DISCUSSION

The gross and histopathological features as well as the site of the soft-tissue lesion deep to the scapula were consistent with the diagnosis of elastofibroma dorsi. As yet, the only other site reported has been in the region of the deltoid muscle.[3] One should always be aware of this condition, since it may be incorrectly diagnosed clinically as a sarcoma.[4] However, elastofibroma never behaves like an aggressive neoplasm and lacks the morphological appearance of one. The natural history suggests a benign lesion apparently associated with a reactive or degenerative process.[5,6] Mackenzie *et al.*[7] have reported that these lesions may result from trauma, which appears to have been the case in the patient described, since there was a definite association of underlying trauma in the development of the lesion. Local excision seems to be adequate treatment.

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Hodgkin's Disease and Acute Promyelocytic Leukaemia

A Case Report

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SUMMARY

A case of Hodgkin's disease is reported in which acute promyelocytic leukaemia developed within 5 months of initiation of chemotherapy. Only 3 other cases, possibly of a similar nature, were found in the literature; these had occurred 15, 77, and 226 months respectively after the initial diagnosis of Hodgkin's disease.

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During the past 6 years it has become increasingly apparent that patients with Hodgkin's disease (HD), especially those treated with both high-level radiation and intensive chemotherapy, have a greatly increased risk of developing leukaemia. Coleman *et al.*[1] reported an incidence of nearly 4% in those patients treated with combination radiation and chemotherapy; the overall incidence was only 2%. It has been suggested that the leukaemia may be a part of the natural history of HD, seen more often now because of improved survival; or that it is a complication of aggressive therapy.[1-3] The latent period from the diagnosis of HD to the diagnosis of acute non-lymphocytic leukaemia (ANLL) ranged from 8 months to 19 years.[4,5] In cases in which the leukaemia was diagnosed within 6 months of the diagnosis of HD, the leukaemia has been regarded as co-incidental, probably not secondary to HD or to its therapy.[4]

One hundred and sixteen patients with HD were treated at Tygerberg Hospital between 1970 and 1979; 1 of these

patients developed acute promyelocytic leukaemia (APL). It is the purpose of this article to report the development of acute APL and diffuse intravascular coagulation within 5 months of initiating chemotherapy in a patient with HD.

CASE REPORT

A 33-year-old man was admitted in October 1978 with symptoms of fever, loss of weight and enlarged left axillary lymph nodes. Two years previously he had sustained an injury to the left arm; a swelling subsequently developed medially to the elbow. One month before admission he noticed swelling of the left pectoral area and enlargement of the lymph nodes in the left axilla (Fig. 1). These increased progressively, fever and sweating ensued, and he lost 7 kg in weight. The spleen was palpable 12 cm below the costal margin. The liver was not enlarged. Biopsy of the elbow mass showed a subacute abscess, while histological examination of the axillary lymph nodes revealed HD (nodular sclerosing type). Several Reed-Sternberg cells were present (Fig. 2). The haematocrit was 30% and the white cell count was 24×10^9/l with 85% neutrophils, 13% lymphocytes and 2% eosinophils. The platelet count was 220×10^9/l and the reticulocyte count 80×10^9/l. The blood smear showed normochromic, normocytic red blood cells. Blood urea and electrolyte values and liver function were normal. Staging trephine biopsy of the bone marrow revealed no signs of HD, and aspiration showed the marrow to be normal and active. The patient was regarded as having clinical stage IIIb HD.

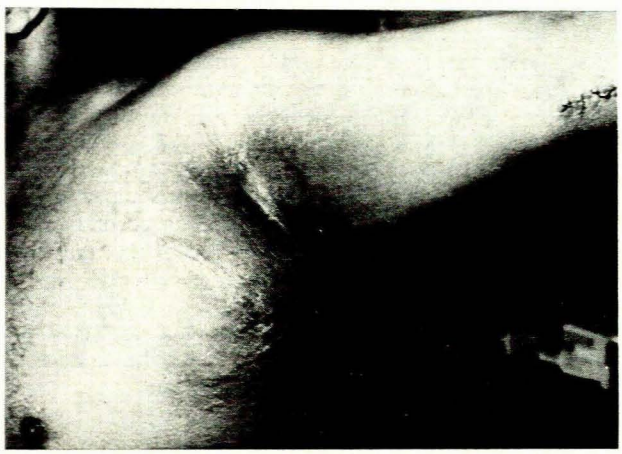

Fig. 1. Photograph of left axilla demonstrating massively enlarged lymph nodes.

Treatment was commenced. Five courses of nitrogen mustard, vinblastine, procarbazine and prednisone were administered from November 1978 to March 1979. The haematocrit and the white cell count returned to normal. The serum copper value, initially 38 μmol/l, reverted to normal levels and the 12 cm enlarged spleen shrank to 2 cm below the costal margin.

Five months after initiation of therapy the patient returned to the hospital because of persistent severe epistaxis. No rash or peripheral lymphadenopathy was found, and the liver and spleen were normal in size. The heart and lungs were normal. No enlargement of the mediastinal lymph nodes was seen on chest radiographs. The haematocrit was 20%, the platelet count 30×10^9/l and the white cell count $5{,}3 \times 10^9$/l. The red blood cells were normochromic with numerous fragmented red blood cells observed on the smear. Only a few platelets were visible. The granulocyte series was shifted to the left with 5% promyelocytes. Bone marrow aspiration and biopsy disclosed myeloid hyperplasia with suppression of erythropoiesis. The predominant cell (42%) was an atypical promyelocyte (Fig. 3), containing numerous Auer body-like inclusions, and the megakaryocytes were reduced in number. The appearance was consistent with APL.

Plasma and urine muramidase levels were within normal limits. The bleeding time was 14 minutes (normal 0 - 7 minutes), prothrombin activity 23% (normal 70 - 120%), the prothrombin ratio 1,62 (normal 1,0 - 1,3), and the

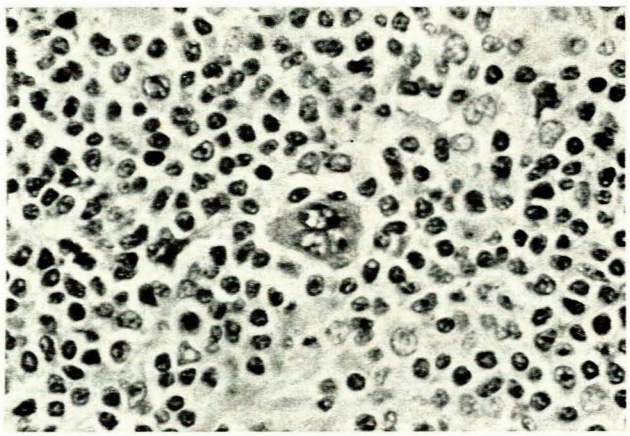

Fig. 2. Lymph node biopsy showing nodular sclerosing type HD (H and E × 400).

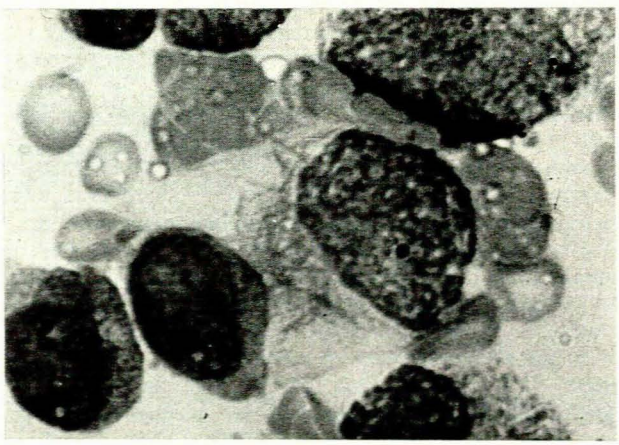

Fig. 3. Photomicrograph of bone marrow showing densely staining granules and crystalline inclusions in cells of the myeloid series. The predominant cells are atypical promyelocytes (May-Grünwald-Giemsa × 1 000).

partial thromboplastin time 35,5 s (normal 25 - 45 s). Other biochemical values were fibrinogen 570 mg/dl (normal 200 - 400 mg/dl) and fibrinogen degradation products 40 μg/ml (normal less than 10 μg/ml); the fibrinogen monomer test was positive (ethanol gelation test). The picture was consistent with diffuse intravascular coagulation.

Fresh-frozen plasma, single donor platelets and thawed frozen red blood cells were transfused. Adriamycin, arabinoside C, and a continuous intravenous infusion of heparin 6 000 U/24 h were commenced, reverse barrier nursing procedures were initiated, and intravenous cephalosporin, aminoglycoside and oral co-trimoxazole were administered. Two days after admission the patient became comatose, developed neck stiffness and decerebrate rigidity, and died. Autopsy was refused.

In summary, the patient suffered from HD and developed APL with diffuse intravascular coagulation within 5 months of beginning chemotherapy.

DISCUSSION

The term 'acute promyelocytic leukaemia' describes a special type of acute non-lymphocytic leukaemia characterized by severe bleeding manifestations which are frequently fatal. Atypical promyelocytes are present in the peripheral blood and bone marrow and contain large azurophilic granules. Thrombocytopenia and abnormal clotting tests reflect disseminated intravascular coagulation.[6] APL probably represents 6% of all cases of acute leukaemia or 13% of all cases of ANLL.[7,8]

Acute leukaemia has been reported to be the terminal event in more than 100 patients with HD.[1,2,4,5,9] The estimated incidence of leukaemia in treated HD patients is about 1%.[4] Only 1 of 116 patients treated at Tygerberg Hospital developed ANLL.

The mean interval from the diagnosis of the HD to the occurrence of ANLL in reported cases was 6,5 years,[2] with a range of 8 months - 19 years.[5] Although all patients had acute myelocytic leukaemia or one of its variants, the term 'acute promyelocytic leukaemia' was not used. APL rarely presents as a terminal event following another haematological disorder.[10]

Newman *et al.*[11] reported 2 patients who developed acute myelomonocytic leukaemia 18 years 10 months and 15 months after the onset of HD. Both had received radiotherapy. One of them was without complaints when a routine check-up revealed thrombocytopenia and 63% blast cells in the peripheral blood. The bone marrow aspirate was hypercellular, with a decrease in erythropoiesis and 80% promyelocytes. Ten per cent of the granulocyte series were blasts with frequent Auer bodies. No megakaryocytes were present in the specimen. The patient died 1 month later owing to progression of the disease, which was complicated by a bleeding gastric ulcer, haematuria, ecchymosis and neurological involvement. Although this was regarded as acute myelomonocytic leukaemia, the symptoms could well have been those of APL also. Newman's second patient presented with anaemia, leucopenia, purpura and haematuria 15 months after HD had been diagnosed. The bone marrow aspirate was hypercellular, and the predominant cell was an atypical promyelocyte, sometimes containing 40 - 50 Auer bodies. The patient died of intracerebral haemorrhage, and the case appeared to be a typical one of APL.

In a comprehensive review of 74 cases Rosner and Grünwald[2] reported 8 patients treated by themselves who had HD and acute leukaemia. Of these, patient 7, who is described as having a nodular sclerosing type of HD, had received radiotherapy initially, followed 6 years later by 3 courses of nitrogen mustard, vinblastine, procarbazine and prednisone. Five months later she developed aplastic anaemia, and chemotherapy was discontinued. One month later the bone marrow showed leukaemia with hypercellularity and 18% blast cells and 80% promyelocytes. She died of a cerebral haemorrhage. The authors did not find any Auer bodies and did not discuss APL.

These are the only possible cases we found in the English literature till 1979, after consulting the computerized MEDLARS request facilities of the South African Medical Research Council. The acute leukaemia occurred a considerable time after initiation of therapy. Chlorambucil, used as maintenance therapy in the treatment of HD, was proved to initiate acute leukaemia.[12] Nitrogen mustard and procarbazine may also contribute. Cadman *et al.*[4] presented a critical analysis of 109 cases reported in the world literature until March 1976, and proposed that when the leukaemia was diagnosed within 6 months of the diagnosis of HD, it should be considered to be coincidental, and probably not due to the HD therapy.

In our patient the occurrence was not simultaneous, since the bone marrow was normal at the time of diagnosis of HD.

The relationship between HD and acute leukaemia remains unclear. There are no apparent characteristics of HD which predict which patients will develop ANLL. In all of the well-documented cases the patients had received either radiation or chemotherapy or both.

It appears that HD does not evolve into acute leukaemia, but rather that ANLL develops as a second malignancy in these patients, whether or not they still have active HD.[1,5] 'Whether the leukemogenic effect is due to an immunologic defect or is the result of a direct injury to myeloid cells by radiation and chemical agents is not established and will have to await a better understanding of the cause and pathogenesis of leukemia'.[13]

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