The Very Acute Leukemias

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SUMMARY

Among 593 cases of acute leukemia, 65 cases were very acute; their courses were 1 month or less. This study emphasizes the special nature of promyelocytic leukemia and notes the expected frequency of myeloblastic leukemia.

This study is based on the analysis of records of 593 patients with acute leukemia admitted to the Hematology Service of the Hospital St. Louis in Paris during the years 1959–64. We have selected as very acute leukemias those that have run courses of 1 month or less from the 1st hematologic examination confirming the diagnosis, except that cases in which the examination was clearly belated. The number of cases satisfying this definition amounts to 65, or 11 % of all case records.

The cytologic classification of these leukemias follows the nomenclature recently proposed to the World Health Organisation (6). Our cases are divided thus: 33 myeloblastic leukemias, 19 promyelocytic, 6 monoblastic, and 5 lymphoblastic; 2 cases could not be classified.

PROMYELOCYTIC LEUKEMIAS

We have previously pointed out the particular nature of acute, promyelocytic leukemia (1–4), a disease characterized by 3 elements: promyelocytes, a marked hemorrhagic tendency, and a very acute course. The present study confirms the description. In our present series there are 19 cases of acute, promyelocytic leukemia. This figure represents 51.3 % of the cases of acute promyelocytic leukemia observed during the period covered by the study. The disease strikes both sexes—11 men, 8 women—and principally adults. Signs of a hemorrhagic diathesis are very frequent—18 cases out of 19—and severe; they are diffuse bleeding and large purpuric plaques. On the other hand, signs related to tumor are rare and moderate. Anemia is constant, and thrombocytopenia is very marked: in 14 cases, less than 50,000 platelets/cu mm; 18 times, less than 100,000/cu mm. The WBC is usually low, less than 10,000/cu mm on 14 occasions and less than 5,000/cm mu on 12 occasions—or 63 %. The percentage of promyelocytes in the peripheral blood was more than 70 % in 8 cases, about 50 % in 6 cases, and less than 10 % in 2 cases; they were absent in 3 cases. The marrow shows a massive invasion by promyelocytes, which always constitute more than 80 % of the marrow cells. Clotting studies revealed grave disorders: fibrinogen of less than 200 mg % in 10 cases with lytic activity in 7 cases. The cerebrospinal fluid was normal in the 2 cases in which it could be studied. In the 16 cases that could be followed to their end, death was always marked by hemorrhages, cerebromeningeal hemorrhages dominating the clinical picture 8 times and gastrointestinal hemorrhages, 3 times. In the blood the terminal WBC was less than 1000 in 6 cases. Autopsy was performed in 9 cases and showed leukemic infiltrations in the majority: massive infiltrates in 6 cases, of which 1 with massive hepatic infiltration and icterus; infiltrate limited to the marrow in 1 case; infiltrates absent in the 2 remaining case, of which one had diffuse hemorrhages and the other, hepatic hemorrhages.

The following therapies were tried: combined corticosteroids and methotrexate in 12 cases; methylglyoxal in 2. The treatment was administered for only a few days, in most cases, the longest duration of therapy being 3 weeks.

MYELOBLASTIC LEUKEMIAS

The group of myeloblastic leukemias is numerically the largest—33 cases—and represents 10.6 % of the total of 310 cases of myeloblastic leukemias in this series. This group is divided equally between the 2 sexes, with 18 men and 15 women. The disease strikes all ages, but there are 2 peaks of incidence—in the 3rd and 5th decades of life.

The clinical signs are marked from the beginning. The frequency of hemorrhagic signs and signs of tumor, in the sense of splenomegaly and adenopathy, are noteorthy.w Gingival hypertrophy, considered to be more frequent in monocytic leukemia, was found in 25 % of the cases of this group. Anemia is constant, and thrombocytopenia usual, 27 patients having had less than 100,000 platelets/cu mm.

The WBC is usually elevated; it was more than 10,000/cu mm in 27 cases (81 %) and more than 50,000/cu mm in 18 cases (54 %). Blast cells are constantly present in the peripheral blood, most often in great numbers; there were 70 % or more in 28 cases (84 %) and 25 % or less in only 2 cases. In the marrow the invasion by blasts has extended to more than 70 % of the medullary elements in 31 cases; in the only 2 cases remaining, the initial percentages were 40 and 50 %; in every case the marrow was of normal or increased density. Aside from the thrombocytopenia, the clotting abnormalities were not striking: fibrinogen of less than 200 mg % in 4 cases; deficiencies in Factors V and VII in 1 case. The cerebrospinal fluid was examined in 9 cases and was normal in every case. The preterminal clinical manifestations have been the following: hemorrhagic syndromes in 21 cases, of which 11 had cerebromeningeal mani-

festations and 10 had gastrointestinal bleeding; acute abdominal pain in 3 cases, in 1 of which the autopsies revealed a mesenteric infarct, in another, a ruptured spleen, and in the 3rd, necrotizing pancreatitis. In 2 cases cardiovascular manifestations dominated the terminal picture: in one 24-year-old patient a myocardial infarct was the event disclosing the leukemia, and it terminated fatally in 3 days; the 2nd patient died in congestive heart failure, and autopsy findings disclosed a leukemic infiltration of the myocardium. Terminal icterus was observed in 2 cases. Streptococcal septicemia was observed in 1 case. The hematologic picture was similar to the initial picture in 27 cases. In 6 cases the WBC diminished to less than 1000/cu mm, and there was an aplastic marrow. It should be noted that of these 6 patients only 1 had had an initially high WBC, the 5 others having had less than 15,000/cu mm initially. Therapy could be initiated 30 times and consisted in 15 cases of corticosteroids with methotrexate, in 4 cases of corticosteroids alone, in 4 cases of steroids with methotrexate and 6-mercaptopurine, in 3 cases of methotrexate, in 2 cases of methylglyoxal and 6-mercaptopurine, in 1 case of vincristine, and in 1 case of 2 exchange transfusions.

In the 6 patients dying with marrow aplasia, the therapy had consisted of the following for the various cases: corticosteroids and methotrexate for 10 days; steroids and methotrexate for 15 days; steroids for 12 days; methylglyoxal and 6-mercaptopurine for 15 days; steroids then methotrexate and 6-mercaptopurine for 21 days; vincristine for 15 days.

Autopsy was performed in 16 cases and in 14 cases revealed massive leukemic infiltrates. In 1 case autopsy revealed only a necrotizing pancreatitis with diffuse hemorrhages and a pulmonary infarct. In another case the marrow was poor and showed no apparent leukemic infiltrate. One patient with terminal icterus was autopsied and had a leukemic infiltrate of the liver.

MONOBLASTIC LEUKEMIAS

The series includes 6 cases of monoblastic leukemia, a diagnosis that is rarely made. Our series includes only 10 cases in its 6-year period, indicating that the very acute cases constitute 60%. The group consists of 3 adult men and 3 adult women. Hypertrophic gingivitis was observed in only 1 case; no particular skin manifestations were noted in this small group. Anemia was constant; thrombocytopenia was in every case between 50,000 and 100,000/cu mm; the percentage of blast cells in the peripheral blood was over 80% and in the marrow was 100%. Cytologic examination showed in 2 cases numerous monocytoid cells associated with the "monoblasts"; the other cases showed only "monoblasts." Clotting studies showed fibrinogenopenia in only 1 case. In 3 cases the preterminal clinical lesions could be determined: there was 1 case of cerebromeningeal hemorrhage; 1 case of anuria in a patient with interstitial nephritis; and 1 sudden death in a patient having massive leukemic infiltrates of the brain and heart. In the 3 cases autopsied, leukemic infiltrates were massive. Therapy was very limited and in no case could be administered for more than 6 days: corticosteroids and methotrexate in 2 cases; methotrexate and 6-mercaptopurine in 1 case; corticosteroids in 2 cases.

LYMPHOBLASTIC LEUKEMIAS

Only 5 lymphoblastic leukemias of the 234 cases accumulated in 6 years had a very acute course (2.1%). These were 4 boys and a girl, all less than 20 years old. Hemorrhagic signs were present in all 5 cases, and tumoral signs were also present, 1 case presenting a mediastinal tumor. Anemia was constant and thrombocytopenia was always very intense—less than 35,000/cu mm. The initial WBC was very variable: 600, 1,600, 6,000, 267,000, and 450,000/cu mm. The presence of peripheral blast cells was also variable; they were absent in the 2 leukopenic patients and represented more than 90% of the cells in the 3 other patients. The cerebrospinal fluid was normal in 2 patients. Death occurred in 1 case in association with a staphylococcal septicemia, and in 3 cases in association with a hemorrhagic syndrome including, in 1 case, a pericardial syndrome. The remaining patient died highly febrile on the 8th day. Only 3 autopsies could be performed; they revealed massive leukemic infiltrates. Therapy was not administered to 1 patient. In 3 patients corticosteroids were administered for 1, 3, and 15 days, and in the last patient, corticosteroids and 6-mercaptopurine were given for 10 days.

DISCUSSION

Is it possible to predict a very acute course for a leukemia?

The 65 cases of very acute leukemias have occurred at very varied ages and have been of very diverse symptomatology.

Frank signs of tumor, a large number of blast cells in the peripheral blood, a very high WBC, and an intense thrombocytopenia are unfavorable elements but are not formal evidence.

The cytologic type is the best index of the gravity of the case. The low relative and absolute number of lymphoblastic leukemias should be emphasized. It is difficult to evaluate the relative frequency of the so-called monoblastic leukemias; in spite of the progress of cytochemical methods (4, 5), it is often hard to determine whether the process is an authentic reticulohistiomonocytic leukemia or an atypical myeloblastic leukemia. The frequency of myeloblastic leukemias in the very acute group is expected. The chief interest lies in the promyelocytic leukemias. The dramatic hemorrhagic syndrome associated with profound fibrinogenopenia and the finding on the marrow smear of atypical promyelocytes should lead one to anticipate a very acute course.

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