Beware a ‘rash diagnosis’

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CASE

The patient (Mrs JR) noted a rash on her left hairline for two years (Figure 1), with ill-defined, indurated plaques. The rash has been stable in appearance since its development. In the past two months, she has also noted a new erythematous right cheek rash (Figure 2). She has used hydrocortisone 1% and clotrimazole 1% on the rash with no effect. Since the onset of the hairline rash, she has also noted low-grade fevers and night sweats. Mrs JR has no background medical conditions and takes no regular medications. She has had no history of travel to high-risk locations. There is no family history of autoimmune conditions.

QUESTION 1

What would be your next step in investigation?

QUESTION 2

What are the histological differential diagnoses of a non-necrotising granuloma?

QUESTION 3

What further investigation(s) would one undertake?

QUESTION 4

What does the chest X-ray show in Figure 3?

ANSWER 1

Further investigation should involve a 4-mm punch biopsy of both lesions on the forehead and right malar cheek for histopathology investigation.

Histopathology showed non-necrotising granulomas composed of epithelioid histocytes, few multinucleated giant cells and rare small lymphocytes surrounded by a population of interstitial lymphocytes, resembling naked granulomas.

ANSWER 2

The histological differential diagnoses of a non-necrotising granuloma are long, and clinical correlation needs to be considered. Common differentials include sarcoidosis, infectious disorders (such as tuberculosis), foreign body reactions, drug reactions, lymphoma, lymphomatoid granulomatosis, antineutrophilic cytoplasmic antibody-associated vasculitis, rheumatoid nodules and inflammatory bowel disease.[1]

ANSWER 3

Given the clinical picture and the histopathology, the most likely diagnosis is sarcoidosis. Any diagnosis of cutaneous sarcoidosis warrants investigation for extracutaneous sarcoidosis. Further initial investigations for a suspected or confirmed sarcoidosis should include:[2,3]

- posteroanterior chest X-ray
- lung function tests
- electrocardiogram

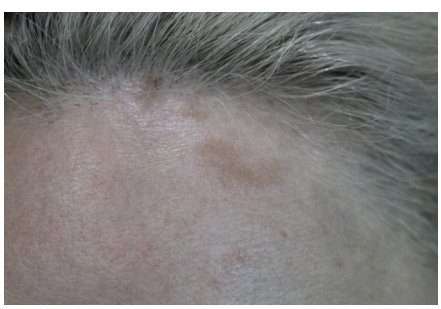

Figure 1. Left forehead rash with ill-defined, indurated plaques.

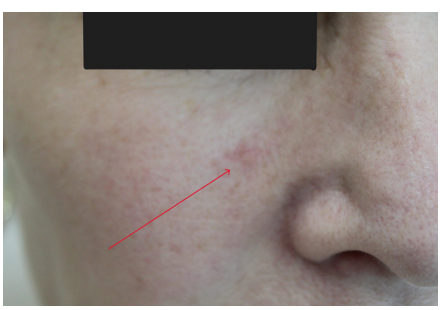

Figure 2. Right cheek macular and erythematous rash (arrow).

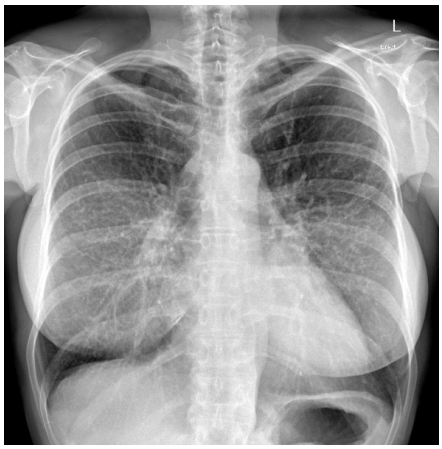

Figure 3. Chest X-ray of the case study (Mrs JR).

- blood tests: full blood count (FBC); calcium; electrolytes, urea and creatinine (EUC); liver function tests (LFTs), serum angiotensin-converting enzyme (ACE)
- urinalysis
- ophthalmologic exam
- tuberculin skin test or interferon release assay to exclude tuberculosis.

ANSWER 4

The chest X-ray shows a reticulonodular pattern in the mid zones bilaterally, consistent with a diagnosis of sarcoidosis.

CASE CONTINUED

Further investigations were performed on Mrs JR to investigate for extracutaneous sarcoidosis. Bloodwork showed elevated serum ACE levels of 125 U/L (reference range 8–70), with normal FBC, calcium, EUCs and LFTs. Elevated serum ACE greater than 50% of the upper limit of normal are highly suggestive of sarcoidosis but are not specific enough to use as a diagnostic test.[2] A high-resolution computed tomography was also performed, which showed extensive reticular nodular interstitial changes throughout the upper lobes and the right middle and lingular segment left upper lobe, and this is most consistent with a sarcoidosis diagnosis. Given systemic involvement, Mrs JR was referred to a respiratory specialist for further investigations and management of her sarcoidosis.

QUESTION 5

What are the cutaneous manifestations of this condition?

QUESTION 6

What are the treatment options?

ANSWER 5

Cutaneous manifestations occur in approximately 25% of patients diagnosed with sarcoidosis[2] and might be the initial manifestation of the disease.[4] These are further categorised into specific lesions, which show non-caseating (sarcoidal) granulomas on histology,[4] and non-specific lesions, which include all other cutaneous manifestations of sarcoidosis. Table 1 explores some of the more common cutaneous manifestations of sarcoidosis.

ANSWER 6

High-quality evidence to support the efficacy of treatment of cutaneous sarcoidosis is lacking.[3,5] Treatment can be challenging and is not required for all patients, as up to two-thirds will have spontaneous remission. The decision to treat will depend on both the patient and the nature of the cutaneous manifestations.[6] Indications for treatment include cosmetic disfiguration (such as with lupus pernio), psychological impact or if lesions are progressive.[7]

First-line therapy for limited disease involves intralesional triamcinolone and topical ultra-potency corticosteroids.[5,7] Systemic agents are used for patients with widespread disease or who do not respond to initial therapy. These include hydroxychloroquine, chloroquine, methotrexate and tetracyclines. Oral glucocorticoids can result in rapid improvement in symptoms; however, given the side-effect profile, they are mainly considered for severe or disfiguring cutaneous sarcoidosis.[5] Biologics, most commonly infliximab, are used for refractory disease.[7] Laser surgery has been reported to improve some disfiguring lesions that have been refractory to other forms of treatment.[7]

Key points

- Cutaneous sarcoidosis is the 'great imitator' and has a wide range of clinical presentations.
- As 25% of patients diagnosed with sarcoidosis have cutaneous manifestations, patients should also be assessed for extracutaneous disease.
- Treatment of cutaneous sarcoidosis varies from topical steroids to systemic immunosuppressants, depending on the extent of the disease and cosmetic or psychological impact.

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Table 1. Cutaneous manifestations of sarcoidosis[4,5]

Specific lesions	Non-specific lesions
Lupus pernio (pathognomonic for cutaneous sarcoidosis)	Erythema nodosum (most common non-specific finding)
Infiltrated plaques	Calcinosis cutis (calcium depositions, most commonly in the skin and subcutaneous tissue)
Maculopapular eruptions	Acute febrile neutrophilic dermatosis (Sweet syndrome; characterised by fever, neutrophilia and tender erythematous plaques or nodules)
Subcutaneous nodules	Nail clubbing
Scars	Erythema multiforme

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