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Case Report

Darier Roussy Subcutaneous Sarcoidosis from Nepal: A case report

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ABSTRACT

Introduction: Sarcoidosis is a common, multisystemic non-caseating granulomatous disease of unknown etiology with cutaneous lesions present in about one-fourth of patients. Darier Roussy sarcoidosis is a rare variant of sarcoidosis with distinct cutaneous presentation characterized by multiple deep-seated nodules on the trunk and extremities which could either be asymptomatic or may present mild tenderness.

Case presentation: A case of 35 yrs male with cough and fever for 3 months was initially diagnosed as a case of tubercular lymphadenitis and started with ATT following which ATT-associated cutaneous adverse drug reaction was suspected due to development of rashes with generalized redness and mild itching a few weeks after starting ATT. He then developed multiple, skin-colored, deep-seated, subcutaneous lesions over the legs then over the arms, forearms, thigh, and trunk. FNAC and histopathological examination of the lesions revealed non-caseating granulomas composed localized to the subcutaneous tissue. A diagnosis of subcutaneous sarcoidosis was made. Subsequently, steroid therapy was started.

Discussion: Clinical manifestations of sarcoidosis range from asymptomatic (mostly) to progressive and relapsing disease. A family history of the disease raises the risk; those with one afflicted first-degree relative face a 3.7-fold increase in risk. Sarcoidosis is diagnosed based on three key criteria: a consistent clinical presentation, the discovery of non-necrotizing granulomatous inflammation in one or more tissue samples with confirmed histology, and the elimination of other origins of granulomatous disorders. . Diagnosis should be confirmed with a biopsy of the lesion, with the histological finding of non-caseating granuloma

Conclusion: Clinically localized subcutaneous sarcoidosis can be confused with ATT induced drug reaction due to the difficulties in diagnosing granulomatous skin disease. The prognosis is good with subcutaneous disease and if there are no disfiguring skin lesions or other critical organ involvement, corticosteroid therapy might suffice

1. Introduction

Sarcoidosis is a multisystem chronic granulomatous disease of unknown etiology, characterized by non-caseating granuloma in various organs and tissues - skin, lungs, lymph node, kidney, and heart. Sarcoidosis affects people of all races and ethnic groups, as well as both sexes, with a small female predominance [1]. Cutaneous symptoms of Sarcoidosis occur in up to 9%–37% of individuals and can sometimes be the first sign of systemic presentation of the disease. Previous estimates of the prevalence of subcutaneous sarcoidosis varied from 1.4% to 6%, with more recent research indicating an occurrence rate of 11.8% to 16% [2] (see Figs. 1–6)

Subcutaneous sarcoidosis, a rare skin manifestation of sarcoidosis, also known as 'Darier-Roussy sarcoid', is a cutaneous disorder characterized by multiple deep-seated nodules measuring 0.3–0.5 cm on the trunk and extremities which could either be asymptomatic or may present mild tenderness [3].

Although immunopathogenesis is unknown, it is hypothesized that presenting a putative antigen to a cluster of T cells ($CD4^+$ T cells) triggers a cellular immune response and cytokine secretion (tumor necrosis factor-alpha, interleukin-12, interleukin-15, interleukin-18, and macrophage inflammatory protein-1) that results in granulomatous inflammation [4]. Few cases of cutaneous sarcoidosis is believed to be an abnormal host response to various types of a microbial organism - M. paratuberculosis, histoplasmosis, and fungi.

Angiotensin-converting enzyme, gallium 67 scan, and bronchoalveolar lavage are the three primary assays that determine activity. In sarcoidosis patients, ACE levels in the blood are frequently increased.

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The synthesis and secretion of ACE by the epithelioid cells of sarcoid granulomas are responsible for the increase. It can be used clinically to assess the granuloma load, although it has limitations [5].

The disease usually resolves by itself and does not require treatment in the majority of cases.

Topical or intralesional (i.e. injected) corticosteroids are the first-line treatment for localized and mild cutaneous sarcoidosis, and are typically advised for disfiguring, aesthetically unpleasant, and symptomatic diseases [6]. Individuals requiring prolonged use of corticosteroids are better treated with a second line of drugs or glucocorticoid-sparing anti sarcoidosis medicines like Methotrexate, azathioprine, leflunomide, mycophenolate and hydroxychloroquine. Hydroxychloroquine is effective in the treatment of individuals with cutaneous nodules, increased calcium levels, and neurological involvement. If the first and second line of drugs are ineffective, the third line are used (Infliximab and adalimumab) [1].

This case report has been reported in line with the SCARE 2020 criteria [7].

2. Case presentation

A 36-years male presented to the hospital with complaints of cough and fever for 3 months. The cough was non - productive and dry. There was no history of wheezing, stridor, hemoptysis, chest pain, breathlessness or seasonal variation. He then developed fever after 3–4days. Fever was insidious on onset and continuous in nature (99–100°) with evening rise of temperature up to 101°. Initially, the individual was treated with paracetamol and antibiotics which didn't result in the resolution of signs and symptoms. Multiple visits were carried out by the individual in the next 2 months for his symptoms. As there was no resolution of fever and cough he was also suspected to have Pyrexia of unknown origin (PUO). During this period, the patient became anorexic and there was an approximate weight loss of about 10 kgs. He was admitted for an extensive evaluation of his condition. HRCT chest was done which depicted normal results. However, the patient continued to have the symptoms. Thereafter, CECT (chest and abdomen) was performed after 2 months, which showed mediastinal lymphadenopathy mostly in the right paratracheal, pre tracheal, and subcarinal region. He underwent bronchoscopy 3 times with normal results. EBUS-TBNA from the mediastinal lymph node was performed which showed positive culture results for AFB. The aspiration smear showed multiple granulomas formed by aggregates of epithelioid cells. However, caseous necrosis and atypical cells were not seen. Clot core biopsy from EBUS-TBNA revealed fibrinous material and few inflammatory cells consisting of neutrophils and lymphocytes. A provisional diagnosis of Tubercular Lymphadenitis was made following which he was started on ATT. Rashes with generalized redness and mild itching appeared a few weeks after starting ATT. ATT-associated cutaneous adverse drug reaction was suspected and ATT was stopped immediately, and antihistamines were started. He then developed multiple, skin-colored, deep-seated, subcutaneous lesions measuring 1x2x3 cm initially over the legs then over the arms, forearms, thigh, and trunk. The lesions were mildly tender on palpation. The number of lesions increased gradually over time. Dermatologic consultation was done and FNAC of the upper limb nodule was performed which revealed discrete, multiple, small, well-formed, non-caseating granulomas composed of epithelioid cells and lymphocytes localized to the subcutaneous tissue. Lymph node biopsy showed numerous confluent naked granuloma surrounded by a moderate amount of lymphocytes. Numerous multinucleated giant cells and

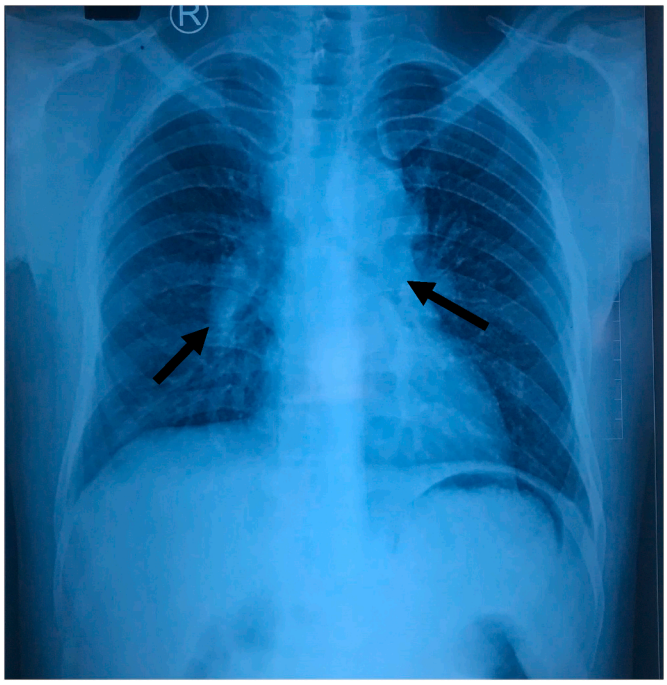

Fig. 2. Chest radiograph showing bilateral hilar adenopathy (right more than left). Multiple small homogenous opacities seen in the mediastinal region. (shown by arrow).

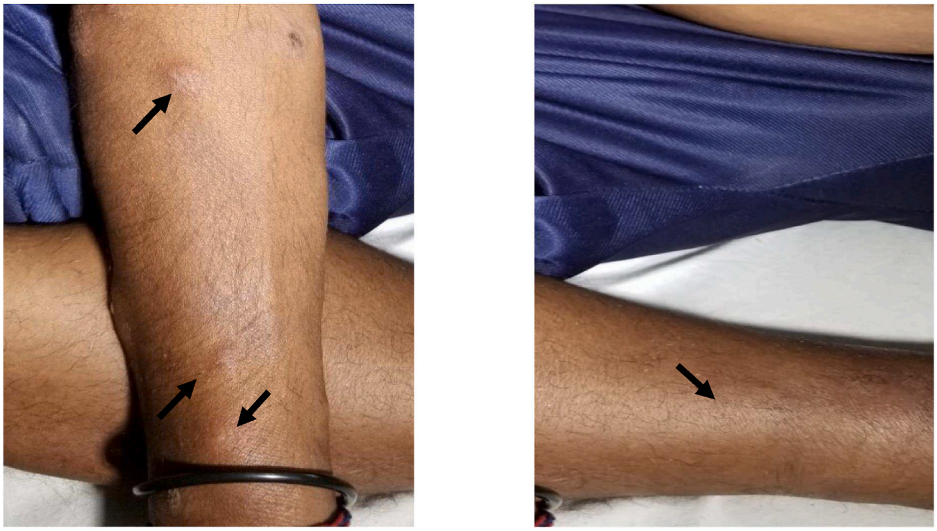

Fig. 1. Multiple, skin-colored, deep-seated, subcutaneous lesions over the arms and legs (shown by arrow).

langhan type giant cells were also noted. Serum ACE level was found to be elevated (199.00U/L) which was consistent with sarcoidosis. A diagnosis of subcutaneous sarcoidosis was made and Steroid therapy was started.

2.1. Treatment

A tapering dose of Prednisolone 1mg/kg/day (60mg) was started. Fever and cough subsided after 15 days of starting the treatment. Same dose of prednisolone was continued for 2 months and then the dose was tapered by 5 mg every two weeks. Presently, he is on prednisolone 5mg/day. The subcutaneous lesions have resolved completely. The treatment plan is to continue prednisolone@ 5mg/day for 2 more months and stop thereafter.

3. Discussion

The clinical manifestations of sarcoidosis range from asymptomatic (mostly) to progressive and relapsing disease. It may lead to dysfunction of various systems (CNS, CVS, musculoskeletal, ocular, pulmonary, lymphatic systems). Non severe form of pulmonary sarcoidosis with bilateral hilar adenopathy is the most prevalent systemic finding in patients with sarcoidosis.

Skin manifestations caused by sarcoidosis are highly variable and can resemble many skin diseases. Cutaneous sarcoidal lesions include papules, scar-associated sarcoidosis, erythema nodosum, lupus pernio, plaques, alopecia, calcifications, erythema multiforme, hypo- and hyper-pigmentation, occasionally, subcutaneous nodules (so-called Darier–Roussy sarcoidosis) [6,8]. Subcutaneous sarcoidosis which are sarcoidal granulomas restricted to the subcutaneous tissue, can be the sole manifestation of sarcoidosis without systemic involvement. It is characterized by a peak incidence during the fourth decade, female predisposition, asymptomatic to slightly tender lesions. Men's incidence is said to peak between the ages of 30 and 50, while women's are 50 and

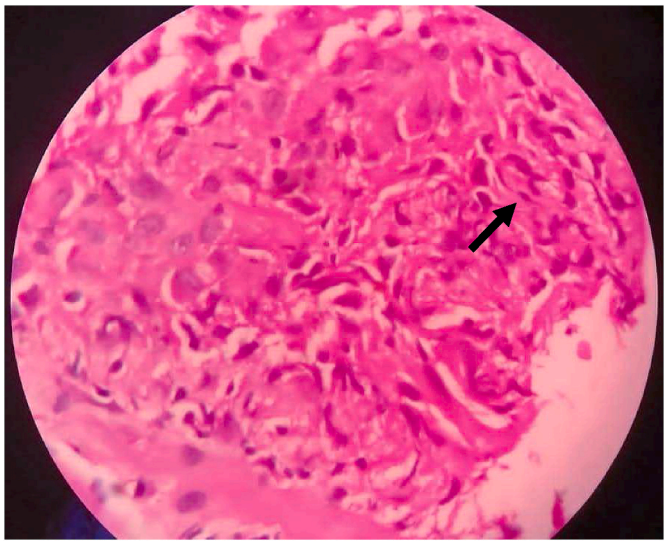

Fig. 4. Aggregates of epithelioid histiocytes (shown by arrow).

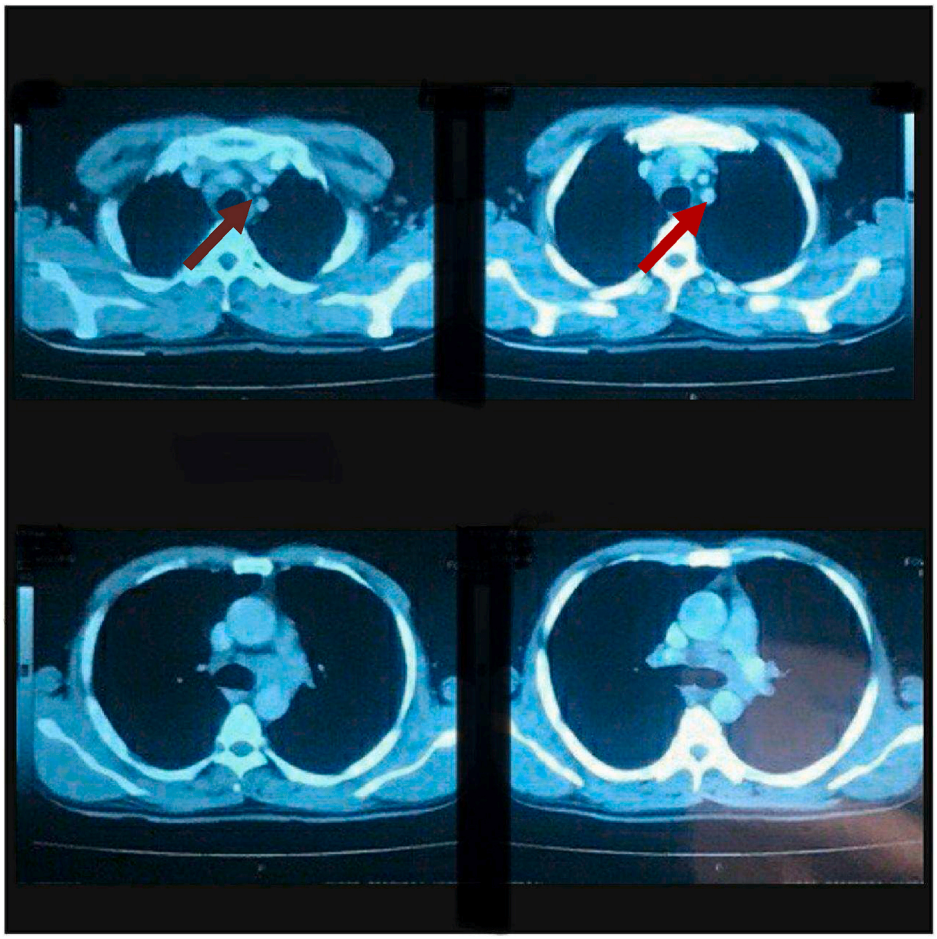

Fig. 3. CECT of chest showing multiple, enlarged, hypoenhancing, mediastinal lymph nodes in the right paratracheal, pretracheal stations along with enlarged lymph nodes in the left hilum. Few subcentimetric lymph nodes are seen in right hilum. (shown by arrow).

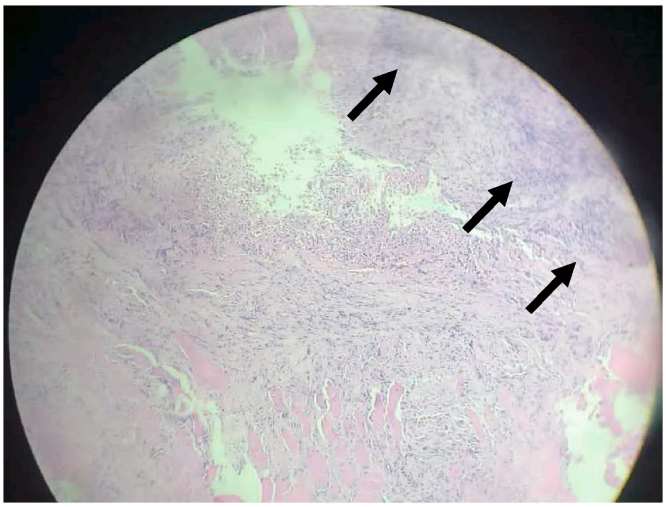

Fig. 5. Numerous multinucleated giant cells and langhan type giant cells (shown by arrow).

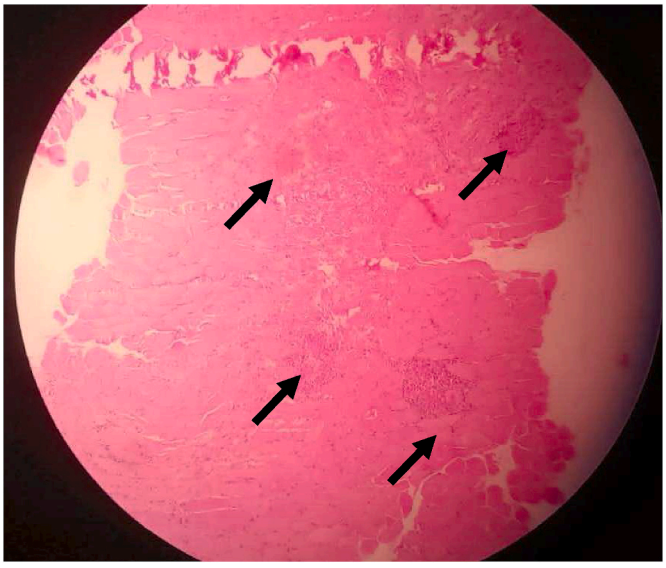

Fig. 6. Multiple unencapsulated tissue bits with fibrocollagenous tissue comprising of numerous well-formed, non-caseating granulomas composed of epithelioid cells and lymphocytes (shown by arrow).

60. A family history of the disease raises the risk; those with one afflicted first-degree relative face a 3.7-fold increase in risk [1].

Sarcoidosis is diagnosed based on three key criteria: a consistent clinical presentation, the discovery of non-necrotizing granulomatous inflammation in one or more tissue samples with confirmed histology, and the elimination of other origins of granulomatous disorders [9].

In most places, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has lately acquired a popularity for sarcoidosis diagnosis. Although TBNA outperforms the CD4/CD8 ratio, it does necessitate the presence of mediastinal lymphadenopathy. or negative. Furthermore, in more advanced radiographic stages of sarcoidosis, the BALF CD4/CD8 ratio is lower [10].The physician must recognize this group and start treatment right away. The Practitioners should be conscious of various factors or conditions that might change BALF (Bronchoalveolar Lavage Fluid) CD4/CD8 ratios, such as active smoking and advanced age, when considering a CD4/CD8 ratio in situations when EBUS is unknown, unattainable or negative [5].

Because sarcoidosis-related skin eruptions are very varied and can resemble a variety of skin illnesses, diagnosing cutaneous sarcoidosis solely based on signs and symptoms can be challenging. Diagnosis should be confirmed with a biopsy of the lesion, with the histological finding of non-caseating granuloma.

4. Conclusion

This case demonstrates that clinically localized subcutaneous sarcoidosis can be confused with ATT induced drug reaction due to the difficulties in diagnosing granulomatous skin disease.

According to the recommendations, for disfiguring illness Intralesional followed by oral corticosteroids should be used initially, followed by hydroxychloroquine if the former is not tolerated or effective. Although the period of treatment is unpredictable, the end goal is frequently resolution [8].

The prognosis is good with subcutaneous disease and if there are no disfiguring skin lesions or other critical organ involvement, corticosteroid therapy might suffice.

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Ethical approval

This is case report: therefore, it did not require ethical approval from ethics committee.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal on request.

Author contribution

All authors: writing the paper, collection of Data, revising it critically for important intellectual content, review and editing.

Registration of research studies

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

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Declaration of competing interest

The authors declare that they have no competing interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104164.

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