Leukaemoid Reaction and Disseminated Tuberculosis

A CASE REPORT

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SUMMARY

Four cases of leukaemoid reactions to tuberculosis, notwithstanding the presence of Auer's rods in the myeloblasts, have previously been reported. A fifth case of disseminated tuberculosis in which Auer's rods were similarly observed, is described. However, we believe that this association does not mean that Auer's rods occur as part of a leukaemoid response, but rather that it indicates the simultaneous presence of acute leukaemia and tuberculosis.


Disseminated tuberculosis is known to produce a variety of haematological disorders, including both granulocytic and lymphocytic leukaemoid reactions. The distinction between a leukaemoid reaction and leukaemia may be of great significance for the patient, and the presence of Auer's rods in the cytoplasm of leukaemic myeloblasts has been held to be of diagnostic value in separating the two conditions. Whether this criterion is absolute has been questioned since 4 cases have previously been reported of Auer's rods in association with disseminated tuberculosis,1-3 and we now report a 5th such case and reassess its possible relevance.

CASE REPORT

A 22-year-old Black fisherman presented with a 1-week history of rectal bleeding and shortness of breath. He had experienced generalised weakness and fatigue for several weeks with recent onset of anorexia and loss of weight. He did not bruise easily or have any cough or night sweats. On examination, he was ill with a high fever, pallor and generalised abdominal tenderness. There was no enlargement of liver, spleen or lymph nodes and no petechiae, ecchymoses, fundal haemorrhages or bone tenderness. The remainder of the clinical examination was normal. A tentative diagnosis of amoebic liver abscess was made at a peripheral hospital, and the patient was treated with metronidazole. No improvement had occurred after 3 days and the patient was transferred to Cape Town for further management.

On his arrival, the clinical features were essentially unchanged. Twenty-four hours after admission, the patient developed a well-marked pericardial friction rub. Pulse rate was 120/min without paradoxus. Blood pressure was 120/70 and heart sounds were normal. Radiography (Fig. 1) showed the presence of a pericardial effusion with mediastinal lymphadenopathy. Haemoglobin was 8.3 g/100 ml, total white cell count 35 700/mm³ and platelet count 35 000/mm³. A differential blood cell count showed

Fig. 1. Anteroposterior radiograph of chest showing pericardial effusion and mediastinal lymphadenopathy.
46% myeloblasts, 18% myelocytes and metamyelocytes. 6% promyelocytes, 7% neutrophils, 5% lymphocytes and 15% band forms. Auer's rods were present in many of the granulocytes (Fig. 2). Aspiration biopsy of the bone marrow showed this to be hypercellular with 60% primitive cells, most of which contained Auer's rods. There was a significant reduction in the number of megakaryocytes and the red cell series showed well-marked dysplastic changes. Heaf test was positive grade 3 and blood cultures grew no bacteria at 10 days.

Fig. 2. Photomicrograph of bone marrow showing Auer's rods in myeloblasts (x 1200).

The patient received induction chemotherapy for acute leukaemia with rubidomycin 1.5 mg/kg and cytosine arabinoside 2 mg/kg. Because of his fever, penicillin and gentamicin were administered parenterally. Haematological remission was not achieved at any stage and the peripheral blast count ranged from 1% to 60%. An episode of hepatocellular jaundice, thought to be due to septicemia, developed and the antibiotic regimen was changed to a combination of Keflin and carbenicillin (Pyopen). Since it was felt that tuberculosis had not been excluded, ethambutol and isoniazid were also administered in full therapeutic dosage. Terminally the patient developed acute renal failure, became hypokalaemic and died suddenly 1 month after admission.

Autopsy Findings

Postmortem examination was carried out 48 hours after death. The positive features were limited to mediastinal and abdominal lymphadenopathy with extensive caseation in the presence of numerous acid- and alcohol-fast bacilli. The liver contained many 2-mm nodules with similar histology (Fig. 3). There was widespread haemorrhagic and fibrinous exudation in the pericardial sac without evidence of tuberculosis or leukaemic infiltration. The remaining organs, including numerous sections from bone marrow, failed to demonstrate any evidence of tuberculosis or leukaemia.

Fig. 3. Section of liver showing classical tuberculous granuloma (x 50).

DISCUSSION

The patient whom we describe here apparently had acute myelomonocytic leukaemia. Our diagnosis is based on the presence of large numbers of myeloblasts in peripheral blood and marrow, a severe degree of anaemia...
with very dysplastic red cell precursors in the marrow, marked megakaryocytopenia and numerous Auer’s rods. The simultaneous occurrence of all 4 features in one patient was thought to constitute a sufficient basis for the diagnosis of acute leukaemia, although some aspects were unusual. Lymphadenopathy, as shown on the chest radiograph, is uncommon in myeloblastic leukaemia, while pericarditis is rarely the initial mode of presentation of acute leukaemia. Sternal tenderness, absent in our patient, is a common finding in acute leukaemia, and Twomey and Byrd, in a review of 41 leukaemoid reactions to tuberculosis, comment that none had bone tenderness.

There has been considerable controversy as to whether disseminated tuberculosis can induce leukaemia or produce a leukaemic reaction indistinguishable from leukaemia, or whether it is simply the simultaneous presence of the two diseases. One form of proof that tuberculosis causes a given haematological abnormality would be the disappearance of the blood disorder with successful antituberculous therapy alone. Twomey and Byrd quote Bulgarelli and Creyx as evidence for recovery from leukaemoid reactions on antituberculous therapy. They comment that a peripheral blast count of 16% in Creyx’s patient was restored to normal on antituberculous treatment. Creyx does not, however, give a percentage of blasts, and the 16% refers to myelocytes. Thus, although the blood cell count returned to normal in 10 days, the abnormal count probably did not indicate acute leukaemia. Many authors have reported leukaemoid reactions to tuberculosis, but none of their patients have survived on antituberculous treatment.

Is this failure to survive owing to late or incorrect diagnosis? Twomey and Byrd comment that the correct diagnosis was made in only 8 of 41 patients reviewed in the literature. However, 3 patients were treated by them for 40, 43 and 14 days without success. Rosenthal treated 3 patients for over 4 months and Withers treated 1 patient for more than 2 months without their recovering. It would then appear that although the diagnosis is often not made, patients who have been adequately treated have failed to recover.

Other than recovery on treatment of tuberculosis, how else can the entities of leukaemia and leukaemoid reactions be separated? Numerous authors have commented that the absence of organ infiltration at autopsy excludes the diagnosis of leukaemia. However, various reasons have been given as to why this may occur. Furthermore, we believe that there is no sound evidence either in reported cases or in experimental work to suggest that tuberculosis can induce acute leukaemia. Leucopenia, leucocytosis, monocytosis and anaemia are accepted criteria for leukaemia are present in a patient with tuberculous leukaemia. Failure to demonstrate organ infiltration was probably a consequence of antileukaemic therapy.

On the basis of our review we suggest that when the accepted criteria for leukaemia are present in a patient with tuberculosisois, the simultaneous presence of 2 common diseases rather than a leukaemoid reaction to tuberculosis must be assumed. Furthermore, we believe that Auer’s rods should continue to be regarded as an important diagnostic feature specific for leukaemia.

REFERENCES