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Case Report

A Misdiagnosed Case of Cutaneous Sarcoidosis: A Case Report and Review of Literature

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Abstract:

Background: Sarcoidosis is a multi-systemic disease that may affect any organ or system. The lungs are the most common affected organ. Extrapulmonary sarcoidosis is rare and cutaneous involvement is the most common extrapulmonary presentation. Cutaneous sarcoidosis is a challenging disease due to its diversity and resemblance to various skin diseases. **Case Report:** We present here a case of cutaneous sarcoidosis without pulmonary involvement. A 47-year-old woman presented with red papules on face one year ago. She was diagnosed as a case of acne vulgaris, however, the skin lesions were resistant to treatment. The patient then developed similar papules on nose, arms, and chest. A skin biopsy showed non-caseating granulomas and systemic workup for sarcoidosis was positive. The patient was eventually diagnosed with sarcoidosis and she was treated by mometasone furoate 0.1% cream and tacrolimus. The skin lesions resolved completely after two months of the treatment. **Conclusion:** This case report spots the light on the importance of considering sarcoidosis in the differential diagnosis of any refractory skin lesions and underscore the significance of early identification of skin manifestations of sarcoidosis, which may predict the development of systemic disease. Patients with CS should be regularly followed up and closely monitored to detect early systemic involvement regardless of the extent of cutaneous involvement.

Keywords: sarcoidosis, cutaneous sarcoidosis, extrapulmonary sarcoidosis, non-caseating granulomas, angiotensin converting enzyme, interleukin-2

1. Introduction

Sarcoidosis is a multisystemic disease with worldwide distribution that characterized by the presence of non-caseating epithelioid granulomas, the latter can be found in any organ. However, the lung is the most common organ involved followed by bilateral hilar lymphadenopathy [1]. Cutaneous sarcoidosis (CS) are the most common extrapulmonary presentations, and may be the only clinical manifestation in the patient [2].

Cutaneous lesions can appear before, during, or after systemic involvement. A biopsy from skin lesions is more accessible and less invasive than a biopsy from the lung or other visceral organs. Therefore, identifying skin lesions can help in early diagnosis and in predicting the outcome of the systemic disease [3,4].

CS varies markedly in morphology, hence the name "great imitator" and it may present with single or multiple red, skin-colored or violaceous macules, papules, plaques or nodules and the diagnosis can be very challenging and often requires clinicopathological and radiographic correlation and laboratory workup as well [4].

CS is classified based on the presence of non-caseating granulomas into: specific lesions which have non-caseating granulomas in skin biopsies and non-specific lesions which do not have such granulomas. The former includes: maculopapules, plaques, subcutaneous nodules, lupus pernio (LP) and infiltrative scars [3,4]. Erythema nodosum is the most common form of the non-specific lesions. Maculopapules and subcutaneous sarcoidosis have a good prognosis. On the other hand, plaque and Lupus pernio have poorer prognosis and are more challenging to treat. [5]

Managing skin lesions of sarcoidosis can be very challenging and the treatment is often frustrating, as lesions may be refractory to therapy or may recur. Treatment options include: topical, for localized involvement, such as: high-potency topical corticosteroids, intralesional triamcinolone injections, tacrolimus in refractory cases, and topical retinoids.

For patients with disfiguring, widespread, extensive or refractory skin lesions systemic treatment may be required such as: corticosteroids, immunomodulatory therapies such as chloroquine and tetracyclines, immunosuppressive treatments such as methotrexate, leflunomide, azathioprine, and biologicals such as tumor necrosis factor antagonists [6].

2-Case Report

A 47-year-old woman presented with red papules on the face for one year which was treated as an acne vulgaris. The patient received topical treatment for acne (Tretinoin and topical antibiotic) with no improvement. The patient then developed similar papules on nose, arms, and chest over a period of 4 months. Dermatological examination showed multiple, rounded, indurated, small (less than 0.5mm), red, firm, not tender, non-pruritic, smooth, papules over the face (Figure 1), nose, both arms and chest. The differential diagnosis included: lymphoproliferative disorders, Hodgkin's lymphoma, leishmaniasis, toxoplasmosis, leprosy and tuberculosis, sarcoidosis, granulomatous rosacea, benign appendageal tumors.

Multiple punch biopsies were taken from the papules on the face and arms and revealed the presence of naked non-caseating epithelioid cell granulomas with giant cells (Figures 2). The majority of these granulomas had no peripheral mononuclear inflammatory infiltrate, while rare granulomas have very thin rim of lymphocytes.

Two types of giant cells were seen within the granulomas; Langhans-type with an arch-shaped arrangement of nuclei at the periphery of the cell and

a foreign-body type with random distribution of nuclei (Figure 3). The giant cells had star-like intracytoplasmic asteroid bodies (Figure 4) and Schaumann bodies which are round calcified protein inclusions within the cells. No evidence of organisms on culture or staining was detected.

Laboratory investigations were done and revealed elevated levels of : C-reactive protein (CRP) (13 mg/dl, normal range is 0.8-1.0 mg/dL mg/dl), erythrocytes sedimentation rate (ESR) (34 mm, normal range is less than 20 mm/hr), serum angiotensin-converting enzyme (ACE) level (114 IU/ml, normal range: 20-95 IU/ml), interleukin-2 (IL-2) (1080.45 pg/mL; reference range: 175.3-858.2 pg/mL), IL-6 (24.26 pg/ml, normal range is up to 7 pg/ml). Total serum calcium was slightly elevated (11.4 mg/dl, normal range is 8.1-10.4 mg/dl).

The patient had no respiratory symptoms. There were no systemic and constitutional symptoms, and she was otherwise well. General physical and systemic examinations were unremarkable and dermatological history was not significant. Chest x-ray was unremarkable and both lung fields were clear. Lung function tests were normal. Renal function tests were performed to exclude renal sarcoidosis due to the presence of hypercalcemia and they were normal.

Based on the patient's history, physical examination, histopathological and laboratory findings (elevated, ACE, IL-2, IL6, and calcium); a diagnosis of cutaneous sarcoidosis without systemic involvement was made. Therefore, our patient was treated by local mometasone furoate 0.1% cream, 30 g twice daily for two weeks then two times/week for two months and tacrolimus 0.1% ointment once a day twice weekly. The cutaneous papules started to fade gradually after one month and resolved completely after two months of the treatment course with no subsequent relapse. The patient was followed up by a regular chest x-ray after 3 months that shows no involvement of both lungs.

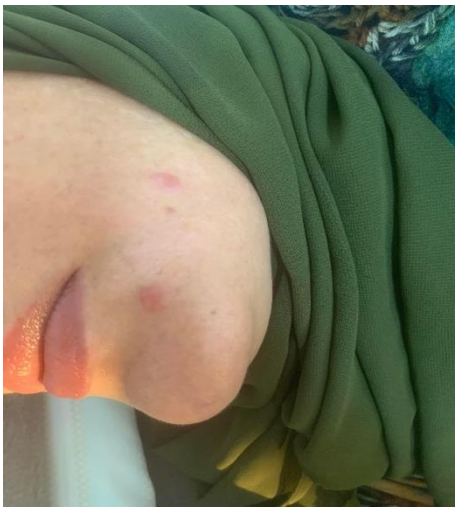

Figure 1: Multiple red papules on the face.

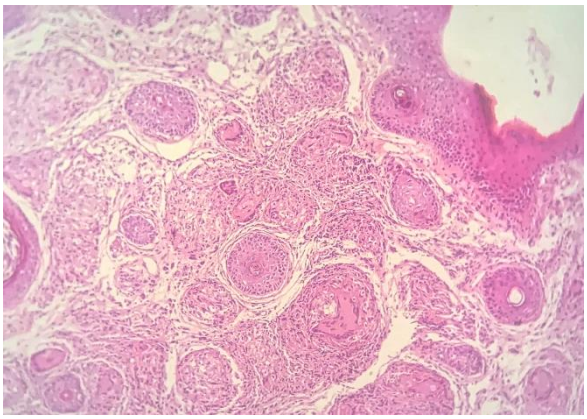

Figure 2: Low power view showing multiple dermal non-caseating granulomas (H & E ×40).

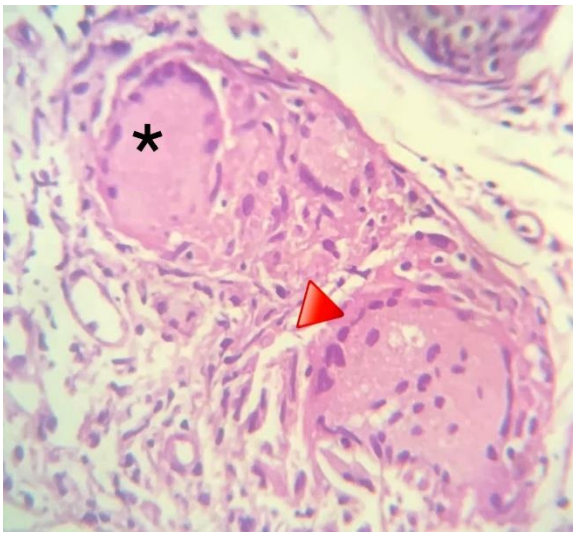

Figure 3: Two non-caseating granulomas showing Langhans giant cells (asterisk) and foreign-body type giant cells (arrow head) (H & E ×200).

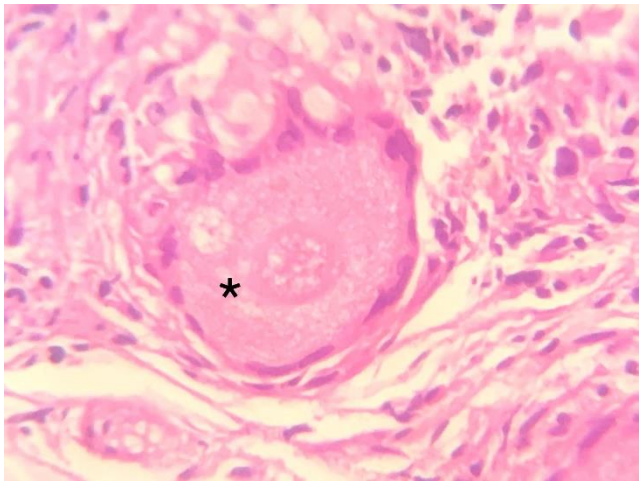

Figure 4: Giant cell containing star-like intracytoplasmic asteroid bodies (asterisk) (H & E ×400).

3-Discussion

Sarcoidosis is a diagnosis of exclusion due to its markedly variable clinical presentation and multisystemic involvement and it is a diagnostic challenge to all physicians. Diagnosis depends on a compatible clinical and radiological picture, the presence of non-caseating granuloma in a biopsy from affected site [7].

It was shown that almost 25 % of patients had CS before the development of systemic manifestations and the prevalence of systemic involvement in CS varies from 29–90%. Female sex, younger age (<54 years), high levels of ACE, IL-2R and CRP were significantly associated with systemic manifestation [1].

Our patient was initially misdiagnosed as a case of acne vulgaris, and she had received local treatment for acne for one year with no response, therefore, a punch biopsy was taken which revealed the presence of classical naked non-caseating granuloma, a finding consistent with that

of existing literature which documented that naked granuloma is pathognomonic for sarcoidosis [8,9]. However, Mahabal et al., found naked granulomas in only 55.3% of cases in their series, while the remaining 44.7% of cases exhibited non-naked granulomas [10].

The histopathological findings of sarcoidosis were supported by laboratory tests which revealed elevated levels of CRP, ESR, serum ACE, IL-2, and IL-6, and slightly elevated total serum calcium. ACE is a marker of sarcoid activity, it is produced in the epithelioid cells of the sarcoid granuloma under the stimulation of T-cells and its level is elevated in about 60-80% of patients. However, it is not sensitive nor specific to sarcoidosis [7]. On the other hand, IL-2 is a recent biomarker and is more sensitive and superior to ACE for diagnosing sarcoidosis. Elevated serum ACE and IL-2 levels were reported to be significantly associated with systemic involvement and low IL-2R levels were detected in patients without pulmonary disease [1].

A comprehensive history taking from our patient and complete physical examination were performed to detect the presence of extra-cutaneous disease. Furthermore, the patient performed chest x-ray and pulmonary function tests to exclude respiratory disease and no extra-cutaneous disease could be identified.

Boch et al in their cohort study, found that 38% of patients had an isolated cutaneous disease, while 62% of patients developed a multi-systemic disease during follow-up [1]. Similarly, mahabal et al reported that six patients had isolated cutaneous sarcoidosis without systemic disease [10].

Of note, this patient has mildly elevated serum calcium. Hypercalcemia in sarcoidosis may indicate renal or rarely bone marrow involvement [7]. However she did not suffer from renal or bone marrow sarcoidosis.

Once our patient was correctly diagnosed and received topical steroid and tacrolimus ointment, the papules started to fade gradually and resolved

completely after two months and she was kept in a regular follow-up every 3 months with clinical and radiological monitoring to detect any systemic manifestations which could be developed later on during the course of the disease

4-Conclusions

This case report casts the light on the value of skin biopsy in diagnosing the cutaneous lesions of sarcoidosis and highlights the importance of considering sarcoidosis in the differential diagnosis of any refractory skin lesions. Our patient has been misdiagnosed as a case of acne and treated for one year without improvement, therefore, recognizing the different manifestations of CS can help in early diagnosis. Furthermore, early identification of cutaneous manifestations of sarcoidosis may predict the presence of systemic disease. Patients with sarcoidosis limited only to skin should be regularly followed up to check disease activity and to detect early systemic involvement regardless of the extent of cutaneous involvement.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) of [THE BIOMEDICAL RESEARCH ETHICS COMMITTEE] (Approval No. (HAPO-02-K-012-2024-02-2041) and date of approval:03/04/2024).

Informed Consent Statement: The authors obtained written consent from patients for their photographs and medical information to be published in print and online and with the understanding that this information may be publicly available

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