

Case Report

Acute Sarcoidosis: 3 Cases in an Acute Medical Clinic

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Key Learning Points

- In the presence of arthralgia and erythema nodosum, check the chest radiograph for bilateral hilar lymphadenopathy, and investigate accordingly to exclude causes other than sarcoidosis
- Unlike the other cutaneous lesions in sarcoidosis, erythema nodosum is not granulomatous; it therefore does not require biopsy to confirm diagnosis of sarcoidosis
- Most acute sarcoidosis presentations, especially Löfgren syndrome, will not require treatment with steroids
- A clinical diagnosis of sarcoidosis requires follow-up in clinic
- Good communication with the patient with suspected sarcoidosis is essential, as the spectrum of outcome and therefore prognosis is wide – use patient information leaflets¹

Abstract

Sarcoidosis is a cryptogenic multisystem granulomatous disorder. We present three patients who presented acutely with erythema nodosum in our Medical Assessment Unit (MAU) or attended our clinic, subsequently diagnosed with acute sarcoidosis. In doing so, we aim to demonstrate that this presentation can easily be seen on the acute medical take, focussing on the management of acute sarcoidosis in association with erythema nodosum. Although patients will often not display florid systemic upset on presentation, we recommend follow-up after initial presentation, to ensure good resolution of symptoms.

Keywords

Sarcoidosis, erythema nodosum

Introduction

Sarcoidosis is a multisystem inflammatory condition characterised histologically by non-caseating granulomata. Although pathophysiological mechanisms have not been confirmed, the development of sarcoidosis is suspected to be dependent on environmental factors (a toxin or infectious agent)² triggering an immune response, in genetically susceptible populations, with a number of HLA haplotypes (and recently an oncogene) implicated.^{3,4}

It is specifically the Th1 subtype of T cells that is responsible for sarcoidosis; indeed interferon, which increases the Th1 response, has been reported to trigger or exacerbate sarcoidosis.⁵ It is possible that failure of the immune system to clear a particular antigen of low virulence can lead to the chronic Th1 response, resulting in granulomata (see Table 1)

Sarcoidosis typically affects those of Scandinavian or African origin between 20 and 40 years of age; the modes of presentation of sarcoidosis are legion.⁷

Due to the elusive pathophysiology, there is no single diagnostic test which can confirm sarcoidosis – instead, diagnosis relies on a pattern of clinical, radiological and pathological findings, with exclusion of other disease.

Here, we present three cases of sarcoidosis, seen over a period of one year in the Medical Assessment Unit of

- CD4+ T-cell activation
- increase in B-cell activity
- increase in nonspecific immune-complex formation⁶
- reduced delayed-type hypersensitivity responses
- cutaneous anergy to tuberculin intradermal testing

Table 1. Components of immune response in sarcoidosis.

Huddersfield Royal Infirmary. In describing these, we hope to remind physicians in acute medicine that sarcoidosis may need to be considered as a differential when faced with a skin lesion resembling erythema nodosum, and to describe a practical approach to the classical presentation of acute sarcoidosis.

Case 1

A 34 year-old Asian man presented with a four week history of painful ankles and lower legs which had become erythematous and swollen over the past week. The pain had responded well to ibuprofen and etorocoxib, but the erythema persisted and spread, despite a course of oral flucloxacillin. The GP organised Doppler ultrasound, which demonstrated no thrombus in the calf veins. The patient was then referred to the acute medical clinic.

Prior to presentation, he had not experienced a fever, cough or sore throat. Blood results were unremarkable apart from a mildly elevated C-reactive protein (CRP).

In clinic, the erythematous lesion on his right leg was believed to be erythema nodosum. A chest radiograph showed bilateral hilar enlargement suggesting lymphadenopathy. The working diagnosis was Löfgren syndrome (acute sarcoidosis with erythema nodosum).

Further blood tests were taken during the clinic visit (Table 2). An ECG was unremarkable.

The patient was prescribed diclofenac, and seen in clinic two weeks later, with good resolution of the arthralgia and erythema nodosum. Pulmonary

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Figure 1. Chest radiograph demonstrating bilaterally bulky hila, with mild right paratracheal node enlargement.

function showed a mild restrictive defect and a normal transfer factor; review in respiratory clinic is ongoing, with no specific treatment currently required.

Case 2

A 34 year-old caucasian man presented with general malaise, rigors, a migratory asymmetrical polyarthralgia and multiple skin lesions on his arms and legs. He reported no sore throat or recent cough. The skin lesion had commenced as a small erythematous nodule on the anterior surface of his left lower leg, and gradually increased in size over a period of one week. In the past two days he had noted other similar raised areas of erythema overlying the extensor aspect of his right arm just above elbow. The lesions were not pruritic, but painful to touch.

He reported difficulty weight-bearing, with pain predominantly in small, medium and large joints.

There was no significant past medical history or family history. His only current medication was amitriptylline. He was a non-smoker, did not consume alcohol, and was in a stable relationship with his wife.

Examination revealed erythematous patches which were indurated and warm to touch, overlying the left tibia (Figure 2), and on the extensor aspect of his arm above the elbow. His cardiovascular, respiratory and abdominal systems were unremarkable, apart from a pyrexia of 38.9°C.

The chest radiograph showed bilaterally bulky hila (Figure 3) An ECG showed normal baseline cardiac conduction.

The clinical impression was erythema nodosum with bilateral hilar lymphadenopathy due to acute sarcoidosis. A variety of blood tests were requested (Table 2).

Having been seen by a rheumatologist, he was commenced on a reducing course of prednisolone (commenced at 40mg daily), which prompted a dramatic improvement in his symptoms. A follow-up appointment with a respiratory physician was organised.

Case 3

A 35 year-old Asian male patient attended MAU clinic with a history of bilateral pre-tibial erythematous nodules for a 3 weeks. He also complained of arthralgia of medium and large joints. He had been treated with simple analgesics and anti-inflammatories without effect. As the



Figure 2. Photograph of the patient's right pre-tibial area with near-circumferential erythema



Figure 3. Chest radiograph demonstrating bilateral hilar enlargement

skin lesions resembled erythema nodosum, a chest radiograph was performed – this confirmed bilateral bulky hila suggestive of lymphadenopathy. As his symptoms were not helped by non-steroidal anti-inflammatories, a reducing course of prednisolone (commencing at 40mg daily) was instituted and the patient was referred to respiratory clinic. He is under follow-up in respiratory clinic and is currently not requiring any further investigation.

Discussion

This case series illustrates the most common pattern by which sarcoidosis may present to the acute medical clinic. Erythema nodosum (EN) commonly causes pain, erythema and swelling of the lower limbs and may mimic deep vein thrombosis or cellulitis, both common conditions presenting to acute physicians. As demonstrated by these 3 cases, sarcoidosis is an important condition to consider when EN is suspected. Careful consideration of the differential diagnosis may reveal an alternative explanation (see table 3). Initial investigation of these patients should include a chest x-ray; the finding of bilateral hilar lymphadenopathy should increase the clinician's suspicion of sarcoidosis, although other conditions such as tuberculosis and haematological malignancy may require exclusion. CT scanning of thorax

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FBC	Hb (13.5 – 7.0)	13.0↓	Electrolytes	Na ⁺ (135 – 45)	133↓
	WCC (3.5 – 11.0)	8.50		K ⁺ (3.5 – 5.0)	3.4↓
	Platelets (140 – 400)	191		HCO ₃ ⁻ (22 – 32)	23
CRP (<10)		111↑	Renal	Cr (48 – 128)	95
ESR (<22)		42↑	Liver	Bili (3 – 17)	24↑
Anti-streptolysin O titre (<200)		400		ALP (30 – 130)	105
AI Antibody screen		-ve		ALT (<35)	55↑
Blood cultures		-ve			

Table 2. Blood test results from Case 2.

Infection	Bacterial	Drugs	Sulphonamides
	Streptococcal		Oral contraceptive pill
	Tuberculosis		Penicillin
	Mycoplasma	Inflammatory	Sarcoidosis
	Viral		Behcet's disease
	HIV		Inflammatory bowel disease
	EBV	Lymphoma/leukaemia	
	Hepatitis C		

Table 3. Causes of erythema nodosum.

and abdomen may be required in some cases.

The diagnosis of sarcoidosis in this context is usually based on the clinical features illustrated by these cases. Tissue diagnosis is not usually required, and biopsy of the skin lesions in erythema nodosum does not usually give any specific diagnostic information⁸. Other investigations which may be useful include the serum calcium, often raised in sarcoidosis. Serum angiotensin converting enzyme (ACE) level may be elevated, but its low specificity and sensitivity mean that this is rarely useful in the initial diagnosis. Anti-streptolysin O and anti DNAse B titres may be helpful to exclude post-streptococcal EN. A 12-lead ECG is important to rule out conducting-system abnormalities, which may indicate cardiac

Uncontrolled symptoms (Pyrexia, arthralgia, cough, dyspnoea, chest pain, exercise limitation)
Organ dysfunction (Lung, eye, heart, CNS, heart)
Organ derangement (Lymphadenopathy, splenomegaly, parotid swelling, cutaneous lesions)
Abnormal serum tests (Raised calcium, progressively elevated LFTs)

Table 4. Indications for initiation of corticosteroids in acute sarcoidosis (adapted from *Harrisons Principles of Internal Medicine*, 16th ed.)¹⁰

sarcoidosis, as well as abnormalities associated with co-existent hypercalcaemia.

This form of sarcoidosis, often termed Lofgren syndrome, usually runs a self-limiting, benign course. In one of our cases resolution occurred following treatment with non-steroidal anti-inflammatory drugs (NSAIDs). The use of corticosteroids is controversial due to the high rates of spontaneous remission. Criteria for institution of corticosteroids are listed in table 4. In two of our cases corticosteroids were used due to persistent symptoms which had not resolved with simple analgesics and NSAIDs. In both cases rapid resolution of symptoms followed initiation of a reducing course of prednisolone, starting at 40mg per day. Discussion with a specialist rheumatologist may be advisable prior to initiation of corticosteroid therapy, with appropriate follow-up. Failure to respond to corticosteroid therapy should raise the suspicion of another cause for the patient's symptoms.

Sarcoidosis is a recognised cause of interstitial lung disease, and close liaison with a respiratory physician is important in all cases. Baseline lung function testing, including transfer factor may reveal a restrictive defect even in the absence of chest symptoms, as in one of our cases. Less well recognised is the potential to cause an obstructive defect due to endobronchial inflammatory changes⁹. Most cases will require follow-up in a respiratory clinic with serial lung function testing.

Conclusion

The combination of erythema nodosum and bilateral hilar lymphadenopathy should alert the acute physician to the possibility of sarcoidosis. A structured approach to assessment will enable exclusion of other important differentials; corticosteroid therapy should be considered for severe, or refractory cases and follow-up in a respiratory clinic following lung function testing is recommended.

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