

Chronic Myelomonocytic Leukaemia

A Case Report

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SUMMARY

A case of chronic myelomonocytic leukaemia and its therapy are reported, and the response to the new agent, VP 16-213, is indicated.

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Since 1913, when acute monocytic leukaemia was described by Reschad and Schilling-Torgau,¹ the entity has become well accepted by haematologists, and the existence of a subacute or chronic form is now also accepted. In the majority of cases there appears to be a well-defined preleukaemic phase of refractory megaloblastic anaemia, or persistent monocytosis, or both.

The intravenous epipodophyllotoxin, VP 16-213, has been used in the treatment of myelomonocytic leukaemia with encouraging results, and it seems that this agent is particularly effective against cells of the monocytoid series.²

It is the purpose of this paper to record a patient with chronic myelomonocytic leukaemia, and to document his favourable response to treatment with VP 16-213 as the only form of therapy.

CASE REPORT

A 67-year-old White man presented in February 1975 with symptoms of anaemia of some 6 months' duration, and angina pectoris precipitated by his anaemia.

Examination revealed that he had anaemia and a soft ejection systolic murmur, that the haemoglobin concentration was 6 g/100 ml with a mean corpuscular volume of 119 μm^3 , and that there was electrocardiographic evidence of ischaemic heart disease. Bone marrow aspirate and trephine biopsy showed granulocytic hyperplasia with an increase in monocytes and promonocytes. There was also megaloblastic change in the marrow. Serum B₁₂ and folic acid levels were normal. The patient was given a blood transfusion and was followed up. He was given no specific therapy, but required frequent transfusions with packed red cells.

A repeat bone marrow examination 6 months later in August showed an elevated monocyte count, and the cells were positive for alpha-naphthyl acetate esterase. Serum muramidase was 900 mg/ml and urine mura-

midase 800 mg/ml. The patient continued to receive regular transfusions. A splenectomy in September 1975 showed the splenic cords to be widened and infiltrated with mononuclear cells with indented nuclei. In December 1975 administration of intravenous VP 16-213 began with a dose of 60 mg/m² body surface for 5 days. This led to an immediate fall in the white cell count from 25 000/ μl to 6 700/ μl , accompanied by a fall in the absolute monocyte count. The relative monocytosis remained, while serum and urine muramidase fell rapidly to normal levels.

Since April 1976 he has been treated with oral VP 16-213 in doses of 120 mg/m² body surface daily for 5 days. The rest periods between treatment have been extended from 2 to 5 weeks. He has remained well, but requires intermittent transfusion. Withdrawal of the VP 16-213 therapy leads to a prompt rise in the monocyte count and a drop in the haemoglobin value. His platelet count has always remained within normal limits. His marrow blast count has varied between 7% and 13%. Blasts have not been observed in the peripheral blood. His only untoward symptom has been a partial loss of hair.

DISCUSSION

There is considerable variation in the nomenclature of cases such as this, and they have been variously called preleukaemia,³ subacute myelomonocytic leukaemia,⁴ chronic myelomonocytic leukaemia,⁵ smouldering acute leukaemia⁶ and chronic monocytic leukaemia.⁷ It seems that this illness represents part of a spectrum with preleukaemic monocytosis at one end, and frank acute monocytic leukaemia at the other. In Saarni and Linman's⁷ series of 34 patients with preleukaemia, 10 had an absolute monocytosis during their illness. A further 5 patients had a relative monocytosis from 9% to 40%. Saarni and Linman⁷ concluded that monocytosis is a common and important preleukaemic manifestation, although none of the marrow specimens was involved by the monocytosis. Nine of the 34 patients had 'a slight increase' in blasts.

Sinn and Dick⁸ reviewed 14 cases of chronic monocytic leukaemia and added 8 of their own. For inclusion in their series, it was required that patients should have had the disease for longer than 1 year, or that there should have been no evidence of acute leukaemia in the marrow at the time of diagnosis. They also included in their series those in whom the disease was of less than 1 year's duration, and in whom there were never any haematological changes of acute leukaemia in blood or marrow, and in whom death appeared to occur prematurely as a result of secondary complications such as infection. Many of their patients had lymphadenopathy, and/or buccal ulceration and gingival hypertrophy. Only

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3 of the patients were less than 40 years of age, and the length of survival was between 12 and 43 months. Pearson and Diamond⁷ have described a case in a child. Their first patient, however, appears to have had an acute myelomonocytic leukaemia with a remittent course. Their second patient was more like those reviewed by Sinn and Dick,⁸ in spite of the finding of peripheral blasts early in the course of the disease; his marrow specimens repeatedly failed to demonstrate malignant change.

In only 3 of the patients reviewed by Sinn and Dick⁸ was there an appreciable monocytosis over an extended period of time. Of the 22 patients with chronic monocytic leukaemia, 9 seemed to be preleukaemic and 8 others had aleukaemic leukaemia. In most of the patients, leucocytosis and monocytosis typical of acute leukaemia were noted during the terminal period. In a few, leucopenia persisted until death. Seligsohn and Ramot⁹ have described a patient who survived for 8 years. However, 78 months of this course were preleukaemic and 20 months were leukaemic.

The French-American-British (FAB) Co-operative Group¹⁰ has recently classified the leukaemias, and recognizes chronic myelomonocytic leukaemia. The monocytic count is at some stage of the disease higher than $1 \times 10^9/l$, and the monocytes often appear atypical. The absolute neutrophil count is variable. Blasts and promonocytes are rarely present, and the neutrophils may show the same abnormalities as in refractory anaemia with excess of blasts. The bone marrow is hypercellular, and usually shows an increase of up to 30% in myeloblasts and promyelocytes. There is also an increase in promonocytes and monocytes, but cytochemical staining may be necessary for identification. Serum lysozyme concentrations are raised in chronic myelomonocytic leukaemia, but not in refractory anaemia with excess of blasts.

CONCLUSION

There is clearly no uniformity of opinion about what has been described as preleukaemia, subacute myelomonocytic, chronic myelomonocytic, smouldering subacute leukaemia, and chronic monocytic leukaemia. We would suggest that

the term 'preleukaemia' be restricted to those patients with an unexplained monocytosis who subsequently appear to develop acute leukaemia, but in whom there were no signs of leukaemia at diagnosis. In view of the fact that there is usually an increase in marrow myeloblasts in those patients with a peripheral blood and marrow monocytosis, their condition should be termed chronic myelomonocytic leukaemia, as suggested by the French-American-British Co-operative Group.

Saarni and Linman³ concluded that the preleukaemic syndrome should not be treated until there is evidence of haematological malignancy since it may in rare instances extend for up to 20 years. In other patients, the condition of the bone marrow may appear to be more malignant than the peripheral blood would indicate, but they may have a prolonged survival. Some patients have an acute terminal phase which resembles myelomonocytic leukaemia.

Geary *et al.*⁵ have felt that these patients are probably best managed without intensive therapy. In view of this, we have treated our patient with VP 16-213 with good results. We have not made any attempt to render his marrow hypoplastic. Withdrawal of the VP 16-213 leads to an increase in monocytes, elevation of serum and urine lysozyme, and an excessive fall in the haemoglobin value. The only untoward effect we have observed has been a partial loss of hair. We feel that oral VP 16-213 may be the drug of choice in the therapy of this condition.

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