Cutaneous Sarcoid Reaction in a Case of Acute Lymphoblastic Leukemia

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Abstract
Sarcoid reactions are noncaseating granulomas that simulate sarcoidosis. Since they do not fulfill the rest of the criteria to diagnose systemic sarcoidosis, they have a separate identity. They are often reported in draining lymph nodes of malignancies. However, they can also occur in the skin forming “Cutaneous sarcoid reaction” – such as this case. We report the case of a 17-year-old female with itchy papules persistent for 3 months while she had no other complaint. The papules were present on the trunk and lower extremities. The general examination was unremarkable except for cervical lymphadenopathy. Bone marrow aspirate and biopsy revealed features of “acute lymphoblastic leukemia (ALL)”. As the peripheral blood smear showed no blasts, it was hard to diagnose her leukemia. Skin biopsy showed features of granulomatous reaction simulating sarcoidosis. Her final diagnosis was compatible with “aleukemia form of ALL”. The patient was started on chemotherapy and her itching was relieved with treatment. The skin papules were resolved leaving behind hyperpigmentation. The link between sarcoïdal reactions and malignancies still needs further research. However, cutaneous sarcoïdal reactions may be the first presentation of systemic malignancy. Patients presenting with sarcoïdal reactions should be investigated to exclude the associated malignancy.

Keywords: Cutaneous sarcoïd granulomas, hematological malignancies, sarcoïd reactions

INTRODUCTION
Sarcoïd reaction (also referred to as sarcoïdal or sarcoïd-like reaction) is an inflammatory condition in which noncaseating granulomas develop within one or several body sites. They occur in patients who have clinical and histological features resembling sarcoidosis but not fulfilling the diagnostic criteria for systemic sarcoidosis.[1]

Several malignancies, especially hematological malignancies and lymphomas, have been linked with sarcoïd reactions. In addition, sarcoïd reactions might be the only presentation of their underlying disease.[2] These reactions most commonly develop within draining lymph nodes of tumors but may also develop in other organs such as skin, lungs, and spleen.[3]

We report a case of cutaneous sarcoïd reaction as a presentation of an underlying aleukemia form of “acute lymphoblastic leukemia (ALL)”.

CASE REPORT
A 17-year-old female was presented with painful reddish lesions of 3 months’ duration. The lesions were very itchy and were distributed on the chest [Figure 1] and both legs. There was no drug intake before the onset of skin lesions. Skin examination revealed reddish papules of different sizes ranging from 0.5 cm to 1 cm distributed over the trunk and on lower extremities. The general examination was unremarkable except for cervical lymphadenopathy.

Investigations showed microcytic hypochromic anemia, absolute neutropenia, and lymphopenia. Erythrocyte sedimentation rate was normal; tests for viral markers (Epstein–Barr virus, human immunodeficiency virus), antinuclear antibodies (ANA), anti-DsDNA, anti-RNP, and the tuberculin test were negative. Serum calcium, chest X-ray, and urine and stool analyses were normal. C3 was normal while C4 was elevated.

Skin punch biopsy was taken from one of the papules on the upper back. The clinical differential diagnosis included leprosy, and were distributed on the chest [Figure 1] and both legs. There was no drug intake before the onset of skin lesions. Skin examination revealed reddish papules of different sizes ranging from 0.5 cm to 1 cm distributed over the trunk and on lower extremities. The general examination was unremarkable except for cervical lymphadenopathy.

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Skin punch biopsy was taken from one of the papules on the upper back. The clinical differential diagnosis included leprosy,
cutaneous leiomyomas, and sarcoidosis. Histopathologic examination demonstrated intact stratified squamous epithelium. Granulomatous masses were scattered in the dermis with no central caseation [Figures 2-4]. Granulomatous masses were formed of epithelioid cells, plasma cells, lymphocytes, and multinucleated giant cells resembling sarcoidosis. There was no evidence of cytologic atypia. Tissue stains for acid-fast bacilli (fite stain) and reticular fibers (reticulin stain) were negative.

Radiographic examinations including abdominal ultrasound and computed tomography chest and abdomen showed hepatosplenomegaly with pretracheal, para-aortic lymph node enlargement. X-rays on skull, chest, and long bones were normal.

Bone marrow aspiration and biopsy showed hypercellular bone marrow with diffuse proliferation of lymphoblasts counting for more than 25% of bone marrow cells. The erythroid and myeloid series were depressed, while the megakaryocytes had good platelet separation. She was finally diagnosed with “aleukemic form of ALL”. This diagnosis was made as there were no blast cells in the peripheral smear. Based on the correlation of the clinical presentation, histopathologic findings, and laboratory studies a diagnosis of “cutaneous sarcoid reaction”. secondary to ALL was made.

The patient was started on chemotherapy sessions with L-asparaginase and doxorubicin. Her itching sensation was relieved and the skin lesions resolved leaving hyperpigmentation following treatment. But unfortunately 4 months later, she developed relapse of her condition and died shortly thereafter.

**Discussion**

The first account of sarcoid reaction was described in 1869, by British physician Jonathan Hutchinson.\[^3\] It may occur following various causes such as infections (bacterial, fungal, or viral).\[^4\] In addition, chemicals and foreign materials such as silicates in talc that is used as a glove powder can induce granulomas in surgical wounds.\[^2\] In addition, it was reported that sarcoid reactions can occur at the site of tattoos.\[^5\]
Although the association between systemic sarcoidosis and malignancy is well known, the link between sarcoid reactions and malignancy still needs further investigations. Sarcoid reactions have been described in association with numerous hematological malignancies and solid tumors, but the exact mechanism has not yet been elucidated.

It has been postulated that the development of sarcoid-like granulomas with malignancy represents a host immune defense mechanism to tumor cells,\[6\] or an immunological reaction to antigenic substances released from the tumors and transported along the lymphatic system.\[6,7\]

They most commonly develop within draining lymph nodes, but these granulomas may also develop in other organs such as skin, lungs, and spleen\[1\] or in the tumor itself.\[8\] These reactions are most commonly presented with Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, and leukemias.\[2\] They are also reported with breast cancer, prostatic cancer, colon cancer, renal cancer, lung cancer,\[9\] and squamous cell carcinoma.\[10\]

This case report aimed to direct dermatologist’s attention to exclude internal malignancy with any case of cutaneous sarcoid reaction. As skin lesions can be the only presentation, full checkup must be done for early detection of the underlying cause.

In our case, absence on blasts in peripheral blood picture made her case harder to diagnose “aleukemic type of ALL.” However, rapid resolution of patient’s skin lesions after chemotherapy sessions confirmed the relation with her leukemia.

**Conclusion**

Cutaneous sarcoid reactions can be the first presentation for the underlying malignancy. Patients are referred to the dermatologists for their skin lesions and dermatologists must be aware of such conditions as they play a critical role in the diagnosis and in suspecting their underlying malignancy. While treatment the underlying condition, skin lesions will mostly recover too.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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Indian Journal of Dermatopathology and Diagnostic Dermatology • Volume 5 • Issue 1 • January-June 2018