Chronic lymphatic leukaemia terminating as erythroleukaemia

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Summary
Terminal development of acute leukaemia in chronic lymphatic leukaemia is well recognized but often difficult to classify. A case with an unequivocal erythroblastic termination is described, occurring after 18 months' treatment with chlorambucil.

Introduction
Chronic lymphatic leukaemia has terminated in blast cell crisis and has been reported increasingly. Both lymphoblastic and myeloblastic terminations occur and the subject has recently been reviewed (Zarrabi, Grünwald and Rosner, 1977). The authors now report a case of chronic lymphatic leukaemia terminating in erythroleukaemia.

Case report
A 67-year-old man presented in May 1978 with malaise and splenomegaly. Initial blood count showed haemoglobin 12·1 g/dl, total white cell count 25·7 x 10^9/l (polymorphs 5%, lymphocytes 93%, eosinophils 2%), platelet count 98 x 10^9/l. Bone marrow examination showed a 66% infiltration by mature lymphocytes. Haematopoiesis otherwise was morphologically normal. A diagnosis of chronic lymphatic leukaemia (Fig. 1) was made and chemotherapy started with chlorambucil 4 mg daily. Splenomegaly regressed on treatment and he remained on chlorambucil until April 1979 and recommenced therapy in October 1979.

In March, 1980, he was admitted to hospital complaining of tiredness and dizziness associated with dyspnoea, and occasional night sweats. On examination he was anaemic and in congestive cardiac failure. There was no lymphadenopathy but hepatosplenomegaly (liver 5 cm, spleen 6 cm) was present. Haematological findings included Hb 3·9 g/dl, total white count 2·0 x 10^9/l (6% polymorphs, 90% lymphocytes, 4% monocytes, occasional nucleated red cell), platelet count 15 x 10^9/l, reticulocytes 1%. Bone marrow aspiration showed erythroid hyperplasia and gross dysplasia and multi-nucleate forms (Fig. 2). Myeloblasts comprised 6% of nucleated cells. Normal haematopoiesis was markedly reduced.

FIG. 1. Peripheral blood film (May-Grünwald-Giemsa, x 1200). Chronic lymphatic leukaemia; lymphocytosis with few smear cells.
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PAS stains showed strong block and stippled erythroblast cytoplasmic positivity. Ring sideroblasts were not present. Bone marrow biopsy confirmed the hypercellularity and showed areas of well differentiated lymphoid cells with contrasting areas of predominantly immature erythroblasts with numerous mitotic figures and marked dysplastic features (Fig. 3). Normal haematopoiesis was virtually absent. Direct Coombs' test was negative.

![Fig. 2. Bone marrow aspirate (May-Grünwald-Giemsa, x1200). Erythroid hyperplasia with marked dyserythropoietic features.](image1)

![Fig. 3. Bone marrow trephine biopsy (HE, x500) showing well demarcated zones of mature lymphocytic infiltration and areas of primitive and bizarre erythroid precursors.](image2)

Discussion

Chronic lymphatic leukaemia terminating in acute leukaemia was reviewed by Zarrabi et al. (1977) who noted that the association was seen in both sexes and that the mean age at the diagnosis of chronic lymphatic leukaemia was 65 years. The acute leukaemia was either lymphoblastic or myeloblastic. Although in most of the reported cases the patient had received either chemotherapy, radiotherapy or both treatment modalities, 2 reported cases received no treatment at all and developed acute leukaemia. This suggests that acute transformation may be a part of the natural history of chronic lymphatic leukaemia as is the case in chronic granulocytic leukaemia.

In the present case report, the patient developed an acute dyscrasia after 2 years of chronic lymphatic leukaemia and after 18 months of chlorambucil therapy. This dyscrasia presented as a pancytopenia and the marrow morphology was diagnostic of erythroleukaemia with bizarre erythroid precursors and

There was a marked immune paresis affecting all Ig classes. A diagnosis of erythroleukaemia developing in chronic lymphatic leukaemia was made. He was treated with blood transfusions but died 2 months after presentation in a cachectic state with terminal haemorrhage. Post-mortem was not performed.
strong positivity. While the cytological typing of the acute leukaemia that develops in chronic lymphatic leukaemia may present a problem (Zarrabi, Rosner and Grünwald, 1979), in this case the bone marrow morphology was entirely distinct. While erythroblastic transformation is well recognized in myeloproliferative disorders (Rosenthal, Canellos and Grabruck, 1977; Scott, Ellison and Ley, 1964; Srodes, Hyde and Boggs, 1973; Bank, Larsen and Anderson, 1966; Dammert and Kaipainen, 1960), erythroleukaemia occurring in lymphoproliferations is rare but has occasionally been reported (Durant and Tassoni, 1967; Forbes, 1972; Cardamone, Kimmere and Marshall, 1974). The incrimination of chlorambucil therapy in the causation of malignancy remains difficult to establish in individual cases but has been demonstrated in certain patient groups (Berk et al., 1981; Rosner and Grünwald, 1974, 1975; Carey, Holland and Sheene, 1967; Goldhirsh et al., 1980). It remains an attractive explanation to the present case where clearly an acute, non-lymphoid dyscrasia had developed in chronic lymphatic leukaemia.

References
Scott, R.R., Ellison, R.R. & Ley, A.B. (1964) A clinical study of 20 cases of erythroleukemia (Diguglielmo’s d.). American Journal of Medicine, 37, 162.