caemia" is consistently produced after a 12-hour fast irrespective of the time of day.

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Simultaneous Occurrence of Acute Myeloblastic Leukaemia and Multiple Myeloma without Previous Chemotherapy

THOMAS TURSZ, GEORGES FLANDRIN, JEAN-CLAUDE BROUET, JEAN BRIERE, MAXIME SELIGMANN

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Summary

The simultaneous detection of multiple myeloma and acute myeloblastic leukaemia is reported in two patients who had not undergone chemotherapy. Histological examinations confirmed the infiltration by both myeloblasts and plasma cells. Only the latter contained monoclonal immunoglobulin chains at immunofluorescent studies. The possible relation between the two distinct proliferative processes is briefly discussed.

Introduction

The occurrence of acute myelomonocytic leukaemia or of acute myeloblastic leukaemia (A.M.L.) supervening on multiple myeloma (M.M.) (Kyle *et al.*, 1970; *Lancet*, 1971) has now been recognized in about 30 patients who had undergone long-term chemotherapy with alkylating agents. The simultaneous detection of both M.M. and A.M.L. in previously untreated patients has not yet been described. It is thus of interest to report two such cases.

Case 1

A 77-year-old man was referred for a pancytopenia which had been discovered three years earlier. Physical examination showed nothing abnormal. Haemoglobin was 10 g/100 ml; W.B.C. was 2,000/mm³ of which 44% were neutrophils and 55% were lymphocytes; the platelet count was 80,000/mm³. Bone marrow smears were hypercellular with 51% of peroxidase-positive myeloblastic cells and 23% of grossly dystrophic plasma cells. This picture was consistent with both M.M. and A.M.L.

The serum electrophoretic pattern showed a narrow spike (1 g/100 ml) which was identified as a monoclonal IgA 1 $\times$ on immunoelectrophoresis. The levels of IgG and IgM were greatly decreased. There was no proteinuria. The skeletal survey was normal.

The immunofluorescence study of the marrow cells with antisera to the various immunoglobulin chains showed that all the plasma cells contained alpha and kappa chains whereas the myeloblastic cells were negative for intracytoplasmic and membrane-bound immunoglobulins.

Postmortem examination showed a striking infiltration of the bone marrow and of the spleen by myeloblasts and plasma cells.

Case 2

A 74-year-old man had had a mild pancytopenia since 1967. Extensive haematological studies were performed in 1971. At that time physical examination showed nothing abnormal except a generalized purpura. Haemoglobin was 11 g/100 ml; W.B.C. was 1800/mm³ of which 48% were neutrophils and 32% were lymphocytes; the platelet count was 60,000/mm³. Bone marrow smears were hypercellular with 51% of peroxidase-positive myeloblasts and 15% of plasma cells. A marrow biopsy showed an extensive invasion by both myeloblastic and plasma cells.

Serum electrophoresis disclosed a narrow spike (2.5 g/100 ml) which was identified on immunoelectrophoresis as a monoclonal IgG λ . The levels of polyclonal IgG, IgM, and IgA were very low. There was no proteinuria. Skeletal x-ray examination showed a mild osteoporosis. All plasma cells were shown to be strongly positive with antisera to gamma and lambda chains by intracytoplasmic immunofluorescence study whereas the myeloblastic cells were negative. Despite therapy with mercaptopurine the patient died a few months later. Necropsy was not performed.

Discussion

All previously reported patients in whom A.M.L. supervened on M.M. had been treated for 14 months to eight years with alkylating agents, mostly with melphalan. Many of these patients had also received local radiotherapy. A single patient reported by Videbaek (1971) had not been treated, but the diagnosis of A.M.L. seems very doubtful since the "blastic" cells were shown by immunofluorescence to contain immunoglobulin chains and were thus probably immature cells of plasmacytic origin, similar to those found in the patient reported by Thijs *et al.* (1970).

The leukaemogenic role of long-term chemotherapy is ruled out in our two patients. Other hypotheses should therefore be raised to explain the occurrence of both A.M.L. and M.M., and possibly the prolonged survival induced by therapy in M.M. patients may offer the opportunity to observe hitherto unrecognized aspects of the natural history of M.M. The humoral immune defect in myeloma may facilitate the emergence of other neoplastic clones. A common aetiological agent could be

Institut de Recherches sur les Maladies du Sang, Hôpital Saint-Louis, 75475 Paris

THOMAS TURSZ, M.D., Interne des Hôpitaux
GEORGES FLANDRIN, M.D., Chef de Travaux Assistant
JEAN-CLAUDE BROUET, M.D., Chef de Clinique Assistant
JEAN BRIERE, M.D., Chef de Clinique Assistant
MAXIME SELIGMANN, M.D., Professeur d'Immunologie

responsible for the development of both proliferations since the occurrence of myelomonocytic leukaemia has been noted by Warner *et al.* (1969) in BALB/c mice after intraperitoneal injection of mineral oil, a stimulus usually leading to plasma-cell tumours. Osserman (1967) stressed the possibility that the chronic stimulation of the reticuloendothelial system may lead to the development of both monocytic and plasmacytic dyscrasias. Though many cases of acute leukaemia supervening on M.M. were labelled as "myelomonocytic" leukaemia, it is worth noting that though lysozyme levels were not studied our two patients apparently had true A.M.L.

Khaleeli *et al.* (1973) recently described four patients with M.M. who developed sideroblastic anaemia several months before the occurrence of acute leukaemia. It is interesting, therefore, to note that a pancytopenia was found in both our patients three to four years before diagnosis. In two other patients with M.M. we found an unusual myeloid hyperplasia with splenomegaly and 30,000-50,000 white blood cells with 90-95% of mature neutrophils. In one of these patients acute leukaemia developed four years later after treatment with melphalan.

The relation between M.M. and A.M.L., which involve distinct cell lines, remains puzzling. Long-term chemotherapy may have only a triggering role in patients with M.M. and some kind of pre-leukaemia state.

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PRELIMINARY COMMUNICATION

T-lymphoblastic Leukaemia: A Distinct Variant of Acute Leukaemia

D. CATOVSKY, J. M. GOLDMAN, A. OKOS,
B. FRISCH, D. A. G. GALTON

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Summary

Two cases of acute lymphoblastic leukaemia (A.L.L.) of T-cell type are reported. Clinically they were characterized by very high peripheral blood blast cell counts at presentation, the early development of meningeal leukaemia, and relative resistance to treatment with combination chemotherapy. Leukaemic cells from both patients lacked all the B-cell markers investigated, but 60-65% of their cells formed rosettes with sheep red cells. Cytochemical and surface structure studies helped to define additional features of these cells and confirmed their T-cell nature.

It seems that this variant of A.L.L. may not be uncommon and that it can be distinguished on clinical and immunological grounds from the usual type of A.L.L. which runs a less aggressive course and lacks B- or T-cell markers.

Introduction

The improvement in rate of remission and survival in acute ("childhood") lymphoblastic leukaemia (A.L.L.) (Spiers, 1972 a)

is the major factor that has led to a more optimistic approach to A.L.L., which is still considered to be a homogeneous disease. Certain "bad-risk" cases are now recognized, however. For example, patients who have high blast cell counts, organomegaly, or marked thrombocytopenia at presentation fare relatively badly and also have a higher risk of developing meningeal leukaemia (Pavlovsky *et al.*, 1973). It has been suggested that patients with large blast cells (macroblasts) may obtain little benefit from immunotherapy (Mathé *et al.*, 1971), but morphological features are highly subjective and agreement between different centres is poor. A classification based on more objective criteria would be extremely valuable if specific cellular features could be shown to correlate with prognosis. In recent years markers for lymphoid cell differentiation have been used in the study of lymphoproliferative disorders. Though most cells from patients with A.L.L. seem to lack the surface markers for B and T lymphocytes (Lay *et al.*, 1971; Smith *et al.*, 1973 a) evidence is now accumulating that a significant minority may in fact be of T-cell type (Seligmann *et al.*, 1973; Borella and Senn, 1973; Kersey *et al.*, 1973; McCaffrey *et al.*, 1973). Furthermore, it has been suggested that the T-cell form of the disease is more aggressive (Borella and Sen, 1973). We studied two further cases of T-lymphoblastic leukaemia in which its aggressive clinical course, in contrast to the usual type of A.L.L., was clearly shown.

We report here the results of these studies because we believe that the immunological tests described should be applied to all new cases of A.L.L. The recognition of the T-lymphocyte origin of a proportion of cases of A.L.L. seems to have important therapeutic implications, but its true incidence cannot be assessed until a much larger series of patients has been studied.

Case 1

A 14-year-old boy was admitted to Hammersmith Hospital in December 1973 with a two-week history of spontaneous bruising. He had a petechial rash distributed symmetrically over the anterior aspect of the trunk. The spleen was palpable 6 cm below the costal margin, but the liver was not enlarged. There was no clinical or radiological evidence of mediastinal enlargement. The peripheral blood showed a haemoglobin of 10.1 g/100 ml, total leucocytes 1,004,000/ μ l and platelets 52,000/ μ l. The differential count showed 95% blast cells with nuclear chromatin aggregation suggestive of lymphocytic differentiation (fig. 1). The bone marrow

M.R.C. Leukaemia Unit and Department of Haematology, Royal Postgraduate Medical School, London W12 0HS

D. CATOVSKY, M.D., Lecturer in Haematology
 J. M. GOLDMAN, B.M., M.R.C.P., Honorary Consultant Physician
 A. OKOS, M.D., Research Fellow
 B. FRISCH M.D., Research Fellow
 D. A. G. GALTON, M.D., F.R.C.P., Director of M.R.C. Unit