A MALIGNANT LYMPHOMA SHOWING THE HISTOLOGICAL FEATURES OF MULTIPLE MYELOMATOSIS, HODGKIN'S DISEASE, AND RETICULUM-CELL SARCOMA

REPORT OF A CASE WITH A REVIEW OF THE LITERATURE

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It has long been known that there is an interrelationship between the various lymphomata. There have been many case reports illustrating the numerous manifestations of reticulo-endothelial diseases and the simultaneous occurrence of different forms of these diseases.[1-6]

This brief report deals with a case in which there was neoplastic proliferation of plasma cells and reticulum cells with foci manifesting the histological picture of Hodgkin's disease. Tuberculous lymphadenitis was an additional finding.

CASE REPORT

A.M., a 40-year-old Bantu female was admitted to Baragwanath hospital on 17 November 1958 complaining of generalized body pains, abdominal pain, and a swelling in the left axilla of about 4 months' duration.

On examination she was found to be extremely anaemic and thin with evidence of marked weight loss. The blood pressure was 120/80 mm.Hg and the pulse rate was 80 per minute. A soft systolic murmur was heard at the base of the heart and a third heart sound at the apex. The liver was enlarged to 2 cm. below the costal margin. A swelling was present in the left axilla 4 - 5 cm. in diameter and the clinical impression was that of matted lymph nodes. Laboratory investigations included: haemoglobin of 4·7 g.%, haematocrit 19%, mean corpuscular haemoglobin concentration 25, and leucocytes 9,600 per c.mm.

A transfusion of 2 pints of blood was given. Bone marrow examination on 21 November revealed a conspicuous plasmacytosis, the plasma cells being of the mature variety. Erythropoiesis was normoblastic and active and some of the normoblasts showed evidence of iron deficiency. There was an increase in the amount of stainable iron in the marrow and these findings were interpreted as a non-sideropenic form of hypochromic anaemia, such as occurs in chronic infection, malignant disease, etc.

A biopsy was performed on the axillary lymph nodes. Microscopic examination showed an enlarged lymph node in which there were a few small tuberculous granulomata (Fig. 1). The greater part of the node, however, showed proliferation of reticulum cells with large numbers of plasma cells, some of which were atypical and contained several nuclei, prominent nucleoli and not infrequent mitoses. It was suggested that the patient be investigated for the possibility of myelomatosis. The patient was then given streptomycin 1 g. daily, by intramuscular injection, rimifon 600 mg. daily by mouth, and urethane 150 mg. daily.

Examination of the urine for Bence Jones protein was negative on 2 occasions and microscopic examination of a centrifuged specimen showed hyaline and granular casts, occasional erythrocytes, and 2 - 4 polymorphonuclear leucocytes per high-power field. Electrophoretic studies of the serum proteins showed the following: total protein 7·5 g.%, albumin 13·8% (1·03 g.%), alpha 1 globulin 8·7% (0·65 g.%), alpha 2 globulin 14·5% (1·09 g.%), beta globulin 14·9% (1·12 g.%), and gamma globulin 48·1% (3·61 g.%).

On 22 December the patient had an epistaxis which necessitated plugging of the nose.

The bone marrow examination was repeated on 24 December. There was a very marked plasmacytosis, some of the plasma cells occurring in sheets. The majority of the plasma cells were mature, but some cells resembling 'myeloma cells' were observed. X-ray examination of the chest showed clear lung fields and a soft tissue mass in the left axilla. The skull, pelvis, and right femur showed no translucent areas. A blood count showed no significant change and another transfusion of 3 pints of blood was given. Blood films examined on 13 January 1959 showed 64% neutrophils, 6% monocytes, 26% lymphocytes and 4% plasma cells.

A further transfusion of 2 pints of blood was given on 14 January. Throughout her stay in hospital the patient had remittent pyrexia between 90°F and 101°F. On 20 January she started deteriorating rapidly, and died on 22 January, 9 weeks after admission and 6 months after the onset of symptoms.

Autopsy Findings

The body was that of a markedly emaciated female. An irregular firm mass about 8 cm. in diameter was present in the left axilla. Both parotid glands were enlarged to 5 cm. in diameter, and on section, exuded purulent material.

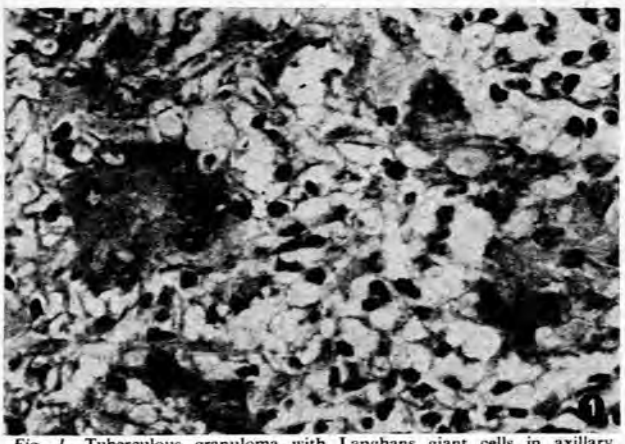

Fig. 1. Tuberculous granuloma with Langhans giant cells in axillary lymph node (haematoxylin and eosin × 480).

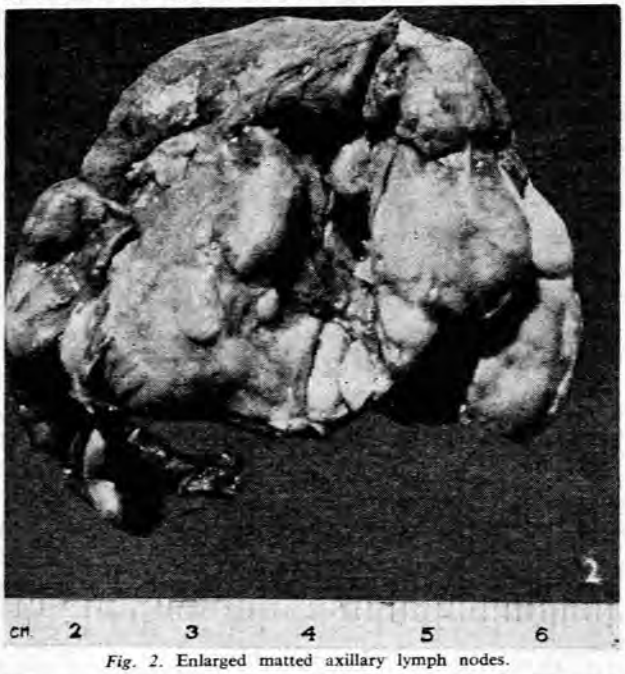

Fig. 2. Enlarged matted axillary lymph nodes.

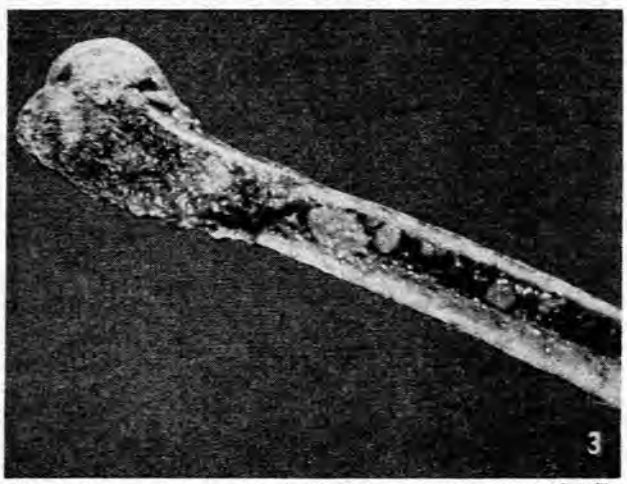

Fig. 3. Cross-section of right femur showing nodular areas of infiltration throughout the bone marrow.

The major morbid anatomical findings were confined to the reticulo-endothelial system.

The mass dissected from the left axilla consisted of enlarged matted lymph nodes measuring 9×4×3 cm. in size. On section they were fairly firm in consistency and pale yellowish-white in colour (Fig. 2).

The left supraclavicular lymph nodes, para-aortic lymph nodes and mesenteric nodes presented a similar appearance.

The spleen (250 g.) was enlarged and on section showed the presence of a well-demarcated yellowish-white subcapsular area 1½ cm. in diameter. The remainder of the pulp had a mottled appearance with yellowish foci alternating with the dark red pulp.

The right femur, on section, showed the presence of numerous well-circumscribed yellowish-white areas of infiltration in the red marrow and to a lesser extent in the white marrow. The distribution of the red marrow appeared normal (Fig. 3).

The remaining morbid anatomical findings were essentially negative.

Microscopic Examination

Sections of the mesenteric, para-aortic and left supraclavicular lymph nodes presented similar features. There was complete loss of the normal architectural pattern due to infiltration by large pleomorphic cells, many resembling large plasma cells with an eccentric nucleus showing clumping of the chromatin and a prominent eosinophilic nucleolus (Fig. 4). Other cells had large horse-shoe shaped nuclei while some contained as many as 5 nuclei; the multinuclear cells resembled the Reed-Sternberg cells seen in Hodgkin's disease (Figs. 5 and 6). In addition, there was considerable reticulum-cell hyperplasia and marked mitotic activity (Fig. 7).

The enlarged left axillary lymph nodes showed a similar picture to the original biopsy, with marked plasma-cell proliferation, moderate reticulum-cell hyperplasia and occasional multinucleated giant cells. Several areas showed deposition of acidophilic homogeneous material which special stains proved to be amyloid.

The spleen showed large areas of necrosis. The remainder of the parenchyma was infiltrated by atypical plasma cells and numerous giant cells of the Reed-Sternberg type. Reticulum-cell hyperplasia was also a prominent feature. Large areas of the spleen were replaced by amyloid material (Fig. 8). The liver showed areas of necrosis, some of which resembled amyloid. At the periphery of these areas there was infiltration by lymphocytes and large atypical plasma cells.

The bone marrow showed a pleomorphic cellular infiltration consisting mainly of neoplastic plasma cells (Fig. 9). In addition there were areas of necrosis and amyloid deposition.

Section of the parotid glands showed an acute suppurative parotitis. The remaining histological findings were negative.

DISCUSSION

This case demonstrates the close association between the various groups of lymphomata. It shows features of Hodgkin's disease, reticulum-cell sarcoma and multiple myelomatosis. According to Lumb[7] the primitive mesenchymal cell may differentiate into either the lymphocyte or the reticulum-cell, and neoplastic proliferations of these two cell types give rise to the lymphosarcoma and reticulum-cell sarcoma respectively. Malignant transformation of both cell types results in the histological picture of Hodgkin's disease.

According to some authors the plasma cell is derived from the reticulum-cell[8] and in view of this it is surprising that tumours showing proliferation of both these cell types are not seen more frequently.

Herbut, Miller and Erf[6] reported 6 cases that at various stages during life were diagnosed as both Hodgkin's disease and lymphosarcoma. At autopsy they showed various combinations of Hodgkin's disease, lymphosarcoma

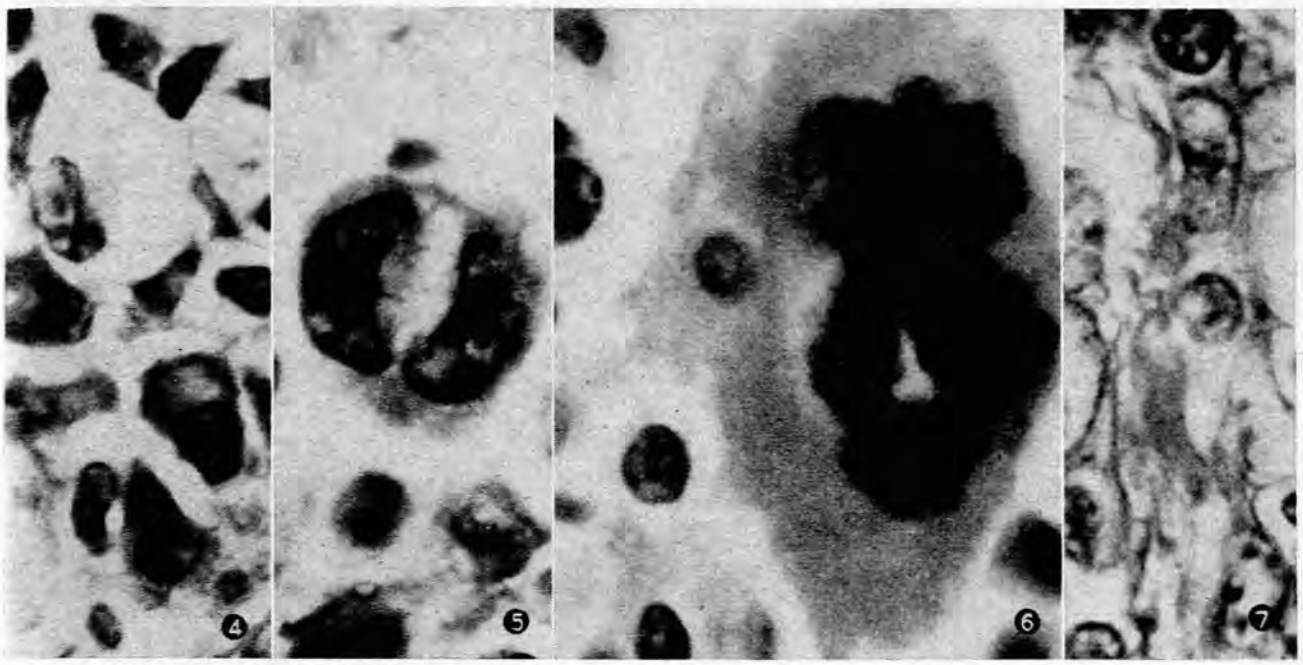

Fig. 4. Photomicrograph of an axillary lymph node showing large, atypical plasma cells (haematoxylin and eosin × 1900).
Fig. 5. Photomicrograph of a mesenteric lymph node showing a characteristic mirror-image cell (haematoxylin and eosin × 1900).
Fig. 6. Multinucleated giant cell surrounded by numerous large plasma cells (haematoxylin and eosin × 1900).
Fig. 7. A further field in the lymph node portrayed in Fig. 5, showing proliferating reticulum cells (haematoxylin and eosin × 1900).

and reticulum-cell sarcoma. They believed that these diseases are not only genetically related but are fundamentally merely phases of the same lesion. The various combinations can be explained only by considering these diseases as arising from a common stem cell and then differentiating in one direction or another according to the amount and type of stimulation as described by Miller and Turner.[9] These authors found 2 substances in increased amounts in the urine of patients suffering from Hodgkin's disease and monocytic leukaemia and separated them chemically into carbinols and noncarbinols. Guinea-pigs inoculated with the carbinols showed increased lymphopoiesis whereas those inoculated with noncarbinols showed increased myelopoiesis. Administration of the 2 products simultaneously resulted in lymphoid and reticulum-cell hyperplasia with foci resembling Hodgkin's disease.

Seife *et al.*[3] reported a case of a man diagnosed clinically as chronic lymphatic leukaemia who was subsequently found at autopsy to have Hodgkin's disease and tuberculosis as well as lymphatic leukaemia.

Co-existent myelogenous leukaemia and Hodgkin's disease has been reported by Samwick *et al.*,[5] and the interrelationship of Hodgkin's disease and other lymphatic tumours was discussed by Custer and Bernhard,[1] who analysed 1,300 lymphatic tumours. They showed a striking fluidity in histological pattern with various transitions and combinations.

The simultaneous occurrence of multiple myeloma and Hodgkin's disease in 2 patients was found by Greenberg and his associates.[2] The first case concerned a patient in whom bone-marrow punctures and lymph-node biopsies performed at the same time showed unmistakable evidence

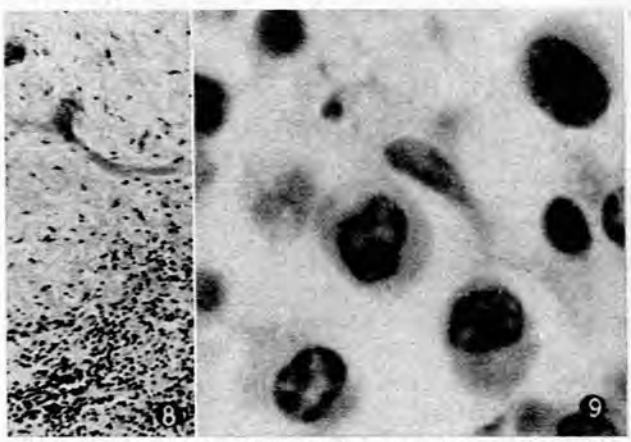

Fig. 8. Section of the spleen showing large deposits of amyloid (haematoxylin and eosin × 120).
Fig. 9. Myeloma cells in a section of bone marrow (haematoxylin and eosin × 1900).

of multiple myeloma (marrow) and Hodgkin's disease (lymph nodes). The second patient had Hodgkin's disease for 10 years after which pathognomonic evidence of multiple myeloma was found. The presence of amyloid in this case is of interest. Amyloidosis may occur in tuberculosis as well as in Hodgkin's disease,[11] and its association with multiple myeloma is often mentioned, but in a review of 51 cases by Glenchur *et al.*[10] it was found in only 2 cases. An earlier study of 51 cases of myelomatosis by Meacham[12] showed only 1 case with amyloidosis.

SUMMARY

A case presenting the pathological features of multiple myelomatosis, Hodgkin's disease and reticulum-cell sar-

coma is described. The interrelationship between the various cell types of the reticulo-endothelial system is discussed and the literature dealing with tumours of the reticulo-endothelial system, exhibiting neoplastic proliferation of several cell types, is reviewed.

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