Case Report

An Unusual Presentation of Sarcoidosis in a Chinese Woman

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Abstract: Sarcoidosis is a multisystem disorder that commonly involves the lung, eye, lymph nodes and skin. Cutaneous involvement is present in up to 35% cases of systemic sarcoidosis and is broadly classified into specific and non-specific lesions according to the presence of typical non-caseating granulomas histologically. Sarcoid specific lesions include a number of cutaneous manifestations but subcutaneous involvement is uncommon. We report on a Chinese woman who initially presented with fever and a subcutaneous lump on the buttock. Excisional biopsy of the lump revealed lobular panniculitis without evidence of vasculitis or granulomatous changes. She subsequently developed arthropathy, interstitial lung disease and mediastinal lymphadenopathy. Lymph node biopsy confirmed the diagnosis of sarcoidosis. The rarity of sarcoidosis in Chinese and the temporal relationship between the diagnosis of panniculitis and the subsequent features of sarcoidosis suggests that panniculitis is the cutaneous manifestation of the disease. Sarcoidosis should be considered as an unusual cause of panniculitis even in the absence of typical non-caseating granulomas.

Keywords: Baker's cyst, cutaneous, dermatological, pulmonary sarcoidosis, skin

Introduction

Sarcoidosis is a multisystem disorder of unknown aetiology characterized histologically by the formation of non-caseating epitheloid cell granulomas. It may affect any organ of the body but the lungs, eyes, lymph nodes and skin are most commonly involved. The disease may also affect the liver, spleen, central nervous system (CNS), heart, bone and marrow and may sometimes be associated with hypercalcemia, hypercalciuria, polyclonal hypergammaglobulinemia, circulating immune complexes, cutaneous anergy and suppressed cell-mediated immunity in-vitro.1 The prevalence of sarcoidosis in the Caucasian white population is around 5/100,000. The disease is approximately eight times more common in the black African Americans than the white Americans. However, it is a very rare disease in the Chinese and the Orientals.2

Two types of presentation of sarcoidosis are well known. In the subacute/transient form, erythema nodosum is typical and may be associated with fever, migratory arthritis, hilar lymphadenopathy and uveitis. Cutaneous manifestations other than erythema nodosum are rare. In the more common chronic/persistent form of systemic sarcoidosis, cutaneous lesions are present in up to 20-35% of cases.3 The commonest lesion is brown-red or purple papule or plaque, which is termed lupus pernio if it occurs on the cheek, nose or ears. Other cutaneous sarcoid lesions include skin nodules, annular, ichthyosiform, erythrodermic, psoriasiform, lichenoid, ulcerative and angiolupoid forms, scars and hypopigmented lesions.

In this report, we describe a middle-aged Chinese woman who initially presented with panniculitis and was subsequently diagnosed to have systemic sarcoidosis.
Case Report

A 44-year-old Chinese woman, previously healthy, presented to the surgical unit in August, 1997 with swinging fever and a painful subcutaneous lump on the left buttock. Physical examination revealed a tender erythematosus nodule of 2x2 cm on the lateral aspect of the left buttock region. There were no other skin lesions and the inguinal lymph nodes were not palpable. She was initially treated as cellulitis with intravenous antibiotics but the fever and tenderness persisted.

A drainage procedure together with excision of the lump was performed. However, her fever did not remit after the operation although repeated cultures from the buttock wound were negative. Histological examination showed marked lymphocytic infiltration; however, there was no evidence of granulomas or vasculitis. The immunohistochemical studies showed that these lymphoid cells were composed of mixed B-cells and T-cells, in keeping with their reactive nature. They were negative for CD56, and in situ hybridization for Epstein-Barr virus was negative (Figure 1). Staining for acid-fast bacilli and fungus was also negative.

Apart from non-specific polyarthritis during the fever spike, the patient did not have other specific complaints. Initial blood tests showed normochromic normocytic anaemia (haemoglobin 8.8 g/dL) but the white cell and platelet counts were normal. Her liver and renal functions were normal except for a low serum albumin level of 29 g/L (normal range 42-54 g/L). Anti-nuclear antibody was weakly positive (1 in 40). Anti-dsDNA, anti-ENA, anti-cardiolipin antibodies, lupus anticoagulant were all negative. A 24-hour urine collection did not show significant proteinuria. Her daughter was diagnosed to have systemic lupus erythematosus (SLE) with probable history of nephritis at her teenage. She did not have the classical features of the disease such as malar rash, photosensitivity or oral ulcers. Moreover, she did not have any abdominal symptoms and the serum amylase level was normal. Initial chest X-ray was unremarkable. There was also no history of trauma to the buttock before the onset of the skin nodule. The working diagnosis was idiopathic lobular panniculitis. With the administration of naprosyn, her fever and joint symptoms subsided. The buttock wound healed satisfactorily and she was discharged from hospital.

Figure 1 (A-C). The 'abscess wall' biopsy shows mixed septal and lobular panniculitis (A&B). The inflammatory infiltrate is formed by plasma cells, histiocytes and lymphocytes (C).
Two months later, she was readmitted because of sudden left lower limb pain and swelling, shortness of breath and recurrence of fever. Physical examination revealed edema of left leg but there was no active synovitis of the knee and ankle joints. There was no new skin lesion or subcutaneous nodules. A doppler ultrasound study did not demonstrate deep vein thrombosis but showed a ruptured popliteal cyst. Examination of the chest revealed bilateral fine inspiratory crackles and a chest X-ray showed newly developed bilateral lower zone reticulonodular shadows. There was no hilar lymphadenopathy. Her blood gas and lung function test were both normal. Electrocardiogram and echocardiogram did not show any features of pulmonary hypertension. A high resolution CT (HRCT) scan of the thorax revealed ground glass opacification of the lung parenchyma, which was compatible with interstitial lung disease. Incidentally, mediastinal and axillary lymphadenopathy was detected. In view of the lymph node enlargement, a conventional CT of the thorax and the abdomen were performed and showed multiple axillary, mediastinal and para-aortic lymphadenopathy and hepatosplenomegaly. A skin tuberculin test was negative.

As there were no externally palpable lymph nodes, the patient underwent a mediastinoscopic biopsy of the paratracheal lymph nodes. The histology of the excised lymph node is shown in Figure 2. The nodal architecture was completely effaced and was replaced by multiple granulomas that were formed by epitheloid cells with relatively few lymphocytes. Caseous necrosis and Langhans' giant cells were not seen and staining for fungus and mycobacterium was both negative. This was compatible with sarcoidosis. As the patient declined an open lung biopsy, confirmation of sarcoid

![Figure 2 (A-B)](image)

**Figure 2 (A-B).** The mediastinal lymph node is replaced by multiple granulomas (A), which show no central caseous necrosis (B).
involvement of the lung could not be made definitely. However, there was no evidence of hilar lymphadenopathy on serial chest X-rays all along.

The patient was treated with prednisolone (0.5 mg/kg/day) for eight weeks, after which the dose was gradually tapered down. She responded dramatically with subsidence of respiratory symptoms and fever. A repeat chest X-ray and HRCT scan of the thorax after three months revealed complete resolution of the ground glass shadows and shrinkage of the mediastinal lymph nodes. There was no recurrence of skin nodules after 10 months' follow-up. Ophthalmological examination did not reveal any sarcoid involvement of the eyes.

Discussion

This is an interesting case of systemic sarcoidosis in a Chinese patient who presented initially with an isolated subcutaneous lump, which was histologically diagnosed to be lobular panniculitis. Although cutaneous manifestation of sarcoidosis is not uncommon and subcutaneous nodule is a well recognized feature, the diagnosis could not be established initially because of the lack of non-caseating granulomas in the adequately excised subcutaneous specimen. Panniculitis other than erythema nodosum as the presenting feature of sarcoidosis has not been reported in the literature.

Cutaneous manifestations in chronic systemic sarcoidosis are diverse but can be broadly grouped into specific lesions that reveal non-caseating granulomas on biopsy and non-specific lesions that may accompany the disease but do not reveal granulomas histologically. Specific cutaneous sarcoid lesions include a variety of nodules/papules, plaques, scars and subcutaneous lesions, while erythema nodosum is the commonest sarcoid non-specific skin manifestations. In the absence of typical non-caseating granulomas, the subcutaneous nodule in our patient should be classified as sarcoid non-specific lesion.

Panniculitis is a pathological condition characterised by inflammation of the subcutaneous adipose tissue. Based on the location of the inflammatory cellular infiltrates, panniculitis can be divided into septal (cellular infiltrates located mainly in the septa of fat lobules), lobular (cellular infiltrates located mainly within the fat lobules) and mixed septal/lobular types. These are further subclassified according to the presence or absence of associated vasculitis. Lupus panniculitis could be a possible differential diagnosis in our patient. Though lupus panniculitis may occur in the absence of systemic disease, it is usually present with other chronic cutaneous manifestations. In the absence of both systemic and cutaneous manifestations of SLE, lupus-related panniculitis was not likely. SLE was excluded in our patient because she did not meet the minimum of 4 American College of Rheumatology (ACR) criteria.

The most common non-specific skin lesion in sarcoidosis is erythema nodosum, which is a septal type of panniculitis. The typical site for erythema nodosum is extensor surface of the lower limb especially shin region. The site and the histological findings of the skin lesion in our patient were not typical of erythema nodosum. On the other hand, there was no evidence of pancreatitis and the possibility of fat/enzyme panniculitis was unlikely. Malignancies such as subcutaneous lymphoma or leukaemia were excluded by immunohistochemical staining. Infection was also unlikely because micro-organisms were not found on special staining of the histological specimen. As there was predominant lymphocytic infiltrate in the fat lobules and in the absence of an obvious cause, the original diagnosis was idiopathic lobular panniculitis or Weber-Christian disease. However, the subsequent development of features of systemic sarcoidosis with arthropathy and interstitial lung disease which responded to steroid therapy suggests that the lobular panniculitis is a cutaneous manifestation of sarcoidosis. Chance co-existence of the two conditions is unlikely in our patient because panniculitis is uncommon and sarcoidosis is very rare in our locality.

Systemic corticosteroids (e.g. prednisone 0.5-1.0 mg/kg/day) are the main stay of treatment of sarcoidosis. However, they are usually indicated for involvement of other organs rather than the skin per se. For chronic cutaneous sarcoid lesions such as lupus pernio and plaques that may cause scarring, oral steroid may be indicated. Topical steroids, intralesional steroid injection and even plastic surgery have been reported to be successful in the treatment of disfiguring cutaneous lesions. On the other hand, the anti-malarials such as
hydroxychloroquine sulphate (200-400 mg/day) and chloroquine (250-500 mg/day)\textsuperscript{4,10} with regular ophthalmological monitoring have been shown to be effective and steroid-sparing in severe cutaneous sarcoid lesions. Methotrexate (7.5-25 mg/week), with regular liver function monitoring, has also been used in the treatment of both systemic and cutaneous sarcoidosis with good effect\textsuperscript{11} but skin lesions may only respond after prolonged therapy for at least six to twelve months. In our patient, systemic steroid was mainly indicated for the treatment of pulmonary sarcoidosis and she responded excellently without any relapses when steroid dose was tailed down. Her subcutaneous lesion had been treated with surgical removal and there was no recurrence of cutaneous lesions either. Close monitoring for systemic and cutaneous relapses is important for our patient and hydroxychloroquine may be considered for the latter.

References