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Acute Leukemia In Adults

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ACUTE LEUKEMIA IN ADULTS

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It is the purpose of this communication to review briefly our current experience with acute leukemia in adults at the Henry Ford Hospital. Comparative data on survival and remissions and comments on clinical points of importance make up the body of the report.

MATERIAL

From late 1957 to April 1960, 18 consecutive cases with which the writer has had personal knowledge have been used for the purpose of this study. Of the 18 cases, 11 had the onset of disease after the age of 50, 17 of the 18 occurred after the age of 30, and one, a 16-year-old boy, had a fulminating acute lymphocytic leukemia of two days' duration. No childhood leukemia is included. In addition five cases of acute leukemia, evolving from chronic granulocytic leukemia are discussed separately.

All of the cases reported herein received the standard supportive measures employed today; i.e., blood transfusions, steroids, analgesics, and sedatives. Antibiotics were employed only when evidence of bacterial infection was reasonably clear. In addition 6-mercapto-purine was the specific anti-leukemia medication employed in the great majority of these cases. In some instances death occurred before any effect from this drug was obtained, or before the patient's general condition would permit its use. However, our aim here is not to exclude such unfavorable situations, but to take an honest look at our experience.

The diagnoses according to cell type were as follows: 11 cases of acute granulocytic leukemia, 4 cases of leukemia reticulo-endotheliosis, 2 cases of acute lymphocytic leukemia, and 1 case of the DiGuglielmo syndrome, terminating in acute granulocytic leukemia.

RESULTS

It will be seen from Figures 1 and 2 that at the end of one month 50% of the patients had died with a survival range of 2 days to 17 months. This compares roughly with the median survival of 1.7 months reported by Tivey[1] in 179 cases from the literature, and by Gunz and Hough[9] who found a 1.0 month median survival in 25 cases of their own. Both of these series were computed on a basis of diagnosis to death, as was ours. No other series is strictly comparable because the duration of disease is computed from apparent onset to death. As we can see in Figure 1 the same 179 cases of Tivey computed on this latter basis give a median survival of 3.3 months, and Ellison's[2] cases are, in similar manner, more optimistic. Southam, et. al.[3] reported on 173 cases of acute leukemia of both children and adults, and arrived at a median survival of 3.8 months, based again upon onset to death. Best, Limarzi, and Poncher[4] employed a method of accumulative analysis on a logarithmic time scale, again measuring first symptom to death, and found a median survival of 3.6 months in their 153 cases of acute leukemia in all ages.

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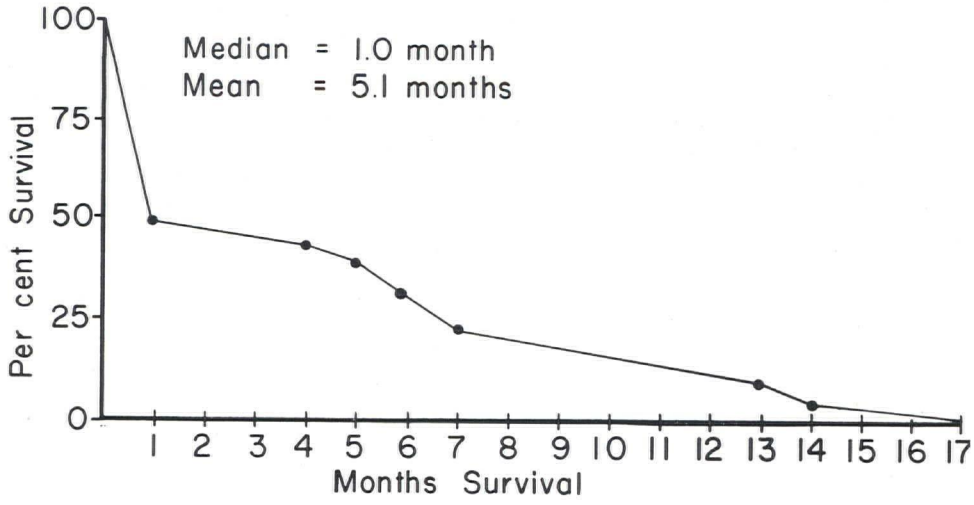

Figure 1

Survival curve in adult acute leukemia, present series. Median survival time is 1.0 month; mean survival time is 5.1 months.

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SURVIVAL DATA

Cases	Source	Treated	Median in Months	Based upon:
179	Tivey[1]	No	3.3	Onset to Death
			1.7	Dx. to Death
94	Ellison[2]	Yes	6.5	Onset to Death
54	"	" (NR)*	4.0	" " "
21	"	" (R)**	11.0	" " "
18	H.F.H. ('57-'60)	Yes	1.0	Dx to Death
	"	" (R)	13.0	" " "

*(NR) = No Remission
**(R) = Remission

Figure 2

Those few cases obtaining any sort of remission in adults are diluted by the fulminating, unresponsive cases. In the present series the remission rate of 22% compares favorably with other series (Figure 3). The four cases having remissions are those whose survival exceeded one year.

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Cases	Source	Remissions	Per Cent
—	Dameshek[8]	—	10—20
94	Ellison[2]	21	22
18	H.F.H.	4	22

Percentage remissions in adult acute leukemia.

Figure 3

Strangely, 16 of the 18 cases under present analysis occurred in males, and conversely, of the 5 cases of acute leukemia evolving from chronic granulocytic leukemia, 3 were women. The size of the respective groups precludes reaching any conclusion from this finding. Previous large series have arrived at a 2.1 ratio for males over females in adult acute leukemia.

Referral to Figure 4 will help clarify the situation with respect to presenting symptoms. Aside from the nonspecific symptoms of weakness, lethargy, and dyspnea (all manifestations of anemia), which occurred in the majority of patients, it will be seen that almost half presented with some form of abnormal bleeding. In most of these cases this consisted of inordinate bruising and/or petechial formation, but unusual bleeding from recent dental extractions, or other mucous membrane bleeding occurred at the onset of disease also. A history of bleeding manifestations, therefore, is the foremost significant clue when this disease is first encountered; and when the symptoms of anemia and fever occur together with bleeding manifestations, the clinician's index of suspicion for acute leukemia should be high. This point is important only because the average case of acute leukemia has no striking lymphadenopathy, hepatosplenomegaly, or other tumefaction, when first seen.

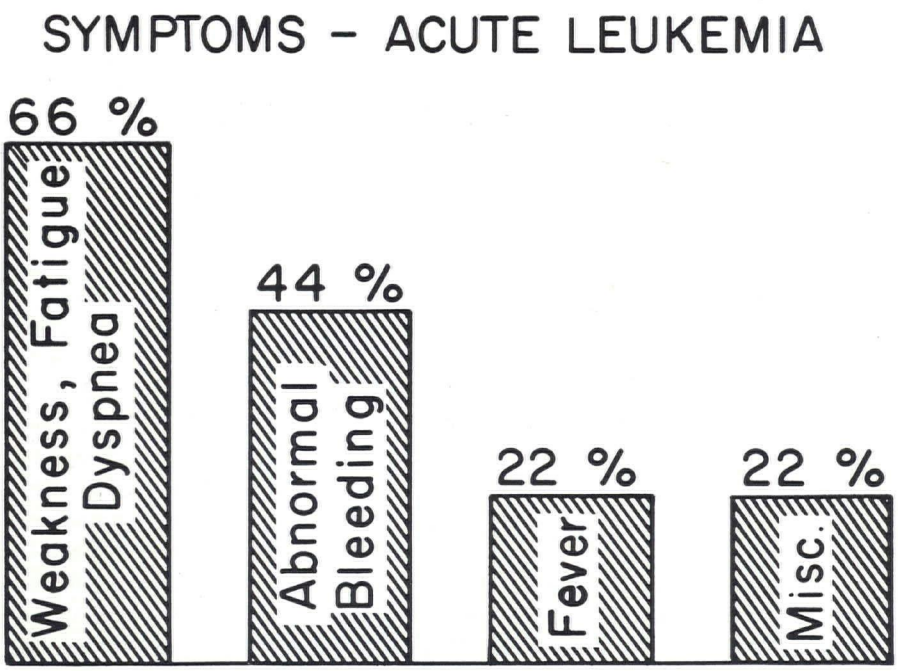

Figure 4

Frequency of symptoms at onset in 18 cases of adult acute leukemia.

Bleeding again plays a prominent role as a major cause of death in acute leukemia (Fig. 5). Sixty-eight per cent of the present series succumbed because of fatal hemorrhage, and 41% had fatal intracranial hemorrhage. Overwhelming sepsis account for 26% of the deaths, and one patient had a fatal myocardial infarct at a time when he was extremely toxic from his primary disease.

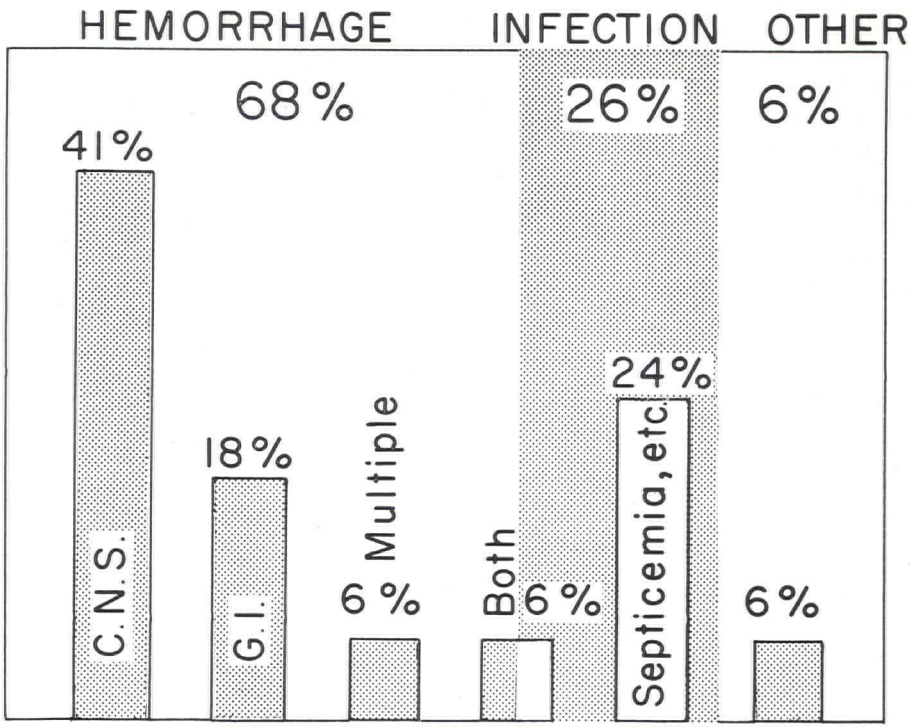

Figure 5
Major cause of death in 17 cases of adult acute leukemia.

DISCUSSION

A. *Prognosis:* In attempting to assess survival in acute leukemia, most authors have fallen into the habit of measuring the duration of disease from apparent onset of symptoms to death. It was not until 1954 that Tivey,[1] reviewing a large number of cases from the literature, stressed the inaccuracy of this method, and urged using the time interval between diagnosis and death. This, of course, shortens the survival considerably (by about one half in Tivey's statistics). Nonetheless, it removes from consideration the uncertain limbo of "preleukemic" states which we know can exist for many months, even years, during which there are recognizable symptoms, but only in retrospect can we surely say that leukemia was evolving. It is true that most cases of acute leukemia present themselves for diagnosis after a period of a month or two of vague non-incapacitating symptoms, but from a practical standpoint it is the period of time after the diagnosis is established that we are interested in, with respect to prognosticating the future and evaluating therapy. Another pitfall to avoid is the use of mean or average survival as a figure to characterize survival in this disease. The survival curve is skewed to the left by the large number of short-lived cases and therefore the median survival figure, which will be considerably shorter than the mean, gives a more accurate picture. McMahon[5,6] stresses this point in recent reviews.

It is apparent from the results of others and those reported herein that the over-all prognosis has not changed appreciably with the advent of antimetabolites and other

chemotherapeutic agents. It is only in the individual case where a remission is induced that a definite prolongation of life can be anticipated, and this happens seldom enough. Nonetheless spontaneous remissions (without chemotherapy) in adults are indeed rare, although well documented instances are reported (Moeshlin),[7] and the present incidence of remissions, (about 20%), is a definite sign of progress.

In general there is no prognostic value in determining the leukemic cell type according to Best, et. al.,[4] who attempted to do this in their 153 cases. If any significant difference occurred, it was that their cases of leukemic reticuloendotheliosis had a slightly better median survival than leukemias due to other cell types. This is in contrast to our impression that leukemic reticuloendotheliosis is extremely resistant to myelotoxic agents and results in rapid clinical deterioration. The present series is too small to draw any concrete conclusion on the basis of cell type. The DiGuglielmo syndrome is said to have a better prognosis than other acute leukemias, and our one case of this type of disease bears this out, in that there was a 13-month survival.

McMahon and Forman[5] have attempted to make prognostic significance out of the degree of leukocytosis when the patient is first seen, stating that the subleukemic cases with normal or neutropenic white blood counts tended to do better than those cases presenting with markedly elevated counts. This would seem to be a somewhat artificial device, for it is not uncommon for the total white counts to swing markedly in either direction in a short period of time with no known extraneous influence, and it would therefore be a matter of chance as to what range the counts were in at the time the diagnosis was established.

There is no ready explanation for the male predominance in adult acute leukemia, and there has never been a prognostic significance in the course of the disease favoring one sex over the other,[3] although it has been said that in childhood leukemia the males do not survive as long.

B. *Clinical Aspects:* The present series stresses the frequency of bleeding symptoms at onset, and the frequency of serious intracranial and gastro-intestinal bleeding terminally, the latter sometimes following upon the former by only a few days. At some time during the course of the disease bleeding can be expected to occur in virtually every case. This is a function of depressed platelet formation, and the deleterious effect that fever and general toxicity have upon vascular integrity. It is not unusual to see bleeding manifestations coincide with toxic relapses while the platelet count remains steady, albeit subnormal.

With regard to the occurrence of infection, it can be said that with or without the harmful effect of our drugs on the bone marrow and reticuloendothelial system, these patients are in a precarious situation. Frequently the infection which occurs is so fulminating in character that prompt treatment is to no avail. Nevertheless we feel that there is nothing to be gained by the use of antibiotics prophylactically. There is no drug with a broad enough spectrum of antibacterial action to protect these patients against the odd or resistant organism which will infect the patient. Therefore we still prefer to treat each infection as it occurs. One of our patients, a 64-year-old male, successfully overcame a bilobar Friedländer's pneumonia while simultaneously acquiring a remission in his acute leukemia, and lived comfortably another 11 months.

C. *Acute Leukemia Evolving from Chronic Granulocytic Leukemia:* In our five cases of chronic granulocytic leukemia, terminating in acute leukemia, there was a uniform lack of response to treatment. The occurrence of this unfortunate phenomenon may intervene at any point in the course of chronic granulocytic leukemia. In our cases the chronic form of the disease had been extant from 4 months to 4 years before the evolution to the acute form. Once having become acute, the range of survival was 1 month to 3.25 months with a median survival of 2 months. Serious bleeding was much less common in this setting, with progressive weakness, weight loss, and general deterioration bringing about the demise. Circulatory failure and pneumonia frequently occurred in the last 48 hours of life.

SUMMARY

1. A review of 18 cases of acute leukemia in adults seen at the Henry Ford Hospital between September 1957 and April 1960 is made.

2. Data on survival and a few salient clinical features are presented.

3. A brief review of the pertinent literature is used for comparison.

4. Data on 5 additional cases of acute leukemia evolving from chronic granulocytic leukemia is also included.

REFERENCES

1. Tivey, H.: Natural history of untreated acute leukemia, Ann. New York Acad. Sc. 60:322, 1954.

2. Ellison, R. R.: Management of acute leukemia in adults, M. Clin. North America 40:743, 1956.

3. Southam, C. M., Craver, L. F., Dargeon, H. W., and Burchenal, J. H.: Study of the natural history of acute leukemia with special reference to the duration of the disease and occurrence of remissions, Cancer 4:39, 1951.

4. Best, W. R., Limarzi, L. R., and Poncher, H. G.: Longevity in leucemia, J. Lab. & Clin. Med. 38:789, 1951.

5. McMahon, B., and Foman, D.: Variation in the duration of survival of patients with acute leukemia, Blood 12:683, 1957.

6. McMahon, B., and Clark, D. W.: Incidence of the common forms of human leukemia, Blood 11:871, 1956.

7. Moeschlin, S.: Subacute Paramyeloblasten-Leukämien mit merfachen längeren Remissionen, Deutches Arch. klin. Med. 191:213, 1943-44.

8. Dameshek, W., and Gunz, F. W.: Leukemia, New York, Grune & Stratton, 1958.

9. Gunz, F. W., and Hough, R. F.: Acute leukemia over the age of fifty; study of its incidence and natural history, Blood 11:882, 1956.