. Examination revealed ulcerative necrosis of the cervix. The hemorrhage could not be controlled by blood transfusion, by administration of vitamin K or by other measures. An abscess of the buttock developed and drained persistently. Scattered petechiae and ecchymoses appeared in the skin, and from time to time she complained of urticaria.

Blood cultures were repeatedly negative. Although the urine contained very few leukocytes, urine cultures were persistently positive for Aerobacter aerogenes, Escherichia coli and Proteus vulgaris. The leukocyte count varied from 40,000 to 85,000. On August 30, she was given 3 millicurie equivalents of radioactive phosphorus in 5% dextrose and isotonic sodium chloride solution intravenously. Similar amounts were given on September 4 and September 22. The leukocyte count rose to 101,000 on September 6 and gradually dropped to 18,000 on October 2. Thereafter it fluctuated from 8,000 to 18,000, with stem cells persisting in high percentage. Anemia and thrombocytopenia persisted, the thrombocyte count falling to 9,000 on October 4.

She was maintained on a highly nutritious, high-fat diet supplemented by yellow bone marrow and vitamin B complex. She received many blood transfusions and several courses of penicillin. There was very little response to any therapeutic measures attempted. She died on October 18.

Necropsy: At necropsy, slight generalized lymphadenopathy was encountered. The liver weighed 1,955 grams and the spleen weighed 205 grams. A few petechiae were found in the pleurae and endocardium. The dilated heart weighed 285 grams. No important changes were observed along the respiratory, gastrointestinal or urinary tracts. The endometrium was represented by a thin, hyperemic irregular surface, to which a few shreds of soft red tissue were attached. The patulous cervical canal was filled with thin malodorous sanguineous fluid, and the hyperemic granular endocervix showed small areas of necrosis. The

ribs and vertebral bodies showed normal density and contained abundant thick, pale red bone marrow.

The bone marrow was heavily infiltrated by cells resembling those found in the peripheral blood and in the bone marrow during life and contained few megakaryocytes, normoblasts or granulocytes. Large mononuclear cells were scattered along the liver sinusoids and along the sinusoids of the lymph nodes, which showed preservation of architectural pattern. However, the architectural pattern of the spleen was obliterated because of proliferation of large numbers of mononuclear cells. The inflammatory process in the cervix proved to be a necrotizing one, characterized by little evidence of repair and by the presence of very few segmented neutrophils and small numbers of large mononuclear cells. Other organs did not show evidence of leukemic involvement.

Effects of Concurrent Infections and their Toxins on the Course of Leukemia

Pelner L; Fowler GA; Nauts HC
Acta Medica Scandinavica 162(Supp 338): 1958; 1-47

Extracted Summary

Of all the recorded cases of so-called "spontaneous" regression in cancer or "spontaneous" remission in leukemia, the great majority have occurred in patients who developed an acute concurrent infection, inflammation or fever, principally streptococcal infections.

Before studying this phenomenon in leukemia, approximately 350 histories of cases of malignant tumors in which such complications may have played a salutary role were assembled for study. In 167 of these patients (152 inoperable, 15 operable, untreated) the neoplasms disappeared, and 62 of these remained free from recurrence or metastases when last traced 5 to 44 years later. Among the 73 determinate operable cases in which infection or inflammation developed before or after surgical removal, 52 patients were traced 5 to 54 years later, free from disease.

However, if the infection developed following heavy radiation or if the disease was very far advanced, only temporary or partial regression of the neoplasms occurred. The beneficial effects of acute concurrent infections or fever on leukemia have also been observed by a large number of investigators. Over 70 such histories have been reported in the literature and many others have been cited briefly.

Often the infection did not occur until the terminal stage of the leukemia, and this may have been one reason why permanent benefit following such infections has not been reported in cases of leukemia, although 36 patients with malignant lymphoma remained free from further evidence of disease after concurrent infection or toxin therapy.

As to how acute infections, inflammation or bacterial toxin therapy may exert their apparently beneficial effects on patients with cancer or leukemia, it is known that neoplastic cells are more sensitive to heat than are normal cells. However, in addition to this factor, it appears that infections or their toxins may activate or mobilize various tissues or systems in the body which may be less active than normal in these patients.

Spontaneous Remission in Chronic Lymphocytic Leukemia

Chervenick PA; Boggs DR; Wintrobe MM
Annals of Internal Medicine 67(6): Dec 1967; 1239-1242

Extracted Summary

A 63-year-old man is described with typical findings of chronic lymphocytic leukemia, diagnosed in 1952 when the patient was 48 years old. Treatment consisted of triethylenemelamine on two occasions in 1952 and 1953, splenectomy for a Combs' positive hemolytic anemia in 1952 and cortisone for a period of 5 months between May and October 1953. There was a marked improvement of the anemia with beginning of cortisone therapy with little effect on other manifestations of his disease.

However, 1 1/2 years after cessation of all therapy the leukocyte count began to decline, and the lymphadenopathy and hepatomegaly disappeared. He has remained asymptomatic and free of any clinical signs of chronic lymphocytic leukemia since 1956.

There is no good temporal relationship between any form of therapy and subsequent remission, and although one cannot definitely exclude an effect from the therapy, it seems quite likely that this represents a spontaneous remission of chronic lymphocytic leukemia. (Permission to reproduce case report denied by publisher.)

Spontaneous Remission of Leukemic Lymphoproliferative Disease

Han T; Sokal JE

Cancer 27(3): March 1971; 586-595

Extracted Summary

Spontaneous remission was observed in 4 of approximately 400 patients with chronic lymphocytic leukemia or malignant lymphoma with leukemic manifestations. Findings prior to spontaneous remission in these patients included generalized lymphadenopathy and splenomegaly. In one patient, the remission followed an acute (presumably viral) infection. Relapse of disease after spontaneous remission, characterized by lymphadenopathy and tissue infiltration only, without lymphocytosis or bone marrow involvement, was seen in one patient with chronic lymphocytic leukemia and one with leukemic lymphosarcoma. Seven well-documented cases of spontaneous remission in leukemic lymphoproliferative disease were found in a survey of the literature. The patterns of normalization of the peripheral blood count seen in the pooled cases included both rapid declines of lymphocyte counts, consistent with active destruction of leukemic cells, and very slow decreases which suggested that the mechanism of remission was cessation of production of leukemic cells, with their subsequent disappearance at a rate consistent with their known long life span. Only one death from lymphoproliferative disease is recorded among these pooled cases.

Selected Case Report

Case 1: H. B., a 69-year-old woman, developed weakness and easy fatigability in 1955. In May 1956, she experienced fullness in the left upper quadrant of her abdomen. She was referred to the Roswell Park Memorial Institute in October 1956, with the diagnosis of chronic lymphocytic leukemia.

Physical examination revealed moderate generalized lymphadenopathy. The spleen was palpable 2 centimeters below the left costal margin, and the liver was palpable 3 centimeters below the right costal margin. Hemoglobin was 11.2 gm/100 ml, platelet count 126,000/mm^3, and the white blood cell count 40,000/mm^3, with 87% lymphocytes. The bone marrow aspirate showed infiltration with "a great number of lymphocytes," with relative depression of other elements; megakaryocytes were normal. She was treated with 2 courses of chlorambucil (first course, November 1956 to January 1957; second course, December 1959 to January 1960) and an excellent partial remission, characterized by disappearance of lymphadenopathy and hepatosplenomegaly, rise in hemoglobin and significant fall in lymphocyte count, was obtained each time. However, mild lymphocytosis and lymphocytic infiltration of the bone marrow persisted.

A gradual increase in lymphocytosis was noted during 1960. In May 1961, slight left axillary lymphadenopathy was found; the white blood cell count was 80,000/mm^3 with 93% lymphocytes. Because of the patient's age (now 75) and excellent clinical status, treatment was withheld. One year later, splenomegaly (5 centimeters below the costal margin) and slight generalized lymphadenopathy was observed. Blood count at that time was as follows: hemoglobin 9.8 gm/100 ml, platelets 190,000/mm^3, white blood cells, 111,680/mm^3, with 96% lymphocytes. The white blood cell counts ranged between 80,500 and 112,000/mm^3, with 90 to 98% lymphocytes, from May 1962 to April 1963. In May 1963, she had an upper respiratory infection and an episode of upper abdominal distress. She was admitted to another hospital in June 1963, because of extreme weakness, generalized aches, and abdominal distress. She was given 2 units of blood and treated symptomatically, with improvement. She was discharged on July 3, 1963.

Between April and September 1963, the total white blood cell count fell to normal levels. On examination in our clinic in September, lymphadenopathy and hepatosplenomegaly had regressed markedly. Hemoglobin was 12.8 gm/100 ml, platelet count 280,000/mm^3, and the white blood cell count 9,943/mm^3 with 67% lymphocytes.

There was a gradual fall in the percentage of lymphocytes during the next 3 years, and a normal lymphocyte count was reached in September 1966. Lymphadenopathy had not been noted since that time, and the liver and spleen have not been palpable. When she was last seen, in May 1968 (at 82 years of age), the hematocrit was 40%, platelet count 106,200/mm^3 and the white blood cell count 5,466/mm^3, with 30% lymphocytes. Bone marrow aspiration and biopsy at that time still showed marked lymphocytic infiltration, however.

Comments: This patient with chronic lymphocytic leukemia had two excellent partial remissions with chlorambucil therapy, followed by relapses, some years before the spontaneous disappearance of all peripheral manifestations of her disease. Despite complete peripheral remission, however, the last bone marrow aspiration showed evidence of residual disease.

Spontaneous Regression of Hematologic Cancers

Wiernik PH

National Cancer Institute Monographs 44: 1976; 35-38

Extracted Summary

Spontaneous regression of hematologic cancer is extremely rare. Data gleaned from the literature and from previously unreported cases allow certain interesting general conclusions. Spontaneous remission of acute leukemia is associated with bacterial infection and is of short duration, weeks to months. Spontaneous regression of lymphoma or plasma cell dyscrasia is often of substantial duration, months or years, and frequently is associated with viral infections. Spontaneous regression of chronic lymphocytic leukemia is also of significant duration and has been associated with the occurrence of a new primary carcinoma in one-third of the cases.

Spontaneous Remission in Chronic Lymphoid Leukemia

Lebedev VN; Kosukhina NV; Lebedeva YL

Terapeuticheskii Arkhiv 48(8): 1976; 26-30

Extracted Summary

The authors give a detailed description of three cases of spontaneous remissions in patients with chronic lymphoid leukemia registered among 287 patients (1.04%) observed during 18 years under conditions of constant prophylactic examinations. In three male patients with the disease in its highest stage who were not subjected to chemotherapy, complete regression of the pathological process occurred. The authors failed to find the causes of remission. Complete remissions lasted for 8 and 10 years in 2 patients, one patient had a severe relapse after a six-year remission.

Selected Case Report

Case 3: A 37-year-old woman was observed with a progressive picture of chronic lymphoid leukemia in whom, during the second year of the disease and without treatment, a spontaneous clinical and hematological remission was observed. The remission lasted 5 years. In the myelogram the lymphocyte count was 21% during the remission (although during the stage of the disease in progress it reached 71%). After five years, the abdominal lymph nodes increased in size and general lymphadenopathy and splenomegaly reappeared, but the peripheral blood count stayed normal: 6,175 leukocytes/ml with 11% lymphocytes, and lymphocyte count in bone marrow no more than 11.4%. The patient died from the general lymphosarcoma (as diagnosed by the authors) despite the treatment with chemotherapy and x-ray irradiation.

(Noetic Sciences translation)

Remission of Chronic Lymphocytic Leukemia After Smallpox Vaccination

Hansen RM; Libnoch JA

Archives of Internal Medicine 138: July 1978; 1137-1138

Extracted Summary

A 78-year-old man with untreated chronic lymphocytic leukemia (CLL) was revaccinated for smallpox. A severe local reaction and generalized rash followed that responded to treatment with vaccinia immune human globulin. After recovery, the leukocyte count fell to normal and all evidence of CLL disappeared. He remains in complete remission three years after smallpox vaccination.

Selected Case Report

A 78-year-old man was first noted to have an elevated peripheral lymphocyte count in 1968 with a leukocyte count of 15,200/mm3 with 36% lymphocytes. A repeat leukocyte count in 1970 was 14,700/ mm3 with 62% lymphocytes. In 1971, a right hip replacement for degenerative arthritis showed diffuse infiltration of the femoral head with small lymphocytes, and a prostatic resection for obstructive uropathy disclosed lymphocytic infiltration of the prostatic tissue. In 1973, a diagnosis of CLL was made on the basis of 1 x 3 centimeter inguinal nodes and a bone marrow showing diffuse infiltration of small lymphocytes, about 50% in number. There was no other organomegaly, and the hematocrit reading was 51%, hemoglobin value 17 gm/ dl, and platelets 245,000/mm3. Generalized hypogammaglobulinemia was present demonstrating the following values: IgG, 600 mg/dl (570 to 1900); IgA, 59 mg/dl (60 to 330); IgM, 23 mg/dl (45 to 145); and IgD, 0 mg/dl (0 to 6). A second strength PPD skin test produced 4 centimeter induration. No treatment was given.

On March 20, 1974, a smallpox revaccination was administered by the patient's primary physician. Two weeks later the inoculation site had not healed but had become a large pustular draining lesion with eschar and severe erythema, induration, and axillary adenopathy. A generalized, maculopapular, nonvesicular rash developed and generalized vaccinia was suspected. However, a skin biopsy showed vasculitis, clinically attributed to contaminating foreign protein from the inoculation. Despite topical applications, the rash worsened, and because the possibility of generalized vaccinia could not be excluded, 20 milliters of vaccinia immune human globulin was given intramuscularly on April 20, 1974. The rash responded dramatically with clearing over the next few days and healing of the inoculation site. Attempts to isolate the vaccinia virus from blood and urine were unsuccessful. Antibody titers for vaccinia before administration of vaccinia immune human globulin were hemagglutination inhibition < 1:5, complement fixation< 1:8, and neutralization test < 1:5.

Over the next several months the patient's absolute lymphocyte count steadily fell and has remained within normal limits since then. Physical examination findings are normal following regression of inguinal lymphadenopathy. Repeat quantitative immunoglobulin values, while not normal, are improved: IgG, 600 mg/dl (normal 422 to 1543); IgA, 290 mg/dl (normal, 56 to 479); IgM, 30 mg/dl (normal, 50 to 391); IgD, 0 mg/dl (normal, 0 to 13). Repeat bone marrow examinations 23 and 35 months after vaccination showed normal bone marrow with scattered small benign appearing lymphoid nodules but no diffuse infiltration of lymphocytes as seen during previous examination. The patient remains in complete remission three years after the smallpox vaccination.

Spontaneous Remission in Acute Lymphocytic Leukaemia: Case Report

Long K; Egan EL

Journal of the Irish Medical Association 72(8): Aug 31 1979; 335-337

Extracted Summary

A seven-year-old girl presented initially with pancytopenia and was treated with supportive therapy alone. Her peripheral blood and bone marrow pictures returned to normal and the blood remained normal for four and a half months. The haematological picture then relapsed and the diagnosis of acute lymphocytic leukaemia was established. It is considered that acute lymphocytic leukaemia was present initially and that it underwent spontaneous remission.

The patient, a seven-year-old girl, was admitted to hospital on 5th July, 1977. She was well until three weeks prior to admission when she developed anorexia and malaise. Twenty-four hours prior to admission she developed a bleeding tooth socket. On examination she was pale, had ecchymoses on both lower limbs and there was blood oozing from a tooth socket. She had a precordial systolic murmur. Her temperature was a 100°F. There was no lymphadenopathy or splenomegaly present. Investigations revealed a haemoglobin of 2.6 gm/dl, white cell count of 1,100/mm3 and platelet count of 11,000/ mm3. The peripheral blood film showed a differential count of 90% lymphocytes (many atypical) and 10% neutrophils. Blast cells were not present. Her urea, electrolytes, vitamin B12, folate, serum iron and iron-binding capacity and coagulation studies were all normal. Cultures of urine, faeces and blood were negative. Chest x-ray showed splenomegaly but was otherwise normal. She was transfused with blood and platelets and was placed on gentamicin and carbenicillin.

Marrow aspiration was unsuccessful on admission. Marrow biopsy revealed marked marrow hypercellularity consisting of an artefacted mononuclear cell population. Specific identification of the nature of these cells could not be made. Repeat aspiration and biopsy forty-eight hours after admission was unsuccessful. Seven days after admission marrow aspiration was again unsuccessful. Marrow biopsy then showed areas of normal red blood cell and platelet precursors with foci of immature white cells. Again, no definite diagnosis could be made.

Thirteen days after admission she had improved and was stable with haemoglobin of 10.7 gm/dl, white cell count of 1,900/mm3 and a platelet count of 41,000/mm3. Differential white cell count showed neutrophils to be 8%, lymphocytes 89%, monocytes 2%, and eosinophils 1%. Blast cells were not present. Marrow aspirate at this time showed a normocellular marrow with an E:G ratio of 1.3. Erythropoiesis was megaloblastoid. Granulopoiesis was left shifted. Megakaryocytes were atypical. There was no evidence of leukaemia. The findings were considered consistent with a marrow recovery state.

Further improvement in her condition occurred and she was discharged from hospital, twenty-one days after admission. She was reviewed at the Outpatients Department on two occasions over the subsequent fourteen weeks. Blood counts were normal on both occasions, and she was well on no treatment. She remained well until the 16th of November, 1977 (16 weeks after the initial presentation), when she was re-admitted to hospital with a three-week history of bruising and with a one-week history of malaise.

On examination she was pale, the temperature was 101°F., and areas of purpura and petechiae were present on both lower limbs. She had slight lymphadenopathy in cervical, axillary and inguinal areas, and the spleen was palpable two centimetres below the left costal margin. A grade II pansystolic cardiac murmur was present. Her haemoglobin was 7.8 gm/dl. The white cell count was 31,000/mm3 and the platelet count was 37,000/ mm3. Peripheral blood film showed 100% lymphocytes, the majority of which were lymphoblasts. Other studies, including urea, electrolytes, serum electrophoresis, chest x-ray, urinalysis and blood cultures, were normal or negative. Throat swab grew haemolytic streptococcus, group A. Marrow aspiration now showed a markedly hypercellular marrow with all normal elements replaced by lymphoblasts. PAS stains were positive. Sudan Black and peroxidase stains were negative. The diagnosis of acute lymphocytic leukaemia was made.

Spontaneous Remission in Acute Myelogenous Leukemia in the Adult

Lachant NA; Goldberg J; Nelson DA; Gottlieb AJ

American Journal of Medicine 67(4): Oct 1979; 687-692

Extracted Summary

A spontaneous complete remission of 17 months duration was observed in a patient with acute myelogenous leukemia. Resolution of all clinical and morphologic abnormalities occurred. The remission was apparently associated with an acute pulmonary infection. At relapse, remission induction was accomplished with cystosine arabinoside and daunorubicin therapy. In-vitro granulocyte-macrophage agar culture studies (CFU-c) showed an abnormal growth pattern at presentation, which persisted during the period of spontaneous remission. Reports of spontaneous remissions of acute myelogenous leukemia in adults have become increasingly rare, and the remissions themselves are short-lived. Despite the association between spontaneous remissions and acute infections or febrile episodes, attempts at remission induction with infectious agents have been unsuccessful. Spontaneous remissions are an uncommon variant of the natural course of acute myelogenous leukemia in the adult.

Selected Case Report

A 67-year-old woman was last known to have a normal "blood count" in 1971. A diagnosis of "anemia" was made in January 1976. In April, the hemoglobin concentration was 6.6 g/dl, and the white blood cell count was 1,400/microliter, including 5% myeloblasts and 1% promyelocytes. Platelets were 45,000/microliter. A bone marrow aspirate was obtained, and a diagnosis of "refractory anemia" was made. The administration of Halotestin, 15 mg/day, and blood transfusions were begun.

The patient was hospitalized in early June 1976 because of pneumonia in the lower lobe of the right lung. The hemoglobin level was 5.6 gm/dl, the white blood cell count was 1,500/microliter, with 24% granulocytes and 76% lymphocytes. Multiple cultures of blood, urine and sputum were negative. The patient remained febrile despite therapy with cephazolin and gentamicin. She was transferred to the Upstate Medical Center on June 29, 1976.

Upon careful review of her records, the patient was found to have received diphenhydramine, acetaminophen, digoxin, thiazide diuretics, ampicillin, cephalexin and blood transfusions during her hospitalization. Her past medical history was negative except for a cervical carcinoma for which she was treated by hysterectomy without radiotherapy in 1948. Positive physical findings on initial examination included a temperature of 38.2°C., scleral icterus, consolidation of the lower lobe of the right lung, a palpable spleen tip, diffuse petechiae and ecchymoses, and moderate ankle edema. The total bilirubin was 6.0 mg/dl with an indirect bilirubin of 2.9 mg/dl. The serum glutamic oxalacetic transaminase was 58 IU. The chest film showed pneumonia in the lower lobe of the right lung with a pleural effusion. Cultures of blood, urine and sputum were obtained.

The hemoglobin level was 8.4 gm/dl. The white blood cell count was 1,100/microliter without circulation myeloblasts. The platelet count was 16,000/microliter, and the reticulocyte count was 0.1%. Review of the bone marrow obtained in April showed a normocellular marrow with 53% myeloblasts, many containing Auer rods. A diagnosis of acute myelogenous leukemia was made. On June 30, a marrow aspirate was hypocellular. The biopsy specimen showed decreased megakaryocytes, normoblasts and granulocyte precursors, whereas the plasma cells and lymphocytes were increased.

The administration of antibiotics was discontinued on admission. The patient's temperature returned to normal over the first 24 hours of observation. All cultures were negative. The pleural effusion was determined to be a sterile exudate. On July 2, the hemoglobin level was 8.0 gm/dl. The white blood cell count was 1,600/microliter, and the platelets were 30,000/microliter. The bone marrow was 20% cellular with normal numbers of megakaryocytes and only 2% myeloblasts. No Auer rods were seen. The marrow was considered to represent a phase of recovery from hypoplasia.

A fiberoptic bronchoscopy was performed on July 6, for evaluation of the persistent infiltrate in the lower lobe of the right lung. Cultures for bacteria, fungi and acid-fast organisms were negative, as were cytologic and histologic examinations, including silver methenamine stains.

The hemoglobin level, white blood cell count and platelets continued to rise without the aid of transfusion. Bone marrow examination was again performed on July 6. Myeloblasts were normal in number, and no Auer rods were observed.

The patient continued to improve throughout the rest of her hospitalization. There was complete resolution of the infiltrates in the lower lobe of the right lung. On July 13, the day of discharge, the hemoglobin level was 9.6 gm/dl. The white blood cell count was 11,800/ microliter, and the platelet count was 248,000/microliter. The bone marrow was 40% cellular with 1% myeloblasts and 1.3% promyelocytes, and fulfilled the criteria for a complete remission. There was no evidence of leukemia, including an exhaustive search for Auer rods on Wright-stained and peroxidase-stained smears.

On August 25, the patient was asymptomatic with no abnormal findings on physical examination. The complete blood count, platelet count and differential were all within normal limits. In April 1977, the hemoglobin level was 15.5 gm/dl, the white blood cell count was 6,800/microliter, and the platelet count was 350,000/microliter. The patient was next seen at the Upstate Medical Center for a persistent upper respiratory tract infection on January 23, 1978, 17 months after her spontaneous remission. Her hemoglobin level was 11.3 gm/dl. The white blood cell count was 2,000/ microliter with 22% myeloblasts. Numerous Auer rods were present. The blasts were peroxidase positive and alpha naphthyl acetate esterase negative. The platelets were 83,000/microliter. The bone marrow was now 50% cellular, with 56% myeloblasts. Megakaryocytes were normal in number. A diagnosis of acute myelogenous leukemia in relapse was made. Induction chemotherapy for acute myelogenous leukemia, according to CALGB protocol #7721, was begun on February 3. Cytosine arabinoside, 100 mg/m^2/24 hours by continuous intravenous infusion for seven days, and daunorubicin, 45 mg/m^2 by rapid intravenous injection daily for three days, were employed. On February 27, the 25th day of therapy, the hemoglobin level was 14.5 gm/dl. The white blood cell count was 12,700/microliter. The platelets were 205,000/ microliter. The marrow was normocellular, with 2.4% myeloblasts and no Auer rods. The patient is in complete remission 19 months after starting induction chemotherapy. Monthly marrow examinations have consistently shown M_I marrow status. The most recent bone marrow was July 11, 1979.

Spontaneous Remission Following Bone Marrow Necrosis in Chronic Lymphocytic Leukaemia

Hughes RG; Islam A; Lewis SM; Catovsky D

Clinical and Laboratory Haematology 3(2): 1981; 173-183

Extracted Summary

This report describes a patient with bone marrow necrosis associated with a haematological malignancy: chronic lymphocytic leukaemia (CLL). Remarkably, our patient showed clinical and haematological recovery which is maintained more than 2 years later.

Selected Case Report

A 58-year-old kitchen porter presented to his local hospital's emergency department with pain of 3 day's duration in his left shoulder. X-rays were normal and a provisional diagnosis of acromial bursitis was made and referral to an orthopaedic clinic arranged. Four days later, on 27 June 1978, he was admitted to hospital with a large swelling over the deltoid region. This was tender and warm showing skin discolouration and restriction of movement of the shoulder. In addition, he complained of upper abdominal discomfort and anorexia.

Further examination revealed a few purpuric scratch marks, small bruises of the lateral aspects of both elbows and haematuria. The liver edge was palpable 3 centimeters below the costal margin. Spleen and lymph nodes were not palpable. A clotting screen and routine biochemical investigations revealed no abnormality. Chest x-ray was normal and osteoarthritis was noted in the cervical and dorsolumbar spine. The blood count at presentation (Hb 15.4 gm/dl; WBC 162 x 10^9/l; platelets 12 x 10^9/l; neutrophils 0%; lymphocytes 39%; prolymphocytes 61%) showed high WBC count with absolute lymphocytosis. A proportion of these lymphocytes appeared immature and resembled prolymphocytes. Bone marrow aspirates from sternum and posterior iliac crest showed marrow necrosis. Antibiotics were started, first oral then intravenous, when he became febrile the following day.

On 3 July 1978 he was transferred to Hammersmith Hospital when he was found to be pale, pyrexial and with some mucosal and skin bleeding. He had very severe bone pain affecting principally the sacrum, but to a lesser extent the ribs, sternum and upper femora. His blood count showed Hb 9 gm/dl; WBC 25 x 10^9/l; platelets 12 x 10^9/l; neutrophils 3%; lymphocytes 78%; prolymphocytes 19%, all values had fallen markedly since presentation. A diagnosis of CLL in prolymphocytoid transformation was made. Direct antiglobulin test, sickle tests, RA latex and tests for autoantibodies were negative. Bone marrow aspirate continued to show necrosis, but with a monomorphic infiltrate of cells. Surface marker studies on his peripheral blood lymphocytes showed 79% mouse RBC rosettes and 5% sheep RBC rosettes. Surface immunoglobulin was negative with all polyvalent and monovalent antisera tested. These findings are consistent with chronic lymphocytic leukaemia of B cell type.

During the subsequent 4-6 weeks, he had severe bone pain requiring diamorphine as often as two hourly. He developed bilateral pneumonia which was treated with intravenous antibiotics. At 4 weeks after presentation, bone marrow continued to show necrotic marrow, but with a few recognizable neutrophils present, and at 7.5 weeks, some normal haemopoietic regeneration.

He received no antileukaemic chemotherapy or steroids while in hospital only antibiotics. He went home reasonably well 12 weeks after admission. Six months later, his blood counts and film appearances were virtually normal with bone marrow showing a mixed picture with necrosis, normal haemopoietic tissue and areas of infiltration with small lymphocytes. He remains clinically well, requiring no further therapy since his discharge from hospital.

Since submitting this manuscript initially, we have found and reassessed the patient, now more than 2 years after first presentation. He is clinically very well, in full-time employment, and there are no abnormal clinical findings. His peripheral blood counts are normal (Hb 14.8 gm/dl; WBC 5.3 x 10^9/l; platelets 187 x 10^9/l; neutrophils 69%; lymphocytes 23%; prolymphocytes 0%) and the lymphocytes are mainly small and well-differentiated with an occasional larger form. Bone marrow aspirate from the manubrium sternum is hypercellular due to infiltration with mainly small lymphocytes. Aspirate from the posterior iliac crest shows a normal distribution of haemopoietic cells, but the trephine biopsy shows areas of normal marrow and areas of infiltration with small lymphocytes.

Spontaneous Complete Remission in Adult T-Cell Leukemia: A Case Report

Kimura I; Tsubota T; Hayashi K; Ohnoshi T

Japanese Journal of Clinical Oncology 13(Suppl 2): 1983; 231-236

Extracted Summary

A 36-year-old man with adult T-cell leukemia gradually improved to the point of complete remission without any anticancer treatment. The patient was referred to our hospital because of the appearance of morphologically abnormal lymphocytes. Thirty percent of the peripheral blood white cells were morphologically abnormal lymphocytes which had lobulated or indented nuclei, and were E rosette-forming and mature T-cell antigen-positive. No hepatosplenomegaly, lymphadenopathy or mediastinal mass was noted. He had a cough with sputum one and a half years before entry. After admission, skin nodules occurred and were diagnosed histologically as non-Hodgkin's lymphoma, diffuse pleomorphic. Serum antibodies against an adult T-cell leukemia associated antigen were detected at a titer of 1:40. Chest x-ray films, a pulmonary function test, bronchographic examination, bronchoalveolar lavage and transbronchial lung biopsy demonstrated no relationship between the pulmonary symptoms and the adult T-cell leukemia. After treatment with antibiotics and a beclomethasone inhaler, the symptoms decreased, and then the abnormal lymphocytes and skin nodules disappeared. The spontaneous, complete remission has continued for four years.

Selected Case Report

A 36-year-old bus driver was admitted to our hospital because of the appearance of morphologically abnormal lymphocytes in the peripheral blood. The patient was born in Onada City, Yamaguchi Prefecture, and lived in Kobe for most of his life. The birthplace of his mother is Saga Prefecture on Kyushu island. He had chronic sinusitis since he was 19 years old. There was no history of blood transfusion. In March 1977, a cough with sputum began and persisted thereafter. One year before he entered Okayama University Hospital, he was admitted to another hospital and was diagnosed as having bronchiectasis. At that time, he noticed on his right elbow a skin nodule, 1 centimeter in diameter, which disappeared spontaneously. Abnormal lymphocytes with indented or lobulated nuclei were first observed in November 1978, and the patient was admitted on January 9, 1979.

He looked healthy but had a slight cough with sputum. A physical examination on admission revealed decreased breath sounds and moderate dry rales bilaterally in the lower lungs. There was no hepatosplenomegaly or lymphadenopathy. The skin was normal.

Laboratory Data: The leukocyte count was 13,000/mm^3 with 20% morphologically abnormal lymphocytes. The cytoplasm was scanty and bluish without granules or vacuoles. The nuclei were irregularly shaped with indentation or lobulation. The chromatin was generally condensed and nucleoli were indistinct. The red blood cell count was 4,750,000/mm^3, hemoglobin 14.5 gm/dl and platelet count 163,000/mm^3. A bone marrow aspirate contained only 1.8% abnormal lymphocytes. C-reactive protein was 1+, RA test negative, erythrocyte sedimentation rates 20 mm/hour and 41 mm/2 hours. Immunoglobulins G, M, A and E in the serum were within normal ranges. Liver function test results and serum electrolytes were normal. The purified protein derivative (PPD) skin test was negative.

Surface Marker: The peripheral venous blood contained 11,000/mm^3 white cells with 33% abnormal lymphocytes which were examined for surface markers. After separation by Ficoll-Conray centrifugation, 73% of the peripheral mononuclear cells were found to be E rosette-forming T-cells which had abnormal nuclei. There were 3% surface immunoglobulin-bearing cells. Lymphocyte differentiation antigens, human thymus leukemia antigen (HTLA), mature T-cell antigen (mT), Ia-like antigen (Ia) and common acute lymphoblastic leukemia-associated antigen (CALLA) were tested for by immunofluorescence by means of absorbed rabbit antisera. The rabbit antisera used in this study were as follows. Rabbit antiMOLT-4 (a T-cell acute lymphoblastic leukemia cell line) serum specific to HTLA and mT and rabbit anti-B411-4 (a normal B-cell line) serum specific to Ia were prepared as described elsewhere (Tsubota et al., JNCI 59: 1977; 845). The anti-MOLT-4 serum further absorbed with normal peripheral blood lymphocytes did not react with mT but still reacted with HTLA (Tsubota et al., 1977, Clin Exp Immunol 41: 1980; 130). Rabbit antiserum against a null-cell acute lymphoblastic leukemia cell line NALL-1, after appropriate absorptions, reacted specifically with CALLA (Uno et al., 1978). Cells with antigens HTLA and mT comprised 89.6% of the total, but only 4.0% had HTLA alone. There were 4.1% Ia-positive and 0% CALLA-positive cells. These findings clearly indicate that the abnormal lymphocytes were mature T-cell antigen bearing T-cells.

Examination of the Lung: Because of the persisting cough with sputum, examinations of the lung were carried out in detail to clarify the relationship between ATL and the pulmonary symptoms. Chest x-ray films revealed no mediastinal masses or other abnormalities. Selective bronchography showed no specific findings of bronchiectasis. A pulmonary function test suggested obstruction of small airways. A bronchoalveolar washing sample contained 26% macrophages, 8% lymphocytes, 63% neutrophils and 2% eosinophils. The lymphocytes showed no morphological abnormalities. A transbronchial lung biopsy specimen revealed mild inflammatory cell infiltration, but no definite leukemic cell infiltration. Repeated examinations for bacteria in the sputum revealed Neisseria, Streptococcus faecalis, Pseudomonas aeruginosa and Candida. The findings indicated that the pulmonary symptoms were due to chronic bronchitis, not to ATL.

Antibody against ATL-Associated Antigen: The serum was tested for antibody against ATL-associated antigen (Hinuma et al., PNCI, 78: 1981; 6476) by Dr. Y. Hinuma and Dr. I Miyoshi, independently. The serum taken in November 1981 was reported to have the antibody at a titer of 1:40 (Hinuma) or 1:10 (Miyoshi). The serum taken one year later showed an antibody titer of 1:20 (Hinuma). These results indicate that the patient had the antibody and may be an ATL virus carrier (Miyoshi et al., Lancet, 1: 1982; 683).

Skin Nodule Biopsy: After admission, two skin nodules, 1.5 centimeters and 1.0 centimeter in diameter with a reddish surface, appeared simultaneously on the back and the left arm. The nodule on the back was resected and examined histologically. Three pathologists diagnosed the nodule as a non-Hodgkin's lymphoma, diffuse pleomorphic or diffuse large cell type. The other nodule disappeared spontaneously 3 weeks later.

Clinical Course: The cough and sputum gradually increased after admission, and a diagnosis of chronic bronchitis was made. For this reason, the antibiotics ceftezole (CTZ), gentamicin (GM), ampicillin (AB-PC) with cloxacillin (MCIPC), cephalexin (CEX) and amoxicillin (AM-PC) were administered. In March 1979, a beclomethasone inhaler was started. In April, another skin nodule appeared but disappeared spontaneously. At that time, the cough and sputum improved and the patient was discharged.

In February 1979, one month after admission, the number of white cells and abnormal lymphocytes began to decrease, the lymphocytes becoming less than 5%. After discharge, the beclomethasone inhaler was continued for 2 years, but no treatment was given thereafter. The morphology of the peripheral blood lymphocytes and the clinical course were followed once a month. No abnormal finding was noted except a negative PPD skin test. A physical examination in December 1982 revealed no skin nodules, no hepatosplenomegaly nor lymphadenopathy. There were no pulmonary symptoms or signs. The leukocyte count was 76,000/mm^3 and no morphologically abnormal lymphocytes were observed.

Spontaneous Complete Remission of CLL

Report of a Case Studied with Monoclonal Antibodies

Buchi G; Termine G; Zappala C; Girotto M; Grosso E; Autino R

Acta Haematologica 70(3): 1983; 198-201

Extracted Summary

A case of complete spontaneous remission of CLL in a 76-year-old woman is reported. Despite the complete remission, the study of the peripheral blood T lymphocytic subsets by the aid of monoclonal antibodies has showed, however, that the ratio between helper-induced and suppressor cytotoxic T cells is still impaired (0.81) as we can see in overt B-CLL. The cause of the remission and its possible connection with the imbalanced distribution of the T lymphocytic subsets is discussed.

Selected Case Report

In March 1977, a 76-year-old woman was admitted to the hospital with a diagnosis of CLL. She was found to have enlarged lymph nodes on both sides of the neck, axillae and supraclavicular areas. The liver and the spleen were not palpable, as confirmed by normal ^{198}Au colloidal liver-spleen scan. The white cell count was 10.3 x 10^9/l with 22% neutrophil, 3% eosinophil, 75% lymphocytes. The lymphocytes were typical small cells and there were numerous Gumprecht shadows; other hematological parameters and serum chemicals were normal. Direct and indirect Coombs' tests, Tinestest, Monotest and Dyetest were negative. The bone marrow aspirate revealed a sharp increase in the percentage of lymphocytes (91%). The left supraclavicular lymph node biopsy showed diffuse infiltration with lymphoid cells appearing as small lymphocytes involving also the capsula. X-ray films and tomographic examination of the chest were normal. Lymphography showed enlarged iliac and lumboaortic lymph nodes bilaterally with a lacy appearance typical of lymphoma.

The disease was classified as stage I CLL according

to the Rai's classification; II B according to the last Binet classification. No chemotherapy was started.

In the following years, we remarked a gradual and more and more striking regression of the lymphadenopathies. In February 1980, the white cell count was 4.2 x 109/l with 60% lymphocytes. Absolute lymphocyte count was 2.4 x 109/l, E-rosettes forming cells were 60%. The detection of surface Ig (sIg) bearing cells showed sIgG 20%, sIgM 8%, sIgA 4%, sIgD 2%, sIg kappa light chain 15%, sIg lambda light chain 2%, Garett's index = 0.76. No hypogammaglobulinemia was found. The bone marrow aspirate disclosed 21% of lymphocytes.

In April 1980, the lymphadenopathies were disappeared; white cell count was 9.9 x 109/l with 16% lymphocytes. Bone marrow aspiration disclosed 8% of lymphocytes. Bone marrow biopsy showed that the structure of the bone was normal. Diffuse infiltration with lymphoid cells or dispersed accumulations of small lymphocytes were not found. A computed tomographic (CT) of the abdomen showed neither an enlargement of the pelvic or lumboaortic lymph nodes nor an involvement of the liver or spleen.

In December 1981, the absolute lymphocyte count was 1.4 x 109/l, the E-rosette-forming cells were 52.4%. The detection of sIg-bearing cells disclosed sIg total 17%, sIgG 1.8%, verified by $F(ab)_2$, sIgM 11.3%, sIgA 6.5%, sIgD 5%, sIg kappa light chain 1.3%, sIg lambda light chain 12.5%.

In May 1982, the patient was asymptomatic. The absolute lymphocyte count was 1.4 x 109/l, the E-rosette-forming cells were 57.5%, the OKT3-binding cells were 59.4%, the OKT8-binding cells 32.5%, the OKT4-binding cells 26.4%. The monoclonal antibody anti Ia-like disclosed 9% of lymphocytes. The study of sIg-bearing cells showed sIg total 8%, sIg kappa light chain 3%, sIg lambda light chain 2%. The patient is well in June 1982.

Adult T-Cell Leukaemia with Spontaneous Remission

Schnitzer B; Lovett EJ III; Kahn LE

Lancet 2(8357): Oct 29 1983; 1030

Extracted Summary

The authors describe a case with antibodies to human T-cell lymphoma virus (HTLV) in which there was spontaneous remission without evidence of residual leukaemia at necropsy.

Selected Case Report

A 73-year-old white man from Michigan was admitted to the University of Michigan Hospital because of altered mental status. He had enlarged inguinal lymph nodes, a serum calcium of 17.1 mg/dl, and a white blood cell (WCC) count of 20,400 x 109/l with 44% lymphocytes. With hydration and steroid therapy, the serum calcium fell to normal over 4 days and the inguinal lymphadenopathy disappeared. The WCC rose to 32,800 x 109/l with 68% lymphocytes, 75% of which had multilobulated nuclei. Less than 10% abnormal lymphocytes were detected in a bone marrow smear. Skin lesions were absent. ATL was suspected. The WCC fell to 20 400 x 109/l with 80% lymphocytes, and during the following weeks returned to normal with only occasional lobulated lymphocytes.

Cell surface antigen phenotyping ('EPICS V' flow cytometer; Coulter Electronics) revealed that more than 80% of peripheral blood lymphocytes had the phenotype T11+, T3+, T4, T10+. Aneuploidy was not detected. 70% of these cells were T4+ (helper/inducer) and 26% were T8+ (suppressor/cytotoxic). The T4+ and T8+ subpopulations were tested for human interleukin-2 receptor with the anti-Tac monoclonal antibody. This receptor is not present on circulating lymphocytes or monocytes, but is present on circulating cells from Japanese patients with ATL. In our patient 33% of lymphocytes were Tac+ and all of these cells bore the T4 antigen. None of the T8+ cells were Tac+. Both the T4+ Tac+ and the T8+ Tac– populations were sorted and examined morphologically. The Tac+ cells had diffuse granular acid phosphatase activity and multilobulated nuclei; the T8+ cells appeared normal. Examination of cytocentrifuge preparations of several pleural and abdominal fluids also revealed the presence of multilobulated lymphocytes. No definite evidence of lymphoma was detected at necropsy, although on careful examination of lymph nodes, scattered lymphocytes with lobulated nuclei were seen. Scalloping of trabecular bone with increased osteoclasts was evident. The cause of death (6 weeks after onset of illness) was cytomegalovirus pneumonia.

Although the hypercalcaemia, absolute lymphocytosis with T4+ Tac+ multilobulated lymphocytes in the blood, lymphadenopathy, and antibodies to HTLV suggested that the patient had ATL, no evidence of neoplasm was present post mortem despite the fact that no chemotherapy had been given.

Hairy Cell Leukemia: A Reversible Disease?

A Report of Two Cases of Spontaneous Remission

Silingardi V; Federico M; Barbieri F; Artusi T; Mauri C

Haematologica 70(5): Sept-Oct 1985; 437-441

Extracted Summary

Between 1967 and 1979 the authors observed 56 cases of hairy cell leukemia (HCL). Twenty patients are still alive and five of them are in good health over ten years after diagnosis. Two out of these five patients never received any specific treatment. The aim of this communication is to report these two cases of spontaneous remission in HCL.

Selected Case Report

Case 1: 53-year-old male. This patient experienced several episodes of upper respiratory tract infections during his early years. Since the age of thirty he attempted periodic anti-inflammatory treatments for rheumatic pains but he never recovered completely. In 1967, he was hospitalized for severe weakness, pallor and persistent headache. He was found to have marked anemia, leukopenia, liver and spleen enlargement. The bone marrow was nearly inaspirable: among the few cells obtained a significant number of atypical lymphoid elements with characteristic hairy-like cytoplasmic projections was detected. Surgical bone marrow biopsy revealed massive replacement by a population of the same type of cells and a diffuse stromal reaction with large amounts of reticulin.

This condition was diagnosed as "lymphoid myelofibrosis" after Duhamel (successively confirmed as typical HCL) and the patient was treated with blood transfusions, androgens and prednisone for his moderate thrombocytopenia. In the following three years he had several hospital admissions due to recurrent infections, such as bronchitis, cystitis and cholecystitis, and to persistent mild anemia. Afterwards, he showed progressive reduction of the hepatosplenomegaly and an improvement of the haematologic picture so that no further treatment was given. Subsequently the patient resumed work and was followed up with periodic blood counts. In 1980 he underwent transurethral prostatectomy for prostatic hypertrophy. In December 1983, the patient was admitted for a re-evaluation of the case. Spleen and liver were no longer palpable; a trephine bone marrow biopsy revealed complete disappearance of lymphoid replacement and absence of fibrosis. In December 1984 he was still doing well without treatment 17 years after the diagnosis of HCL.

Spontaneous Regression of Cytogenetic and Hematologic Anomalies In Ph^I Positive Chronic Myelogenous Leukaemia

Smadja N; Krulik M; Audebert AA; DeGramont A; Debray J

British Journal of Haematology 63(2): June 1986; 257-262

Extracted Summary

We report a case of a 27-year-old man with Ph^I positive chronic myelogenous leukaemia (CML). At the time of diagnosis 100% Ph^I positive cells were found with a trisomy 8 in 50% of them. In absence of therapy, his haematological status remained stable for 3 years. Subsequently a progressive regression of haematologic and cytogenetic data was observed. Eight years after diagnosis the karyotype showed only 37% Ph^I positive cells and the trisomy 8 had disappeared.

Selected Case Report

Mild leukocytosis was first seen in November 1976 in a 27-year-old man with a possible history of professional benzene exposure during a routine haemogram. WBC was 12.2 x 10^9/l with polymorphonuclears 58%, eosinophils 5%, basophils 2%, lymphocytes 16%, monocytes 13% and myelocytes 6%. Erythrocytes and platelets were normal. Splenomegaly was absent. Laboratory findings demonstrated a myeloproliferative disorder with bone marrow aspirate and biopsy showing hyperplasia of granulocytes with normal maturation and a slight eosinophil increase. Megakaryocytes appeared normal, erythroblasts were moderately decreased and fibrosis was absent. Karyotype examination showed the Ph^I chromosome. Regular follow-up without therapy was planned for this patient.

Three phases were observed during the course of the

disease. The first lasted about 3 years and was characterized by stable haematological and cytogenetic condition. The second ran from 1981 to 1983 and showed progressive haematological and cytogenetic regression. In 1982, WBC was normal as was blood vitamin B12 level. Serum histamine was only a third of its maximal value. Scores for leukocyte alkaline phosphatases (LAP) remained decreased. In 1983 a bone marrow biopsy showed only mild granulocyte hyperplasia with normal maturation. Karyotype examination showed complete disappearance of the trisomy 8 and regression of the percentage of Ph^1 positive cells. The third phase began in 1983 and was characterized by a cytogenetic stabilization. In 1985 the bone marrow aspirate was normocellular with 66% granulocytes and 20% erythroblasts. WBC was still normal as was vitamin B12. Histamine level remained increased and LAP decreased. Karyotype examination showed the same result as in 1983. Biological and cytogenetic data were taken at diagnosis and throughout the 8 years of follow-up.

"Spontaneous" Complete Remissions in Chronic Lymphocytic Leukemia

Report of Three Cases and Review of the Literature

Ribera JM; Viñolas N; Urbano-Ispizua A; Gallart T; Montserrat E; Rozman C

Blood Cells 12: 1987; 471-479

Extracted Summary

"Spontaneous" complete remissions (SCR) are a rare event in chronic lymphocytic leukemia (CLL). In this article, we report three cases of SCR observed in a series of 285 patients followed at a single institution during the last 15 years. SCR was documented by clinical and hematologic data, including bone marrow biopsy, and immune cell markers. A delay of 0.9-1.6 years between "clinical" and "clonal" remission was observed. A review of other cases of SCR in CLL is also performed.

Selected Case Reports

Case 1: A 49-year-old woman was referred in April, 1976 because of leukocytosis and lymphocytosis. She was found to have enlarged lymph nodes in both supraclavicular areas and splenomegaly of 1 centimeter below the left costal margin. Hemoglobin level was 14 gm/dl and WBC count 41.9 x 10^9/l with 81% lymphocytes. The platelet count was 215 x 10^9/l. The bone marrow aspirate revealed a 95% infiltration by lymphocytes. Bone marrow biopsy showed an interstitial infiltration pattern. E-rosette-forming cells were 2% and the percentage of sIg bearing cells, 92%. The disease was classified as a B-CLL in stage A(II) according to Binet's classification. No treatment was given.

In December, 1976, enlarged bilateral laterocervical and supraclavicular nodes were found and an infiltration of Waldeyer's ring was observed. Treatment with cyclophosphamide (200 mg/day over 20 days) was started, followed by 22 Gy irradiation of both laterocervical areas. The lymph nodes and the Waldeyer's ring infiltration disappeared and the absolute lymphocyte count was 30.3 x 10^9/l. No further treatment was administered. In February 1980, 23 months after the therapy, the patient had a severe varicella zoster infection. One month later, the number of leukocytes was 4.6 x 10^9/l with 35% lymphocytes. In May 1980, the absolute lymphocyte count was 2.5 x 10^9/l, E-rosettes were 35% and sIg, 63%. A second bone marrow biopsy showed a nodular infiltration pattern. In September, 1981, E-rosettes were 68%; sIg, 22% (kappa: 16%, lambda: 10%). In November 1981, a hiatus hernia was diagnosed and a fundoplicature was performed. No lymphadenopathy consistent with the diagnosis of CLL was found in the abdominal cavity. A biopsy of a perigastric lymph node showed nonspecific lymphadenitis. In May, 1986, the patient remained healthy and the absolute lymphocyte count was 1.5 x 10^9/l The analysis of immune markers showed: E-rosettes, 50%; M-rosettes, 2%; sIg, 11% (kappa: 9%, lambda: 7%); OKT3, 35; OKT4, 30%; and OKT8, 10%.

Case 2: In December, 1972, a 57-year-old woman was referred because of generalized lymphadenopathy and splenomegaly of 3 centimeters below the left costal margin. The liver was not palpable. The Hb level was 11.8 gm/dl, WBC count 19.7 x 10^9/l (98% lymphocytes), and the platelet count was 200 x 10^9/l. The bone marrow aspirate revealed 90% infiltration by lymphocytes. The disease was classified as B-CLL in stage B(II). No treatment was given.

In the following months, the size of lymph nodes and spleen decreased and the absolute lymphocyte count was 4.03 x 10^9/l at 2.5 years after the diagnosis. At that time, E-rosettes were 25% and sIg, 73%. In April, 1976, the physical examination was within normal limits and the absolute lymphocyte count was 1.55 x 10^9/l. E-rosettes were 66%, and sIg, 25%. In October 1976, no lympho-

cytic infiltration was found in the bone marrow aspirate and the analysis of immune markers was normal. In March, 1977, a bone marrow biopsy showed a nodular infiltration pattern. In November 1981, the patient remained asymptomatic, the immunologic studies were normal and a second bone marrow biopsy showed again a nodular infiltration pattern. At the most recent visit (July, 1985), the absolute lymphocyte count was 1.12 x 10^9/l and an analysis of immune markers revealed: E-rosettes, 55%; M-rosettes, 4%; sIg, 5% (kappa: 6%, lambda: 0%); OKT3 positive cells, 68%; OKT4, 49%; and OKT8, 5%.

Spontaneous Remission in Chronic Lymphocytic Leukaemia

Holmes JA; Whittaker JA

British Journal of Haematology 69(1): May 1988; 97-98

Extracted Summary

Chronic lymphocytic leukaemia (CLL) is often an indolent disease which may only produce symptoms and signs at an advanced stage. Spontaneous complete remission in CLL is a rare event. There have been few previous reports (Buchi et al., Acta Haematologica 70 (1983), 198-201 and Ribera et al., Blood Cells 12 (1987), 471-483) and the mechanism for such remissions remains speculative.

It seems likely that spontaneous complete remission in CLL is achieved by an immunoregulatory effect, possibly through endogenous interferon, whose production may be provoked by viral infection. The authors report three cases of spontaneous complete remission in CLL.

Selected Case Reports

Case 1: A 71-year-old woman presented in October 1973 complaining of low back pain. X-rays of the lumbar spine showed osteoarthritic changes. An incidental full blood count revealed a hemoglobin concentration of 14.5 gm/dl, WBC 23 x 10^9/l (91% small differentiated lymphocytes), and a platelet count of 140 x 10^9/l. There was no lymphadenopathy, but the spleen and liver were just palpable. Bone marrow aspiration demonstrated a small lymphocytic infiltrate comprising 30-40% of all nucleated cells. The chest x-ray was normal. Immunoglobulin assay revealed a low IgA level, but with normal IgG and IgM levels.

The patient was not treated and regular review confirmed the splenomegaly and lymphocytosis. She complained of aching and stiffness in small joints and rheumatoid factor was positive at 1 in 128. Immunophenotyping of peripheral lymphocytes done in 1986 showed a marked preponderance of B cells, consistent with a diagnosis of B-cell CLL.

During the past 12 months, both the lymphocytosis and splenomegaly have resolved. All recent full blood counts have been entirely normal and immunophenotyping has demonstrated normal B cell numbers and T cell subsets with kappa and lambda chain distribution not providing any evidence of cloning.

Case 2: A 56-year-old woman presented in August, 1981 complaining of tiredness. Examination revealed multiple small lymph nodes in the right axilla. There were no other abnormal findings. The full blood count showed a hemoglobin concentration of 13 gm/dl. WBC 25.4 x 10^9/l (67% small well-differentiated lymphocytes) and a platelet count of 282 x 10^9/l. Tests of renal and liver function and chest x-ray were normal and viral studies were negative. At no time did the patient receive treatment for this condition. She was seen regularly, without receiving any treatment, until December, 1986, when it was first noted that her white cell count and differential were normal. Since then, over a period of 6 months, two further counts have also proved to be normal. The patient feels well and has no abnormal physical findings. Immunophenotyping of her peripheral blood lymphocytes shows a normal pattern with no evidence of clonality.

Transient Blueberry Muffin Appearance of a Newborn with Congenital Monoblastic Leukemia

Gottesfeld E; Silverman RA; Coccia PF; Jacobs G; Zaim MT
Journal of the American Academy of Dermatology 21(2 Pt 2): Aug 1989; 347-351

Extracted Summary

A full-term male infant was born with skin findings suggesting a blueberry muffin appearance. Biopsy of a cutaneous nodule was consistent with monoblastic leukemia cutis, and bone marrow examination confirmed the diagnosis of leukemia. The infant has remained well 2 years after spontaneous resolution of the cutaneous eruption. Infiltrative neoplasms should be considered along with congenital infections and hematologic disorders in the differential diagnosis of a newborn with a blueberry muffin appearance.

Spontaneous remissions can occur in many cases of congenital leukemia, especially in those infants with Down syndrome. These remissions, however, are often temporary, with recurrences up to 2 years after birth. Our patient has remained in remission for 26 months.

Selected Case Report

A male infant was born on January 1, 1986, to a 22-year-old woman who was blood type A, Rh positive, free of venereal disease, and immune to rubella after a normal gestation, labor and delivery. Several hours after birth, the baby was noted to be tachypneic and was transferred to Rainbow Babies and Childrens Hospital in Cleveland.

Physical examination revealed an alert, active 3.46 kilogram infant with a respiratory rate of 70 breaths/minute. Scattered randomly over the trunk, scalp, and extremities were dusky red to purple macules, papules, and nodules measuring 3 to 15 millimeters in diameter. The nodules did not blanch with vigorous rubbing. Petechiae, adenopathy, and hepatosplenomegaly were absent. The remainder of the physical examination were normal. No features of Down syndrome were observed.

Laboratory studies on admission disclosed the following values: hemoglobin, 15.4 gm/dl; hematocrit, 44.7%; reticulocytes, 1.3%; and a white blood cell count of 14,800 cells/mm3, with a differential of 30% neutrophils (normal 32% to 63%), 39% bands (normal 10% to 18%), 10% lymphocytes (normal 26% to 36%), 9% atypical lymphocytes, and 12% monocytes (normal up to 6%). No circulating malignant cells were observed. The platelet count was 226,000 cells/mm3,. Electrolytes, liver function tests, blood urea nitrogen levels, and creatinine levels were normal. Blood cultures and serologic titers for toxoplasmosis, rubella, cytomegalovirus, herpes simplex virus, and syphilis were negative. The infant was blood type B, Rh positive, and results of a direct Coombs' test were negative. Arterial blood gas analyses revealed a partial oxygen pressure of 42 torr. Chest film studies revealed bilateral pulmonary infiltrates that radiated from the hilum.

Bone marrow aspirate showed 25% of the cells to be immature monocytes and monoblasts. A sample of the aspirate was sent for cytogenetic analysis, but an insufficient number of mitotic spreads were available for a complete chromosome analysis. Taken together, these findings were consistent with a diagnosis of acute monoblastic leukemia.

The infant was treated for possible sepsis and pneumonia. The skin lesions began to fade spontaneously within 1 week and were absent after 4 weeks. New lesions have not occurred. Hematologic parameters have been monitored routinely for 2 years and have remained consistently normal.

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Lymphomas

Malignant Lymphoma in Childhood

Diwani M; Gabr M; Essawy M; Elwi A
Archives of Pediatrics 77(10): Oct 1960; 406-420

Extracted Summary

The classification of malignant lymphoma is reviewed on an embryological and anatomical basis. Malignant lymphoma excluding leukemia constitutes 10% of all causes of malignancy in infancy and childhood.

The follow-up of 3 cases of malignant lymphoma in children is discussed: One case of giant follicular lymphoma in a boy 2 1/2 years old and 2 cases of reticulum cell sarcoma in boys 9 and 10 years old.

The following features are to be noted: An intermittent course may be encountered in giant follicular lymphoma as well as in disseminated reticulum cell sarcoma; exophthalmos which is not a rare feature of giant follicular lymphoma may be due to retroorbital deposits of tumor cells; dissemination of reticulum cell sarcoma may occur all over the body. In the second case presented, tumor cells involved glands, liver, spleen, skull bones, facial nerve, skin and testis. Involvement of the testis by reticulum cell sarcoma is very rare but should be suspected in cases of bilateral malignant testicular swelling especially if associated with skin deposits.

Selected Case Report

Case 1. First admission: G. M., a boy aged 2 1/2 years was first admitted to the hospital in April 1955 with the chief complaint of swelling of the neck. The swelling was noticed one month before admission and has been progressively enlarging since then. The past history and family history were not remarkable. Examination revealed a well-nourished child with bilateral markedly swollen elastic, discrete and painless cervical and submandibular glands. Axillary and inguinal glands were slightly enlarged. Both the liver and spleen were felt 3 fingers below the costal margin. Physical examination was otherwise negative.

Investigations: Hemoglobin: 70%; RBCs, 4,200,000; Total WBCs, 14,200; Polymorphs 63; Lymphocytes 33; Monocytes 5; Normal platelets in film. Bone marrow: cellular, myeloid: erythroid ratio 1.5:1 with a normal differential count: myeloblasts 6; myelocytes 6; Juvenile 13; Staff 15; Segmented 17; Lymphocytes 2, Basophil 1, Eosinophil 0, Normoblast 35, Macroblasts 5. Tuberculin Test: Negative. Radiological examination of the chest, skull and long bones was negative. Urine and stools were free.

Progress: During his stay in the hospital both the cervical and axillary glands progressively enlarged. Edema of the face and of the forearms developed probably from pressure by the glands on the draining lymphatics. One of the neck glands was excised for biopsy and the following pathological report was made: "The lymph node is grossly enlarged. Microscopic examination showed that the capsule is intact and revealed the presence of numerous large follicles uniformly scattered throughout the cortex and medulla of the lymph node which are crowded against each other. The follicular structures are mainly composed of reticulum cells with a narrow ring of lymphocytes. The surrounding lymphoid structure is obviously compressed by the expanding newly formed follicles and in some places a crack separates the two structures. Diagnosis: giant follicular lymphoma." The child was discharged at the mother's request a month after admission.

Second Admission: He was readmitted in October 1955 because of the development of bilateral proptosis and ptosis of the left eye, which the mother noticed one month previously. The edema of face and upper limbs had disappeared by this time and his general condition had improved but the glandular enlargement persisted. Exophthalmus of both eyes was evident with ptosis of left eye. Ophthalmic examination revealed sluggish reaction of right pupil which was more dilated than normal, while the left pupil was widely dilated and fixed. Fundi showed blurring of margin and some congestion of veins, a picture of early papilledema. Investigations done on the second admission were essentially similar to the previous investigations. X-ray of skull was negative.

Progress: The child remained in the hospital for 2 months, on tonics only. During this time the proptosis has markedly regressed and pupillary reactions became active. He was discharged with minimal proptosis and slight ptosis of left eye.

Third admission: He was readmitted for the third time in October 1955 because of development of severe stridor and cyanosis. The mother stated that after the second discharge from the hospital his general condition improved and he started to put on weight. On the night of admission he developed severe dyspnea with labored breathing. Examination revealed a distressed blue child with marked inspiratory stridor and retraction of subcostal margin. Chest was free apart from upper respiratory sounds heard on auscultation. Eyes looked the same; skull circumference was 48 centimeters; liver was 5 fingers below costal margin and the spleen was three fingers enlarged. The neck and axillary glands were much more swollen than before. Mouth and throat were free and laryngoscopy revealed normal findings. Tracheotomy was done two hours after admission with marked relief of the respiratory difficulty. Investigations done on the third admission were essentially negative except for a moderate degree of anemia (Hemoglobin 60%) and marked enlargement of the mediastinal glands was evident radiologically.

Because of technical difficulties the child did not receive deep x-ray therapy. In spite of this the mediastinal shadows gradually decreased in size, the respiratory difficulty disappearing altogether in 3 months' time. The tracheotomy tube was ultimately removed and the child was discharged in February 1957.

The child has been seen sporadically ever since and is still living (March 1959), the mother refusing any medication. During the last year the general condition of the child has deteriorated with emaciation and easy fatigability. The liver has progressively enlarged in size now reaching almost 8 fingers below the costal margin. The neck glands, however, surprisingly have regressed in size.

Follicular Lymphoma of the Skin

KWITTKEN J; GOLDBERG AF

Archives of Dermatology 93: Feb 1966; 177-183

Extracted Summary

An 83-year-old woman with a scalp lesion exhibiting neoplastic lymphomatous follicular infiltrates involving the entire corium is reported. This lymphoma underwent complete and spontaneous regression in approximately 15 months. Subsequently, an enlarged spleen was palpated and lymphoma cells were observed in the blood and bone marrow but peripheral lymphadenopathy and anemia were absent.

SELECTED CASE REPORT

An 83-year-old Puerto Rican woman was referred to the Knickerbocker Hospital skin clinic in September 1963 complaining of "bumps" on her head of approximately two weeks duration.

The patient had been in essentially good health until about 1960 when she developed congestive heart failure secondary to hypertension and arteriosclerotic heart disease. Chest x-rays at that time revealed slight left ventricular enlargement and mild basilar pulmonary fibrosis. Her condition was well controlled with digitalis, oral diuretic, and antihypertensive medication. In 1962 the patient had slightly elevated hemoglobin and hematocrit values consistent with a mild secondary polycythemia. Pulmonary function tests demonstrated abnormalities which were compatible with congestive heart failure and pulmonary fibrosis. Her hematocrit was 54% and her red blood cell count 6,800,000/mm^3; hemoglobin averaged about 16.5 gm/100 cc; and the white blood cell count about 5,000/mm^3, with a normal differential. The sedimentation rate was 15 mm/hour.

In 1963 physical examination revealed multiple, contiguous, smooth, firm, slightly elevated violaceous nodules measuring 5 to 10 millimeters in diameter in the left frontoparietal scalp region. These formed an irregular plaque 4 by 6 centimeters in area. Scalp hair in this area was sparse. The skin elsewhere was dry and callosities with fissures were present on her soles. Blood pressure was 150/80 mmHg with 1+ edema and varicose veins of both legs. Examination of the chest and abdomen were negative. No peripheral lymphadenopathy was present.

Biopsies of the scalp lesion were performed in September and December 1963. There was no gross change in the lesion during this interim. The biopsy revealed the skin and subcutaneous tissues, except for the epidermis, to be markedly infiltrated with lymphoid cells forming discrete and confluent "follicles." The centers of these follicles were composed almost entirely of polygonal reticulum cells. These cells had pleomorphic relatively large nuclei whose nuclear chromatin pattern was relatively fine. Varying amounts of poorly defined pale cytoplasm were present. Mitotic figures and nuclear phagocytosis were prominent features in some follicles and absent in others. The reticulum cells merged with densely packed smaller lymphoid cells at the periphery of the follicles. These latter cells were slightly larger than normal small lymphocytes. Their nuclei were hyperchromatic and the cells had small amounts of cytoplasm. These cells were observed between the dermal collagen bundles, in the subcutaneous fat, and around the skin appendages. Focally, these neoplastic follicles had attenuated the overlying epidermis, being separated from it by a very narrow band of collagen fibers. Condensation and compression of reticulum fibers at the periphery of the follicles were present while their centers contained moderate amounts of branching fibers of varying thickness. The diagnosis of follicular lymphoma, reticulum-cell type, in accordance with the classification of Rappaport et al. was made.

The patient did not return to the clinic until August 1964. During this eight-month period a spontaneous involution of most of the scalp lesions had occurred. Only two small, contiguous, erythematous firm nodules measuring 0.8 centimeters and 0.4 centimeters in diameter remained in the involved region.

In September 1964, physical examination revealed a spleen palpable one finger breadth below the left costal margin. No hepatomegaly or lymphadenopathy was felt. Her hemoglobin was 15 gm/100 cc; red blood cell count, 6,900,000/mm^3; platelets 258,000/mm^3; and reticulocytes 1.1%. White blood cell count was 9,950/mm^3, with 66% neutrophils, 26% lymphoid cells, 6% monocytes, and 2% basophils. Most of the peripheral lymphoid cells were abnormal and of a type seen in patients with lymphosarcoma. These cells were larger than normal and had higher nuclear/cytoplasmic ratios than normal. Their nuclei contained increased chromatin consisting of irregularly shaped chromocenters with chromatin bands of variable length and thickness. Their cytoplasm was light blue with lighter colored "vacuoles." Minute cytoplasmic pseudopods and increased numbers of granules were frequently present, particularly in the larger lymphoid cells. The red blood cells were essentially normocytic and slightly hypochromic. Slight rouleaux formation was present. Platelets appeared normal.

A sternal marrow aspiration was moderately hypercellular. Neoplastic lymphoid cells were present in patchy focal aggregations as well as scattered among normal myeloid elements. These neoplastic lymphoid cells were mainly of the small "mature" type. Some prolymphocytes and lesser numbers of lymphoblasts were present. Transitional cells among these cell types were observed. All of the cells had very high nuclear/ cytoplasmic ratios. Nuclei were generally spherical. Occasionally slightly notched or lobulated nuclei with irregular excrescences were observed. These lymphoid cells had increased nuclear chromatin with a disorganized pattern. This consisted of irregularly sized chromocenters having chromatin bands of variable thickness and length. Prolymphocytes and lymphoblasts had a similar nuclear structure with relatively larger amounts of basophilic cytoplasm. Myeloid cells had a normal maturation and the myeloid erythroid ratio was normal. Erythroid cells were normoblastic. Megakaryocytes were normal. Mast cells were moderately increased in number. These cells were localized either among the lymphoid cells or in the connective tissue reticulum. Malignant associated change (MAC) was present in peripheral blood and bone marrow cells.

Slides were made from material aspirated from the scalp tumor and stained with Wright-Giemsa and Papanicolaou techniques. Most of the lymphoid cells present were small. A lesser percentage of larger immature cells were seen with transitional forms between the two major cell types. The cells had the same structural characteristics as those described in the bone marrow. VDRL and serum complement fixation tests were both weakly reactive. The Reiter protein complement fixation test was 3+. The total serum protein was 7.7/100 cc with albumin 3.2 and globulin 4.5 gm/100 cc. Serum protein electrophoresis revealed albumin 40.5%, $alpha_1$ globulin 2.7%, $alpha_2$ globulin 5%, Beta globulin 17.9%, and gamma globulin 33.9%. The direct and indirect Coombs' tests were negative. Uric acid was 6.1 mg/100 cc. Cephalin flocculation, thymol turbidity, alkaline phosphatase, and serum glutamic oxaloacetic transaminase values were normal.

In October 1964 the smaller scalp nodule regressed and the larger one had softened. These disappeared by December leaving a poorly defined area of atrophic skin, 4.0 by 6.0 centimeters, with zones of hypopigmentation and hyperpigmentation. The patient felt well.

Clinical Evidence Suggesting the Development of An Immunological Response Against African Lymphoma

Burkitt DP

Treatment of Burkitt's Tumour, Burchenal J. H. & Burkitt D., editors
[New York: Springer-Verlag 1967, UICC Monograph Series, Vol 8, 197-208]

Extracted Summary

Clinical observations made during treatment of over 100 patients with African lymphoma, and follow-up of approximately a third of these, suggest that sustained regressions cannot be attributed solely to chemotherapy. Moreover, regressions have been observed following failed chemotherapy and in absence of any chemotherapy. Clinical evidence suggesting an immunological host response is given. Clinical evidence is put forward which appears to suggest some factor additional to chemotherapy which accounts for long-term survivals in patients suffering from African lymphoma.

It is difficult to determine how often spontaneous remission occurs. The success of therapy renders it unjustifiable to delay treatment for more than a short time and it is therefore unlikely to be observed in patients who have reported for treatment. It could be that it commonly occurs, in which case medical advice would not be sought.

In one patient, however, who was taken home by her parents before treatment was commenced but after a biopsy had been obtained, evidence of spontaneous remission has been obtained.

Spontaneous Remission of African Lymphoma

Burkitt DP; Kyalwazi SK

British Journal of Cancer 21(1): March 1967; 14-16

Extracted Summary

The extreme sensitivity to chemotherapy and radiotherapy, and the relatively high incidence of long-term survivals observed in the treatment of African lymphoma is now well known (Burkitt, Hutt, and Wright, Cancer, 18: 1965, 399, Clifford, East African Medical Journal 43 (1966), 179, Ngu, Treatment of Burkitt's Tumour, 1966, 204-208). The observation that long term remissions, amounting to possible cures, can follow a single dose of chemotherapy (Burkitt, op. cit., 1966, 197-203)) suggests a strong anti-tumour response on the part of the patient. This observation naturally prompts the question whether the immunological response in the absence of chemotherapy could be sufficient alone to eradicate a tumour.

Before the availability of suitable chemotherapy these tumours were always observed to grow rapidly during the period the child was retained in hospital. Now that the response to therapy has been shown to be related to the size of tumour when first treated, there is no justification for withholding treatment, and the possibility of observing spontaneous regression is consequently limited to the rare instances where treatment is refused following diagnostic biopsy. Two patients who fall into this category have been followed, and both remain symptom-free.

Selected Case Reports

Case J. 135: A girl aged 4 years was admitted to Mulago Hospital, Kampala, on June 27, 1964, with a malignant lymphoma involving her left maxilla and invading the orbit. After removing tissue for biopsy through the socket exposed in extracting a loose tooth, treatment was postponed until anaemia was corrected by blood transfusion. This was refused by the mother and the child was taken home without receiving blood or chemotherapy. One year later the child's home was traced. There was no evidence of tumour and the gap left by the extracted tooth was confirmatory evidence of identity. The patient was last seen in July 1966, symptom-free over two years after diagnosis.

Case K. 272: A married woman aged 36 was admitted to Mulago Hospital in April 1966, with massive bilateral breast lymphomata and a tumour on her right shoulder. She was breast-feeding a 5-month-old child. These tumours had been present for two months, and a biopsy had been taken at another hospital before her arrival at Mulago Hospital. As there was difficulty in tracing the report of this a second biopsy was taken. Both biopsies showed the typical features of African lymphoma. Therapy was postponed in order to ascertain whether administration of cyclophosphamide would, through the milk, have any deleterious effect on the child. At this time a close relative died and the patient asked permission to attend the funeral, promising to return in a few days for treatment. She did not return for 6 weeks, and by this time all evidence of tumour had disappeared. She was last seen in mid-August when she was symptom-free.

Evolution of an Atypical Case of Burkitt Lymphoma

Jamra M; Carvalho RPS; Dalldorf G
Lancet 2: Sept 26 1970; 672

Extracted Summary

A case of Burkitt's lymphoma is reported. Laparotomy revealed ovarian tumours which were not removed. Without specific treatment, and only a small dose of oral penicillin, there was a spontaneous clinical and haematological remission in March 1970.

Selected Case Report

A girl 12 years old was admitted to hospital on February 5, 1970, with swelling of the left side of the face, fever, and pallor. On examination the gums were swollen; there was no hepatosplenomegaly. A mass was found in both iliac fossae, and on gynaecological examination an elastic tumour was felt, believed to be ovarian.

Laboratory findings were as follows: Red cell count, 2.9 million/mm^3; white cell count, 900/mm^3 (stab neutrophils 2%, segmented neutrophils 8%, mature lymphocytes 78%, monocytes 12% with a few immature monoblasts); platelet count, 116,000/mm^3. Sternal bone marrow showed myeloblasts 10%, paramyeloblasts 2.2%, "monocytic immature cells" 17%, granulocytic cells 14%, erythroblasts 26.8%, and mature lymphocytes 24.4%; no megakaryocytes were seen.

Laparotomy on February 26, 1970, revealed ovarian tumours, the size of oranges, on both sides. Histological examination of biopsy specimens showed a starry-sky pattern with lymphoblastic and reticulum cell proliferation typical of Burkitt lymphoma (Dr. A. Luizi). The ovarian tumours were not removed. Without specific treatment, and only a small dose of oral penicillin, there was a spontaneous clinical and haematological remission in March: the face lesions disappeared; and the red-cell count rose to 5 million/mm^3, the haemoglobin to 13.9 gm/100 ml, the platelets to 275,000/mm^3, and the lymphocytes to 8,700/mm^3, (11.5% lymphocytes). At a second operation on March 5, the tumours were found to be so much smaller that the ovaries appeared almost normal; the ovaries were therefore not removed.

The remission lasted till May when the anaemia, leucopenia, and thrombocytopenia reappeared, and laboratory findings suggested lymphatic leukaemia. The bone-marrow was infiltrated with 66% "reticulum hystiocytic monocytoid immature cells." At this point, cyclophosphamide treatment was started, and there was a prompt response: The blood and bone-marrow pictures became nearly normal. On June 10, the bone-marrow showed only 7% reticulum cells, and the blood contained 4.2 million red cells, 5,300 white cells, and 114,000 platelets/mm^3. This is the picture at the time of writing (August 12).

Regression of Burkitt's Lymphoma In Association with Measles Infection

Bluming AZ; Ziegler JL
Lancet 2: July 10 1971; 105-106

Extracted Summary

There have lately been reports suggesting a beneficial effect of natural measles infection on the course of acute lymphoblastic leukemia. The authors have observed a complete regression of histologically diagnosed Burkitt's lymphoma in an untreated African child who contracted measles shortly after diagnostic biopsy.

Selected Case Report

An eight-year-old African boy was admitted to Mulago Hospital on December 1, 1970, with a four-month history of painless right orbital swelling. Six months before admission a much smaller right orbital mass had been excised at another hospital. At that time the clinical diagnosis was lipoma, although no histological examination of the mass was performed. On December 1 physical examination was remarkable only for right-sided proptosis with conjunctival oedema, loss of vision, and absence of all extraocular movements on the right side. A biopsy specimen of the right retro-orbital tumour taken on December 3 was histologically diagnostic of Burkitt's lymphoma. No blood or blood products were administered at the time of surgery nor at any time thereafter. On December 13, before institution of any form of therapy, the patient was noted to have a generalised measles exanthem. On the same day, the right orbital tumour was first noted to be regressing; over the course of the next two weeks both the exanthem and the tumour disappeared. Measles antibody titers, measured by complement fixation, were absent on December 16, 1/64 on January 8, and 1/16 on March 5. The patient remains in complete remission four months after the measles infection, having received no antineoplastic therapy.

Immunological evaluation included intradermal testing, on January 9 and April 12, with intermediate strength PPD, streptokinase-streptodornase, mumps antigen, and dermatophyton O. On neither occasion was a reaction to any of these antigens observed. Attempted sensitisation to topical dinitrochlorobenzene applied on January 9 was proven unsuccessful at the time of challenge on February 4 and April 12. Iliac crest bone marrow aspirations on December 20 and January 11 disclosed normal cellularity with 20% to 22% erythrocyte precursors. Only 7% lymphocytes was found in the first aspirate; this figure rose to 28% during the three-week period preceding the second bone marrow aspiration.

Spontaneous Remission in Burkitt's Lymphoma

Ziegler JL

National Cancer Institute Monographs 44: 1976; 61-65

Extracted Summary

Three cases of spontaneous regression of Burkitt's lymphoma are reviewed and additional clinical and laboratory observations relevant to the role of host defences are summarized. Spontaneous regression of Burkitt's lymphoma provides compelling evidence for antitumor immunity.

Spontaneous Regression in Non-Hodgkin's Lymphoma

Gattiker HH; Wiltshaw E; Galton DAG

Cancer 45(10): May 15 1980; 2627-2632

Extracted Summary

Two hundred nine cases of non-Hodgkin's lymphoma have been analyzed retrospectively for the occurrence of spontaneous regression (SR). Complete, partial or minor SR was found in 18 out of 140 cases with nodular lymphoma and in 2 out of 69 cases with diffuse lymphoma. Thus, SR occurs far more frequently in nodular lymphoma than in the diffuse type. Within the nodular lymphoma group, SR is associated with long survival. It occurred in previously treated and untreated patients and in nodal and extranodal disease; the duration varied from a few weeks to many years but lasted one year or more in 7 cases with complete or partial SR.

Spontaneous Regression of Non-Hodgkin's Lymphoma

A Report of Nine Cases

Krikorian JG; Portlock CS; Cooney DP; Rosenberg SA

Cancer 46(9): Nov 1 1980; 2093-2099

Extracted Summary

Seven previously untreated patients and two previously treated patients with advanced non-Hodgkin's lymphoma (Stages III and IV) and favorable histologic subtypes had spontaneous regression of their lymphomas. Regressions were either complete or partial and were frequently durable. Six of the seven patients who had spontaneous regression of their lymphomas prior to any therapy have yet to require treatment. Seven of the nine spontaneous regressions occurred in a group of 44 patients who were followed with initial therapy deferred. Six patients had regression of their lymphomas prior to any therapy and one patient had previously received a small field of radiation therapy. Temporary spontaneous regression of lymphoma may be common in selected patients with favorable histologies and advanced disease in whom initial therapy is deferred.

Selected Case Reports

Case 1: B.S. was a 42-year-old man when he first presented in March 1973, with lymphadenopathy measuring up to 2 centimeters involving the right submandibular, right epitrochlear, left axillary, right inguinal, and right femoral regions. He was asymptomatic. Laboratory investigations, including a complete blood count, platelet count, serum chemistries, and chest roentgenogram, were all normal. Biopsy of a right submandibular and right epitrochlear lymph node showed nodular mixed lymphocytic and histiocytic lymphoma. Bone marrow biopsy was normal. A lymphogram was performed in June 1973, and showed markedly enlarged foamy lymph nodes in the para-aortic and common iliac regions bilaterally. Following the lymphogram, a repeat chest roentgenogram revealed an abnormal foamy node in the left supraclavicular region.

He was clinically staged as III-A and because he had no threatening disease and was asymptomatic, he was observed without therapy. Two months following his lymphogram, peripheral lymphadenopathy was noted to regress. Four months following his lymphogram he had no evidence of disease on physical examination and the previously abnormal lymph nodes observed on the abdominal lymphogram and chest roentgenogram had regressed showing equivocal abnormalities but no definite evidence of lymphoma. He has continued asymptomatic and without evidence of disease five years since his initial diagnosis.

Case 2: S.B. was a 68-year-old woman when she first visited Stanford University Medical Center with a four-month history of asymptomatic right posterior cervical lymphadenopathy. Previous biopsy of a lymph node had revealed nodular poorly differentiated lymphocytic lymphoma. Physical examination revealed right posterior auricular, right submandibular, left anterior cervical, and bilateral axillary lymphadenopathy. Laboratory investigations included a normal complete blood count, differential, and platelet count, and normal serum chemistries. Chest roentgenogram showed a left hilar mass. Bone marrow biopsy revealed involvement with lymphocytic lymphoma and lymphogram revealed enlarged, foamy bilateral para-aortic and iliac lymph nodes compatible with tumor involvement. Intravenous pyelography demonstrated no ureteral obstruction. She was staged IV m+A.

Because she had no threatening disease and was asymptomatic, therapy was deferred. Three months later, it was noted that her peripheral lymphadenopathy had regressed. The left hilar mass on chest roentgenogram resolved and the abdominal lymphogram demonstrated marked reduction in the size of the involved lymph nodes. She continues asymptomatic, without therapy, and without clinical evidence of disease two years after her first visit.

The Natural History of Initially Untreated Low Grade Non-Hodgkin's Lymphomas

Horning SJ; Rosenberg SA

New England Journal of Medicine 311(23): Dec 6 1984; 1471-1475

Extracted Summary

To learn more about the natural history of low-grade non-Hodgkin's lymphoma, the authors have studied 83 patients in whom the advanced disease was initially managed without therapy. Actuarial survival was 82% at 5 years and 73% at 10 years. The median time until therapy was required was three years. Histologic transformation to an intermediate-grade or high-grade lymphoma occurred both before and after primary therapy. The actuarial risk of transformation among the initially untreated patients was similar to that in a group of patients treated at this institution immediately after diagnosis. Neither the time to histologic transformation nor the incidence of transformation was influenced by when therapy was started.

The authors considered that spontaneous regression of disease occurred if radiologic or physical examination showed evidence of regression, and the regression had to be documented on two or more occasions over more than two months. The authors defined complete regression of disease as the resolution of all clinical disease, including evidence from radiologic studies.

During follow-up of the 83 initially untreated patients, spontaneous regression of disease was observed in 19 cases (23%), including 30% of patients with nodular, poorly differentiated lymphocytic lymphoma. None of the 19 patients had received treatment for their low-grade lymphoma. The median time from diagnosis to spontaneous regression was eight months. Regressions were complete in 6 patients and incomplete in the remaining 13, and were noted in patients with moderate (>3 centimeters) or minimal adenopathy. One of the complete regressions occurred after a clinical viral illness.

The authors suggest several advantages in witholding treatment until there is evidence of disease progression. First, there are many unpleasant side-effects to cytotoxic therapy, including myelosuppression, which can be associated with serious, even fatal, infectious complications. Second, there have been reports among patients with the low-grade non-Hodgkin's lymphomas of an increased incidence of acute leukemia that is related to the duration of exposure to alkylating agents. Third, spontaneous regression of disease may occur. There have been reports in the literature that indicate that 5 to 15% of patients with low-grade lymphomas have experienced spontaneous regressions.

The mechanism of spontaneous regression is unknown. Disease regression after viral infection, a possible interferon effect, has been reported. The authors speculate that this mechanism may be implicated in one of their patients.

Transient Spontaneous Regression of an Anterior Mediastinal Mass

Weaver GR; Cohn JH; Mintzer RA

Chest 87(4): April 1985; 547-548

Extracted Summary

A case of spontaneous regression of lymphoma is presented. Regression of the tumor occurred during an episode of mechanical small bowel obstruction. Elevated circulating endogenous corticosteroids are thought to have acted against the tumor cells.

Selected Case Report

A 69-year-old woman presented to Northwestern Memorial Hospital with shortness of breath and cough. A chest roentgenogram revealed an anterior mediastinal mass. This was confirmed on CT scan of the chest. Percutaneous aspiration of the mass with an 18-gauge needle yielded cells suggestive of a lymphoma. During the next two days, the patient developed abdominal distention, pain, and an elevated white blood cell count. The focus of attention shifted to her abdomen, and the patient had a laparotomy seven days after admission. A small bowel obstruction was relieved with lysis of adhesions and resection of 59 centimeters of small intestine. After the patient recovered from her abdominal surgery, investigation of the mediastinal mass resumed. On a repeat roentgenogram of the chest, the mass was no longer visible on the 17th day of hospitalization, and a CT scan failed to demonstrate any mass lesion. The patient was discharged to be followed with serial chest x-ray films. Three weeks after discharge, the patient returned with reaccumulation of pleural effusion and reappearance of the anterior mediastinal mass. Thoracotomy and biopsy revealed lymphoblastic lymphoma.

Spontaneous Remission in CNS Lymphoma

Rubin M; Brisson ML; Goldenberg M; Libman I
Canadian Journal of Neurological Sciences 12(2): May 1985; 69

Extracted Summary

We report a case of complete, spontaneous remission of primary CNS lymphoma that occurred within twenty-seven weeks of onset and which, by CT and clinical data, lasted approximately one year before relapse. To our knowledge, this is the first such reported case in the literature and it lends further support to the notion that CNS lymphoma is a heterogeneous disorder. At the very least, it is clearly capricious in its natural history.

Spontaneous Remission in Diffuse Large Cell Lymphoma

Grem JL; Hafez GR; Brandenburg JH; Carbone PP
Cancer 57(10): May 15 1986; 2042-2044

Extracted Summary

A case of spontaneous remission in a Stage IIA diffuse large-cell lymphoma is presented. A review of the literature suggests that whereas spontaneous regressions are a well-recognized phenomenon in indolent lymphomas, it is extremely rare in lymphomas of aggressive histologic subtype.

Selected Case Report

A 54-year-old woman presented in January 1982 with a 2-month history of a foreign body sensation in the throat. Indirect laryngoscopy revealed a mass in the left vallecula, and a mobile tender lymph node was noted in the left neck. There was no evidence of hepatosplenomegaly, and no other nodes were palpable. Direct laryngoscopy was performed and a 3 x 3 centimeter submucosal soft tissue mass arising from the left base of the tongue was observed. A biopsy of the lesion was obtained. The patient received intravenous penicillin G for 5 days followed by oral cefazolin for 1 month to treat a possible bacterial infection.

Histologic examination of an incisional biopsy specimen disclosed a diffuse sheet of large cells with irregular oval vesicular nuclei and with one or more prominent nucleoli and scanty cytoplasm. The mass was covered by an intact squamous epithelium. The diagnosis of malignant lymphoma, diffuse large cell type, was entertained, and the patient was referred to a cancer center for further evaluation.

On their examination, a 2 x 2 centimeter mass was identified at the base of the tongue, and a 2 x 2 centimeter lymph node was palpable in the left cervical area. Pathologic review confirmed the diagnosis of diffuse large cell lymphoma. Laboratory studies including complete blood count (CBC), chemistry survey, and erythrocyte sedimentation rate were normal. A chest radiography, computerized tomographic (CT) scan of the abdomen, lymphangiogram and bone marrow aspirate and biopsy showed no evidence of lymphoma. The clinical stage was II on the basis of the mass in the base of the tongue plus the enlarged regional lymph node. Combination chemotherapy was recommended. Because of geographical

considerations, the patient was referred to the Wisconsin Clinical Cancer Center to receive therapy.

Upon examination at the University of Wisconsin in February 1982, a mobile left cervical lymph node was palpable. Indirect laryngoscopy was performed by an otolaryngologist (JHB); slight irregularity of the left base of the tongue was noted, however, no discrete mass was seen. Pathologic review of the original biopsy specimen again confirmed the histologic diagnosis of diffuse large cell lymphoma. Immunoperoxidase staining for cytoplasmic immunoglobulin was negative. Because of the apparent regression of the primary tumor mass, chemotherapy was withheld, and she was followed monthly with physical examinations by two physicians (PPC and JHB). The cervical lymph node regressed completely and the physical exam was completely normal by late Spring 1982. She remains well and without evidence of recurrent lymphoma 4 years after her original diagnosis.

Spontaneous Regression of a Small Noncleaved Cell Malignant Lymphoma (Non-Burkitt's Lymphoblastic Lymphoma) - Morphologic, Immunohistological, and Immunoglobulin Gene Analysis

Poppema S; Postma L; Brinker M; DeJong B

Cancer 62(4): Aug 15 1988; 791-794

Extracted Summary

Complete spontaneous regression of high-grade malignant non-Hodgkin's lymphoma is extremely unusual. In this report the authors describe a complete spontaneous remission after surgical excisional biopsy of a small noncleaved cell malignant lymphoma (non-Burkitt's lymphoblastic lymphoma) of the tonsil in a 12-year-old boy. The diagnosis was confirmed by immunohistologic and immunoglobulin gene analysis. Similar studies were performed on the cervical lymph node excised 2 weeks later when spontaneous remission had occurred. The patient has remained in good health for over 3 years.

Selected Case Report

A 12-year-old boy was admitted to the University Hospital, Groningen, The Netherlands, because of a mass in the left submandibular region that had been present for 6 weeks. Four months before the admission, he was seen by a physician because of sinusitis. Despite antibiotic therapy, general weakness persisted. At the age of 4 years he underwent adenotomy. Otherwise, his past medical history and family history were noncontributory.

Physical examination confirmed the presence of a left-sided oropharyngeal tumor behind an enlarged necrotizing tonsil. In addition, a cervical lymph node with firm consistency and a diameter of 5 centimeters was palpable in the left neck region. The erythrocyte sedimentation rate was 4 millimeters/hour. Hemoglobin was 135 gm/l; leukocyte count 6.6 x 10^9/l, with 7% eosinophils, 66% neutrophils, 20% lymphocytes and 7% monocytes; platelet count 212 x 10^9/l. Further blood studies including T/B cell ratio and CD4/CD8 ratio determinations were normal. Membrane immunoglobulin studies of peripheral blood B-cells revealed no clonal population. Bone marrow smears and spinal fluid cytologic examination also were normal. Tests for infectious diseases including Epstein-Barr virus, toxoplasmosis, varicella zoster, and cytomegalovirus were negative. A computerized axial tomographic scan of the base of the skull confirmed the presence of a large left-sided oropharyngeal soft tissue mass without bony involvement. A biopsy specimen of the oropharyngeal tumor was taken and diagnosed as a malignant lymphoma, small noncleaved cell (non-Burkitt's lymphoblastic).

During the next days, the size of the tumor diminished rapidly and therefore the cervical lymph node in the left side of the neck also was excised. This lymph node was diagnosed as showing only reactive changes, including fibrohyalinosis. A decision was made to refrain from antitumor treatment and the boy was discharged from hospital after 2 weeks. Since then he was examined at regular intervals and he has now remained in good health for 3 years.

Spontaneous Regression in Non-Hodgkin's Lymphoma

Clinical and Pathogenetic Considerations

Drobyski WR; Qazi R

American Journal of Hematology 1: 1989; 138-141

Extracted Summary

The spontaneous regression (SR) of tumor has been noted in a variety of neoplastic conditions. In non-Hodgkin's lymphoma, this phenomenon has been reported in indolent histologic subtypes, with a frequency of 10-20% in selected series. Investigators evaluating new therapies for lymphomas with a favorable histology need to be cognizant of SR's impact. Mechanisms which have been proposed to explain SR have included the role of contemporaneous bacterial or viral infection, as well as an augmented host immune response which is able to mediate tumor regression via humoral and cellular effector mechanisms. The ability to recapture immunoregulatory control is aptly illustrated by lymphomas developing after organ transplantation where reduction of immunosuppression has, on occasion, resulted in tumor regression. The importance of immune regulation of B-cell lymphoma is also suggested by the tumor's responses to immunotherapy and interferons in-vivo and by the biologic and pathologic characteristic of indolent lymphomas being analogous, in many respects, to benign neoplasms. Indolent lymphomas which differ from aggressive lymphomas in their clinical and biological behavior may be more responsive to these host immunoregulatory influences. Review of clinical experience as well as proposed mechanisms of spontaneous regression in non-Hodgkin's lymphoma are explored in this report.

Spontaneous Regression of Primary Malignant Lymphoma of the Stomach in Two Nontreated Japanese

Shigematsu A; Iida M; Lien GS; Imamura T; Okada M; Fuchigami T; Fujishima M; Itoh H; Iwashita A

Journal of Clinical Gastroenterology 11(5): Oct 1989; 511-517

Extracted Summary

Two patients with primary malignant lymphoma underwent spontaneous regression. One was a 40-year-old woman with a large ulcerating tumor on the greater curvature of the gastric antrum. This tumor shrank spontaneously, leaving only a small shallow ulcer. The resected specimen showed a minute focus of malignant lymphoma in the ulcer base. The other was a 73-year-old man who had a tumor with central ulceration on the posterior wall of the gastric antrum. Endoscopic biopsy revealed a malignant lymphoma. This tumor disappeared 60 days later. The patient refused surgery and remains well with no evidence of recurrent disease at this writing, 44 months later. Although there have been several case reports of spontaneous regression, partial or complete, of gastric malignant lymphoma, our cases seem to be the ones best proven.

Selected Case Reports

Case 1: In March 1983, a 40-year-old Japanese woman complained of epigastric hunger pain. Her past history revealed diabetes insipidus that had been well controlled by a nasal drip of 1-diamino-8-D-arginine vasopressin (DDAVP). A barium meal demonstrated a large hemispherical tumor with a smooth mucosal surface on the greater curvature of the pyloric antrum. Endoscopy revealed an elevated lesion with a shallow saucer-like ulceration and a smooth mucosal surface. The diagnosis of malignant lymphoma was made on biopsy findings. The endoscopic biopsy specimen was composed of diffuse infiltration of lymphoma cells, which were positive for LN-2, but negative for LN-1, LN-3, by ABC method and negative for intracytoplasmic immunoglobulins, lysozyme, alpha 1 antichymotrypsin by PAP method on paraffin sections from formalin-fixed material. Histol-

ogic diagnosis of malignant lymphoma, large cell type, was made according to the Working Formulation.

Physical examination was unremarkable. Laboratory data were all normal, except for a positive fecal occult blood and positive hepatitis B surface (HBs) antigen. Chest radiograph was normal. The next barium meal and gastroscopy revealed essentially the same feature as that at the initial examination. Barium meal follow-through examination and barium enema also were normal. Computed tomography, lymphangiography, ^{67}Ga scanning, and ultrasound study showed that the lesion was confined to the stomach, and elective surgery was considered.

Forty days after the initial examination, a remarkable regression of the tumor, with no chemotherapy or radiotherapy, was observed on gastroscopy. Radiograph examination revealed a further decrease of the tumor, leaving a small ulcer with a slightly elevated surrounding margin, mimicking a benign peptic ulcer in the healing stage. Despite a remarkable diminution in the tumor size, surgical resection was performed 65 days after the initial examination.

Pathologic examination of the resected specimen showed a small shallow ulcer on the greater curvature of pyloric antrum. Microscopically, a minute focus of malignant lymphoma, 2 mm in diameter, was found in the granulation tissue of the ulcer base. The tumor cells revealed the same features as those in the biopsy specimen. The perigastric lymph nodes were free of tumor involvement. The patient remains well, with no evidence of recurrence, 5 years and 9 months later.

Case 2: A 73-year-old Japanese man complained of abdominal pain. Gastroscopy revealed a protuberant tumor with a shallow ulcer and a smooth mucosal surface on the posterior wall of the antrum. Blood clot was evident on the ulcer base. Endoscopic biopsy revealed malignant lymphoma cells that were positive for intracytoplasmic immunoglobulins, with a monoclonal pattern (IgG, lambda-type) by PAP method on paraffin section from formalin-fixed material. Histologic diagnosis of malignant lymphoma, large cell type, was made. Following a barium meal, a polypoid mass with a smooth mucosal surface and central ulceration was detected, and he was admitted. Physical examination was unremarkable. Laboratory data, including complete blood count, routine serum chemistry, serological test, urinalysis, and stool examination, were all within normal ranges. Barium meal follow-through examination and barium enema revealed no abnormality. Computed tomography, ^{67}Ga scanning, and ultrasound study indicated no lymphomatous lesion outside the stomach.

Twenty-one days after the first examination, gastroscopy revealed that the tumor had decreased in size, even though chemotherapy or radiotherapy had not been given. Forty days later, a double-contrast upper gastrointestinal study revealed slight fold convergency, suggesting a healed ulcer on the posterior wall of the pyloric antrum. On a compression study, the tumor with the central ulceration had almost entirely disappeared. Gastroscopy performed 60 days after the initial examination also showed the disappearance of the tumor with the central ulcer. A discolored area was present where the tumor had been. The endoscopically obtained biopsy specimens showed no malignant cells. Although surgical resection was strongly recommended because a reappearance of the tumor was anticipated, the patient refused. Careful follow-up, including a gastroscopy with biopsy showing only erosive gastritis 8 months later, has been done thereafter. Recent barium studies of the upper gastrointestinal tract showed no sign of recurrent disease, 44 months after the tumor disappeared.

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Australian and New Zealand Journal of Medicine 14(5): Oct 1984; 676-677

Extracted Summary

We report a case of a 59-year-old woman who presented in end-stage renal failure with Stage III b lambda light-chain myeloma (LLCM). Despite a large tumour burden and refusal to accept cytotoxic chemotherapy, she was started on continuous ambulatory peritoneal dialysis (CAPD). With dialysis therapy alone she has shown considerable hematological improvement and remains well 18 months after diagnosis. The extremely poor prognosis attributed to light-chain myeloma is largely due to death from uremia.

As the natural history of this disease in patients offered dialysis therapy is unknown, dialysis should not automatically be withheld from patients with LLCM. (Permission to reproduce case report denied by author.)

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Other Lymphatic and Hematopoietic Tissue Malignancies

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Dutcher JP; Wiernik PH
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Spontaneous Regression of Extramedullary Plasmacytoma: A Case Report
Arunabh S; Dutta Gupta S; Bal S; Sarda AK; Vijayraghavan M; Shukla NK; Kapur MM
Japanese Journal of Surgery 18(4): Jul 1988; 455-459

Benign Neoplasms

Cystic Hygroma in Children: A Report of 126 Cases

Ninh TN; Ninh TX
Journal of Pediatric Surgery 9(2): April 1974; 191-195

Extracted Summary

One hundred twenty-six cases of cystic hygromas were seen in 10 years. More than two thirds of the cases were seen at birth or shortly thereafter. Inflammation occurred in 15.8%; hemorrhage into the hygroma in 12.6%. Radiotherapy has no place in management. Total excision is the only effective treatment.

The natural history of lymphangiomas has not been studied extensively. Spontaneous regression is not given credence by most authors. We think that this notion should be re-examined. In our series, we have had two cases of spontaneous regression. Both patients were seen at the neonatal period; one had a fairly large cystic hygroma arising from the right supraclavicular fossa, the other had an even bigger one on the right side of the neck. Both tumors regressed spontaneously.

Cervical Axillo-Mediastinal Lymphangioma With Tendency to Spontaneous Regression

Bollinger A; Brühlmann W
VASA 11(1): 1982; 66-70

Extracted Summary

The case of a 29-year-old woman suffering from a cervical axillo-mediastinal lymphangioma is described. Comparison of chest X-ray with pictures taken in early childhood revealed spontaneous regression of the cystic tumor, especially the cervical and mediastinal part. Computer tomography of the mediastinum indicates the presence of hemangiomatous tissue in the congenital malformation.

Selected Case Report

Immediately after the birth of the now 29-year-old patient, a forward arching of the right cervical region and the right axilla was observed. The x-ray picture at the age of one year clearly shows the arching supraclavicularly and axillarily. The whole upper right mediastinum shows the arched soft parts. Caudally, the shadow was clearly limited. There were none of the serious symptoms that can be caused by tracheal compression. A surgical and radiotherapeutical treatment was not applied. The picture of the thorax taken at the age of 7 years still showed the axillary and cervical swelling as well as the widened upper mediastinum.

Upon the present examination at the age of 29 years the cervical tumour no longer existed. Only the right supraclavicular cavity was a little more filled than the left one. A firm elastic, roundish growth about the size of a mandarine orange was palpable in the axilla. It was punctated and filled with opaque substance. The cyst was also registered by the computer tomogram.

The lymphography of the arm revealed normally wide lymph vessels with the correct number of valves. In the axilla, however, only 2 conductors could be found. The thinner one goes round the caudal pole of the cyst whereas the thicker one obviously leads directly into the cyst.

The newly carried-out x-ray shows that the shadow of the upper mediastinum has disappeared. It only reveals a flat arching of the right suprahilar mediastinum.

The computer tomogram before and after intravenous administration of opaque substance is interesting. The space-absorbing process is located in the front part of the mediastinum. Before the injection of the opaque substance the density of the tumour was 38H, afterwards 82H. That leads to the conclusion that the process is strongly vascularized and probably contains hemangiomatous elements. For the time being a surgical removal of the persistent axillary cyst was not carried out because it might cause the development of a lymphedema.

(Noetic Sciences translation)

Spontaneous Resolution of a Cystic Neck Mass in a Fetus with Normal Karyotype

Distell BM; Hertzberg BS; Bowie JD

American Journal of Roentgenology 153(2): Aug 1989; 380-382

Extracted Summary

Cystic hygromas are congenital malformations of the lymphatic system that usually are located along the posterior surface of the neck. Prenatal sonographic detection of nuchal cystic hygromas generally is thought to carry a poor prognosis, and these lesions often are associated with chromosomal aneuploidies such as Turner syndrome. We report a case of spontaneous resolution of a prenatally detected cystic neck mass in a fetus with a normal karyotype and a normal outcome. This case demonstrates that in the absence of fetal hydrops, in utero detection of a nuchal cystic hygroma does not necessarily indicate an unfavorable prognosis, but occasionally can be associated with a normal clinical outcome.

Selected Case Report

A 30-year-old woman, gravida 9, para 1, was referred for obstetric sonography because of a history of seven spontaneous first trimester abortions. Obstetric history was also remarkable for an infant with an imperforate anus. Interestingly, a cystic hygroma had been surgically removed from the mother during early childhood.

Sonographic examination revealed a viable twin pregnancy with crown-rump lengths of 6.9 and 7.1 millimeters, corresponding to 6.3 menstrual weeks. Follow-up sonography at 14 weeks showed no abnormalities in twin A, but revealed a bulging membrane with a central septum on the posterior aspect of the neck of twin B. The calvaria and cervical spine were intact, and there was no evidence for fetal hydrops. Findings were considered typical for a cystic hygroma.

A third sonographic examination at 16 weeks, performed in conjunction with amniocentesis, confirmed the presence of a cystic neck mass in twin B. Chromosomal analysis revealed normal 46, XY chromosomal patterns in both twins. Repeat sonography at 18 weeks again showed the mass, but it had decreased in prominence. Follow-up scans at 22 and 27 weeks no longer revealed a cystic neck lesion, although the soft tissues in the nuchal region remained somewhat prominent. Two healthy, morphologically normal twins were delivered by cesarean section at term, both with normal appearing necks, without evidence of webbing or masses. Examination of the products of conception indicated a diamniotic dichorionic gestation.

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Journal of Ultrasound in Medicine 8(2): 1989; 101-103

Spontaneous Resolution of Fetal Cystic Hygroma and Hydrops in Turner Syndrome
Mostello DJ; Bofinger MK; Siddiqi TA
Obstetrics and Gynecology 73(5 Pt 2): May 1989; 862-65

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Meizner I; Levy A; Cohen J
American Journal of Obstetrics and Gynecology 163(1 Pt 1): Jul 1990; 267-269