Long Duration of Complete Remissions in Acute Leukemia

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SUMMARY

Reports are presented of 13 cases of acute leukemia in which the patient has survived for more than 4 years. In 12 of these cases, remission was complete for more than 3 years. Seven patients continue in remission and in good general health variously 8 years 6 months, 6 years 7 months (2 patients), 4 years 9 months (2 patients), 4 years 8 months, and 4 years 3 months after the onset of acute leukemia.

The variety of forms observed, the relatively high proportion of myeloblastic leukemias, and the diversity and occasional mildness of the therapy applied are evidence in this series in favor of the intervention of the defense mechanisms of the individual patient.

The existence of such long-term remissions obtained with proved therapy should be taken into consideration in evaluating the effects of new treatments. Hopes of long-term stabilization of acute leukemias no longer appear completely unreasonable. The aim of all therapy of acute leukemia is to increase the number of patients in long-term remission.

Long-lasting acute leukemia presents large variations. The most interesting ones are those where long survival is related to the long duration of a complete remission.

We have collected in Table 1 our personal cases in which a complete remission (generally the 1st, with 1 exception) lasted 3 years or more.

We had hoped to demonstrate some common features explaining the long duration of those remissions but did not succeed. The diversity of symptoms and data is striking.

The patients consisted of 10 children (5 male, 5 female) and 3 adults (1 male, 2 female); there were 9 acute lymphoblastic leukemias and 4 acute myeloblastic leukemias.

The initial treatments varied and, in the 1st case, consisted solely of large blood transfusions (10 liters within a few days). (As we showed with M. Bessis in 1947, in the era before chemotherapy, exsanguination transfusion is itself able to promote the complete remission of acute leukemia).

The same diversity in maintenance treatments is to be noted: no maintenance treatment in Case 12; amethopterin in the 2nd complete remission of Cases 8, 9, and 11, and in the 3rd and 4th complete remissions of Case 13; 6-mercaptopurine in the other patients.

This diversity is not disappointing. It suggests the presence of an additional common factor responsible, in the various cases, for the duration of the remission. It seems likely that this particular factor has to be looked for among the cases in which leukemic cells are not evident during remission.

In these cases one must postulate the existence of quiescent, silent leukemic cells—of leukemic cells without leukemia.

Nothing is known about these cells. We do not know their number (certainly a small one), their morphology (perhaps stem cells without any distinguishing feature), or their localizations (whether in hematopoietic organs, nervous system, or lymph nodes) or whether these quiescent cells are fixed in one place or, although dormant, are still able to move. We do not know whether they are completely quiescent or whether they continue slowly to proliferate. Do some general or local factors play an essential role in this respect? One may imagine the surviving leukemic cells imprisoned in some area, the nervous system for instance, without any permanent relation with other parts of the organism. It is also conceivable that the main factor is the number of leukemic cells that remain at the end of treatment rather than environment. There may also be an unintentional causal effect of the treatment, for instance in destroying a very large number of viral particles together with the leukemic cells.

These explanations remain entirely hypothetical. But the role played by the general environment has an importance that has been demonstrated: in certain cases an exchange transfusion can bring about complete remission of an acute leukemia. The change of the medium in which the leukemic cells live, therefore, alone has great influence upon the cells themselves.

These are very difficult areas of research, but their investigation probably has great importance for the whole study of cancer.

TABLE 1

THIRTEEN CASES OF VERY LONG COMPLETE REMISSION IN ACUTE LEUKEMIA

During remission 6-mercaptopurine, 2.5 mg/kg/day, was given p.o. to all patients except No. 12, who received no maintenance therapy.

CASE NO.	AGE (yr)	SEX	CYTOLOGIC TYPE	FIRST INDUCTION TREATMENT		DURATION OF COMPLETE REMISSION	DURATION OF THE ACUTE LEUKEMIA
				Agent	mg/kg /day		
1	4	F	Lymphoblastic	Prednisone	1	8 yr 3 mo	Living (8 yr 6 mo)
2	4.5	F	Lymphoblastic	Prednisone	3	6 yr 2 mo	Living (6 yr 7 mo)
3	8.5	M	Lymphoblastic	Prednisone	1	6 yr 5 mo	Living (6 yr 7 mo)
				6-Mercaptopurine	2.5		
4	22	F	Lymphoblastic	Prednisone	3	4 yr 8 mo	Living (4 yr 9 mo)
5	9	F	Lymphoblastic	Prednisone	3	4 yr 8 mo	Living (4 yr 9 mo)
				6-Mercaptopurine	2.5		
6	46	M	Myeloblastic	Prednisone	3	4 yr 7 mo	Living (4 yr 8 mo)
				A-methopterine	0.1		
7	3	F	Lymphoblastic	Prednisone	3	3 yr 11 mo	Living (4 yr 3 mo)
8	25	F	Myeloblastic	Prednisone	3	1st— 4 yr 9 mo	5 yr 6 mo
				6-Mercaptopurine	2.5	2nd—8 mo	
9	7	M	Myeloblastic	Prednisone	3	1st— 3 yr 9 mo	4 yr 9 mo
						2nd—10 mo	
10	5	M	Lymphoblastic	Prednisone	3	1st— 3 yr 10 mo	4 yr 6 mo
						2nd—7 mo	
11	9	M	Lymphoblastic	Prednisone	3	1st— 3 yr 6 mo	4 yr
						2nd—5 mo	
12	19	M	Myeloblastic	Blood transfusion		1st— 3 yr 10 mo	4 yr
13	2.5	F	Lymphoblastic	Prednisone	3	1st— 1 yr	
						2nd—6 mo	
						3rd—3 yr	5 yr 6 mo
						4th—8 mo	