An Unusual Cause of Lymphadenopathy and Rash

A 38-year-old Chinese man who was previously well, presented with one month of fever and a non-pruritic rash involving the face, trunk and upper limbs. There was no oral, ocular or genital involvement. He denied weight loss, night sweats, fatigue or easy bruising and there was no history of cough or haemoptysis. He was not on any medication and had no relevant family history.

He was pyrexial at 38.5ºC and had an erythematous, nodular rash over the face, torso and upper limbs (Fig. 1). Non-tender cervical and axillary lymph nodes measuring 1.5 cm were detected bilaterally. There was no hepatosplenomegaly.

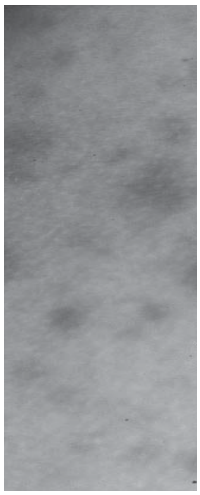

Fig. 1. Erythematous nodular rash over trunk.

Investigations revealed a haemoglobin of 12.4 g/dl, white cell count 2.6 $x10^9$/L, absolute neutrophil count (ANC) 1.5 $x10^9$/L, lymphocyte count 0.88 $x10^9$/L, and platelet count 257 $x10^9$/L. The ANC dropped to a nadir of 0.72 $x10^9$/L, but subsequently recovered.

The lactate dehydrogenase (LDH) was elevated at 2260 U/L and his erythrocyte sedimentation rate (ESR) was raised at 79 mm/hr. A peripheral blood film revealed a few atypical lymphoid cells and liver function tests revealed transaminitis (Aspartate Transaminase 281 U/L, Alanine Transaminase 154 U/L, Alkaline Phosphatase 221 U/L).

A computed tomography scan revealed cervical, axillary and mesenteric lymphadenopathy. Flow cytometry of the peripheral blood revealed reactive lymphocytes.

Excision biopsy of a cervical lymph node revealed necrotising lymphadenitis with prominent nuclear karyorrhexis (Fig. 2). No granulomata or malignant cells were detected. A skin biopsy revealed a dermal infiltrate of histiocytes and lymphocytes with abundant karyorrhectic nuclear dust material (Fig. 3); the histiocytes were found to co-express CD68 and myeloperoxidase. The lymphocytes were mostly T-cells (CD3 positive; CD20 negative) with equivalent numbers of CD4 and CD8 positive cells. Ziehl Neelsen stain and culture for acid fast bacilli were negative.

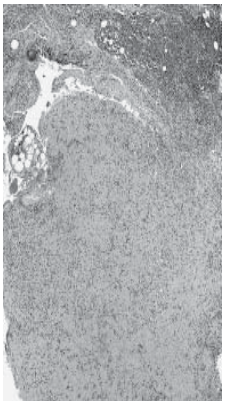

Fig. 2. Lymph node biopsy showing large areas of necrosis (H and E, original magnification x 20).

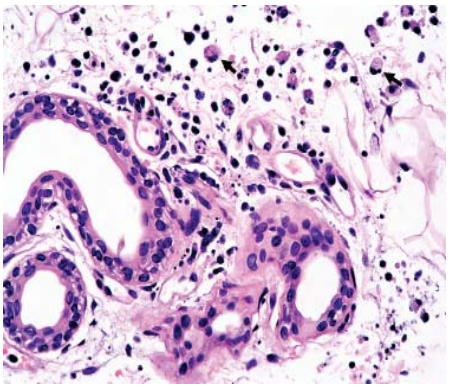

Fig. 3. The skin biopsy shows periadnexal lymphocytes and histiocytes, many of the latter contain crescenteric nuclei (arrows). (H and E, original magnification x 300).

What is the diagnosis?

A. Non Hodgkin Lymphoma
B. Systemic Lupus Erythematosus
C. Kikuchi-Fujimoto Disease
D. Mycoses Fungoides
E. Multicentric Castleman's Disease

Answer: C

Discussion

The lymph node and cutaneous histology are consistent with Kikuchi-Fujimoto Disease (KFD).

The T-cell-rich infiltrate typical of KFD may raise the consideration of a T cell lymphoma. The latter, however, is associated with architectural effacement, monomorphism of the lymphoid population, and lack of histiocytes and apoptosis.

Mycosis fungoides is the most common cutaneous T-cell lymphoma. In the patch stage of the disease, the histopathology is characterised by lesional lymphocytic epidermotropism. Karyorrhectic debris and crescenteric histiocytes typical of KFD would not be expected.

Lupus Erythematosus (SLE) can give very similar cutaneous and lymph node histopathology to KFD. Hallmarks of SLE in the skin- thickened epidermal basement membrane, interface changes and dermal mucinous deposition should be sought for. Haematoxylin bodies and vessels with Azzopardi phenomenon are distinctive of lupus lymphadenitis. Correlation with clinical and serological features is important.

Multicentric Castleman's Disease involves primarily the lymph nodes with very occasional reports of skin disease. Vascular-hyaline changes within germinal centres, onion-skin appearance of follicles and sheets of plasma cells are histological features distinctive of the disease.

KFD is an uncommon cause of lymphadenopathy of unknown aetiology.[1]

Presentation is subacute with lymphadenopathy and fever.[2] Cutaneous manifestations include nodules, crusted papules and erythema multiforme.[2] Laboratory features include anaemia, leukopaenia, and elevated LDH.[2]

Lymph node histology reveals paracortical coagulative necrosis with karyorrhectic debris and abundant histiocytes around necrotic areas.[2] Immunohistochemistry reveals a CD8+ T-cell predominance. Histiocytes characteristically express CD68, myeloperoxidase and lysozyme. Cutaneous histology reveals features typified in the current case.

KFD is associated with autoimmune disease.[2] Our patient had Graves disease (GD) (Free thyroxine 30.3 pmol/l [range, 10.0 to 23.0]), Thyroid Stimulating Hormone below 0.02 mIU/L (range, 0.45 to 4.50), TSH Receptor Antibody (TRAB) 5.0 IU/L [<2.0]. His anti thyroid peroxidase antibody titre was <10 IU/ml (range, 0 to 50) and Anti-thyroglobulin was <20 IU/ml (range, 0 to 40). He was clinically euthyroid, with no family history of thyroid disease. Although rare, GD has been reported in association with KFD.[3] Our TRAB assay is approximately 99% specific, therefore a false positive TRAB in biochemically hyperthyroid patients is unlikely. His anti nuclear antibody and anti double stranded DNA were negative.

Morbidity and mortality are rare and no specific treatment is required although follow-up for recurrence is recommended.[2] Our patient's symptoms resolved within a month. He required no treatment for KFD but received initial treatment for GD with carbimazole.

Our case alerts clinicians and pathologists to avoid misdiagnosing this condition as lymphoma or SLE.

REFERENCES

1. Kikuchi M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytosis. Nippon Ketsueki Gakkai Zasshi 1972;35:379-80.
2. Bosch X, Guilabert A, Miquel R and Campo E. Enigmatic Kikuchi-Fujimoto Disease, a comprehensive review. Am J Clin Pathol 2004;122:141-52.
3. Keogh MA, Williamson RM, and Denaro CP Kikuchi's disease associated with parotidomegaly, thyroiditis and a rash in a young man. Aust N Z J Med 2000;30:633-4.

Sanjay de Mel,[1] *BSc (Hons), BM (Hons), MRCP (UK)*, Chee Wei Teoh,[2] *MBBS (Malaya), MRCP (UK), MSc (Derm) (UK)*, Li Mei Poon,[1] *MBBS, MRCP (UK), FRCPath*, Kong Bing Tan,[3] *MBBS, FRCPA, FRCPath,* Siok Bian Ng,[3] *MBBS,FRCPA*, Kong Leong Toh,[2] *MMed (Int Medicine) (NUS), MRCP (UK), Ph D (Human Genetics) (University of Utah)*

[1]Department of Haematology - Oncology, National University Health System Singapore
[2]Department of Medicine, National University Health System Singapore
[3]Department ofPathology, National University Health System Singapore

Address for Correspondence: Dr. Sanjay de Mel, Registrar, Department of Haematology–Oncology, National University Health System Singapore, 5 Lower Kent Ridge Road Singapore 119074.
E-mail : sanjay_widanalage@nuhs.edu.sg