

A 40-Year-Old Man with Rashes and Palpitations

A 40-year-old Singaporean Indian man with no significant past medical history presented with worsening non-pruritic rashes primarily involving his limbs over a 6-month period. He also reported a near fainting episode associated with recurrent palpitations over the past few weeks. Clinical examination revealed the presence of multiple waxy yellowish-brown dermal papules and plaques over his limbs (Fig. 1) as well as an irregular pulse, but was otherwise unremarkable. A full blood count showed lymphopenia at 200 cells/ μ L, while serum electrolytes including calcium levels, liver and thyroid function tests were normal. Cardiac enzymes were not raised, but an electrocardiogram showed complete heart block (Fig. 2).

What is the diagnosis?

- A. Xanthomas with ischaemic heart disease
- B. Primary systemic amyloidosis with cardiac involvement
- C. Sarcoidosis
- D. Lepromatous leprosy
- E. Adult T-cell leukaemia/lymphoma

Discussion

On histopathological examination of a punch-biopsy specimen taken from a representative lesion on the patient's arm, numerous granulomas without caseous necrosis were seen in the superficial and mid-dermis (Fig. 3). There was no nerve involvement. Periodic acid-Schiff, Gomori methenamine silver and Ziehl-Neelsen stains were negative

for infective organisms. Two-dimensional echocardiography showed a normal left ventricular ejection fraction of 65%, and coronary arteries were normal on angiogram. The patient declined endomyocardial biopsy. Our patient's angiotensin-converting enzyme (ACE) level was elevated at 101 units (normal range: less than 53 units). Computed tomography scan of the thorax and an eye screen were normal.

The above investigations were consistent with a diagnosis of sarcoidosis with cutaneous and cardiac involvement. Lymphopenia may be observed in over 50% of patients with sarcoidosis.¹ Our patient was treated topically with mometasone furoate 0.1% cream, and underwent a pacemaker insertion. He also received tapering courses of oral prednisolone (maximum dose of 50 mg daily) and oral azathioprine (maximum dose of 125 mg daily) for about 2 years. The patient responded well to therapy, with resolution of the skin lesions and no recurrence of his cardiac symptoms after a follow-up period of 2 years.

Eruptive and tuberous xanthomas are possible differentials, with yellow-hued skin lesions favouring the extensor surfaces of the extremities. However, eruptive xanthomas often appear in crops with involvement of the buttocks, and they are frequently itchy. Tuberous xanthomas are usually more nodular in appearance. There is a predominant facial distribution in primary systemic amyloidosis, with firm skin-coloured to pink to yellow-brown waxy papules and plaques that can become purpuric. Lepromatous leprosy is a consideration in view of the finding of granulomas in the biopsy specimen. However, the absence of ear lobe



Fig. 1. A) shows yellowish-brown papules on the patient's right forearm; B) shows similar lesions involving the patient's right knee.

Answer: C

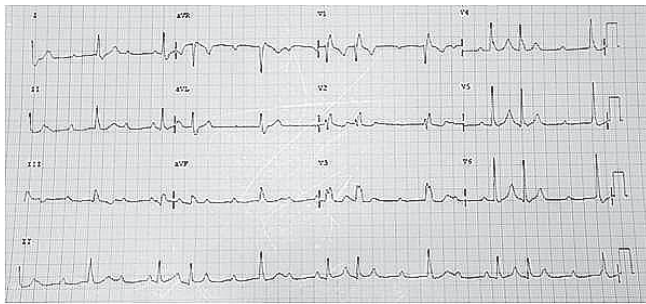


Fig. 2. The patient's electrocardiogram showing complete heart block.

involvement clinically, as well as the presence of intact nerve bundles and the lack of acid-fast bacilli on histology point against this diagnosis. Adult T-cell leukaemia/lymphoma (ATLL) is characterised by skin lesions resembling those found in mycosis fungoides or Sezary syndrome, which can range from atrophic patches to indurated plaques to ulcerated tumours. The acute form of ATLL also presents with lymphadenopathy, hypercalcaemia and bone lesions. Apart from the clinical features, histology also helped to clinch the diagnosis of sarcoidosis in our case.

First described by Sir Jonathan Hutchinson in 1875, sarcoidosis is a non-caseating granulomatous disorder of unknown aetiology that can affect virtually any organ system.

Cutaneous sarcoidosis is seen in about 25% to 33% of cases. Notably, the extent and type of cutaneous involvement does not correlate well with the degree of systemic disease. In general, the skin lesions are typically asymptomatic red-yellow brown dermal papules and plaques. However, sarcoidosis is termed a “great imitator” as it can present with almost any morphology, and more than 1 subtype can be present in the same patient. Cutaneous involvement in sarcoidosis can be classified as either specific or non-specific, with specific lesions showing non-caseating granulomas on histological examination. Some examples of specific disease include lupus pernio, as well as the angiolupoid, annular, erythrodermic, ichthyosiform, lichenoid, maculopapular, nodular, papillomatous, plaque, psoriasiform, scar, subcutaneous nodular, ulcerative, vasculitic and verrucous forms. Lupus pernio is characterised by bluish-red to violaceous infiltrated papulonodules and plaques that usually affect the ears, nose, cheeks and extremities. The angiolupoid variant of sarcoidosis tends to be localised to the malar region, bridge of the nose, or around the eyes, and consists of livid nodular lesions that coalesce to form plaques. Erythema nodosum is the main non-specific cutaneous manifestation. Our patient had a combination of both the papular and plaque forms of cutaneous sarcoidosis.

The prevalence of cardiac sarcoidosis with clinical

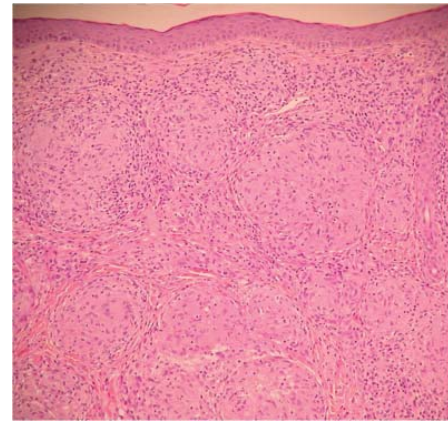


Fig. 3. Histology showing multiple non-caseating granulomas (haematoxylin and eosin stain, original magnification x 40).

symptoms or electrical signs is about 5% in various series, but evidence of cardiac disease has been found in up to 20% to 30% of autopsies.² Arrhythmias, infiltrative cardiomyopathy, pericarditis, congestive cardiac failure and sudden death can occur. As cardiac involvement is responsible for 50% of patient deaths from this disorder, it is imperative that this should not be missed.³

ACE is produced by sarcoidal granulomas but does not correlate with the severity of skin involvement. Although it has limited diagnostic value, it serves as a useful monitor of disease activity.

For mild, localised cutaneous sarcoidosis, potent topical and intralesional corticosteroids remain the treatments of choice. Systemic treatment is indicated when there is disfiguring skin disease and/or myocardial involvement. Corticosteroids as well as immunosuppressants such as azathioprine, methotrexate and mycophenolate mofetil can be considered.

The clinical course of sarcoidosis in general is highly variable. Approximately 60% of cases experience spontaneous resolution within 2 to 5 years. A further 20% settle with treatment, and the last 20% of patients tend to have chronic recurrent disease despite therapy.

Physicians should always consider sarcoidosis as a possible differential in a patient presenting with cutaneous dermal papules and plaques and/or protean manifestations. It is also important to keep in mind that no organ is exempt from sarcoidal granuloma deposition. In all patients, attempts should be made to delineate the full extent of disease to avoid any adverse outcomes. The following tests should be considered: a full blood count, renal and liver function, calcium levels, chest X-ray, electrocardiogram, urinalysis and an ophthalmology evaluation. Other investigations should be guided by each patient's symptomatology.

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