Erythema annulare centrifugum in a case of chronic myeloid leukemia

Prabhat Agrawal¹, Amit Kumar², Nikhil Pursnani¹, Geetika Agarwal³, Satyanand Sathi⁴

¹PG. Department of Medicine, S.N. Medical College, Agra, Uttar Pradesh, ²Dermatologist at Cosmoderma, Sumit Sadan, Hinoo Main Road, Ranchi, Jharkhand, ³MBBS Intern, Safdarjung Hospital, New Delhi, ⁴Department of Medicine, SMMH Government Medical College, Saharanpur, Uttar Pradesh, India

Abstract

Chronic myeloid leukemia (CML), BCR-ABL1-positive, is classified as a myeloproliferative neoplasm predominantly composed of proliferating granulocytes and determined to have the Philadelphia chromosome/translocation t (9;22)(q34;q11.2). Skin is said to be the mirror to systemic diseases, with skin manifestations ranging from nonspecific cutaneous lesions to specific lesions. The cutaneous manifestations of CML are generally reddish-brown to violaceous papules and nodules, indurated or hemorrhagic plaques, perifollicular aceniform papules, bullae, and palpable purpura. Other unusual manifestations could be erythema nodosum, pyoderma gangrenosum, erythema annulare centrifugum, and so on. Here we present a case of a 50-year-old woman with a history of recurrent pruritic skin lesions and erythema annulare centrifugum as the presenting complaint of CML.

Keywords: CML, erythema annulare centrifugum, paraneoplastic erythema annulare centrifugum eruptions

Introduction

Cutaneous lesion in any patient is often dealt by a family physician. So it is important and pertinent for a family physician to know that many times dermatological lesions can be a manifestation of a systemic disease. Chronic myeloid leukemia (CML) is one of the myeloproliferative neoplasms derived from pluripotent hematopoietic stem cells characterized by reciprocal translocation between long arms of chromosomes 22 and 9. Thus, shortening of the short arm of chromosome 22 is a diagnostic evidence for CML. Rare presenting symptoms of CML are tinnitus, diplopia, papilloedema, and priapism. Here, we report a case of a 50-year-old woman who presented to our outdoor department with erythematous annular pruritic lesions which were revealed to be a “paraneoplastic presentation of CML. These lesions regressed after two weeks of starting Imatinib.”

Case Report

A 50-year-old woman presented with multiple itching skin lesions over her abdomen and lower limbs for the past 5 to 6 months. She denied having any history of fever, drug intake, or local application of any cream/ointments. There were no signs or symptoms related to any bacterial, viral, or fungal infections or active systemic disease or any associated history of drug or food allergy. General examination of the patient was unremarkable except for mild pallor. Cardiovascular, respiratory, and neurological examinations were within normal limits. Abdominal examination revealed moderate splenomegaly. On examination, we found multiple erythematous to violaceous annular plaques with central clearing...
measuring around $1 \times 2$ cm to $5 \times 5$ cm with well-defined and raised margins; few lesions were discrete, few coalesced to form larger lesions over the back, and few were also present over the right breast and bilateral thigh. Local temperature was not high, and the lesions were non-tender [Figures 1 and 2]. There were also some discretely arranged purpuric lesions on the anterior aspect of the right leg and the left elbow [Figure 3].

Laboratory investigations reported Hemoglobin 9.9 gm/dl, Total leukocyte count-1,15,610/cu mm, 30% Neutrophils, 10% Lymphocytes, 2% Monocytes, 2% Eosinophils, 2% Basophils, 21% Metamyelocytes, 25% Myelocytes, 6% Promyelocytes, and 2% Blast cells; these were suggestive of the chronic phase of CML. FISH analysis determined the presence of BCR/ABL1 fusion gene representing t (9;22), which is characteristic of CML. The sample showed a typical profile for the signal pattern of the fusion gene confirming the diagnosis of CML. The patient refused for a skin biopsy, and we took the opinion of dermatology department which confirmed that these lesions were erythema annulare centrifugum (EAC). This patient was thereafter diagnosed with PEACE (Paraneoplastic Erythema Annulare Centrifugum Eruptions) based on the characteristics of the lesion and the concurrent presence of lymphoproliferative disease (CML).

We started Tab Imatinib Mesylate 400 mg daily, and follow-up was done every week. The lesions eventually started regressing by Day 14 and completely disappeared by Day 21 of starting Imatinib therapy. Her TLC started decreasing; at the end of third week, she became normal (8900 cu mm); and on peripheral smear there were no immature/abnormal cells.

**Discussion**

CML is a lymphoproliferative disorder often presenting in the middle- to elderly-age group. Early in the course of the disease, patient may be asymptomatic or may have nonspecific symptoms like fatigue, weight loss, and anorexia. Here we reported a case of CML who presented with PEACE that gradually resolved on starting Imatinib therapy.[8]

A previously published case report has revealed similar findings in an Imatinib-resistant CML case with EAC lesions and speculated that the lesions were due to underlying malignancy as they regressed on starting Ponatinib.[9,10] Erythema annulare centrifugum (EAC) when associated with underlying malignancy is referred to as paraneoplastic erythema annulare centrifugum eruptions (PEACE), and it is of utmost importance to diagnose these lesions as they may also lead to the diagnosis of the causative malignancy promptly.[11] It is postulated that in such cases EAC occurs as a consequence of the cytokines and other tumor factors released by the malignant cells, resulting in these reactive cutaneous plaques.[12]

EAC can be categorized as a hypersensitivity reaction or may represent an underlying malignancy in which case it presents as a paraneoplastic syndrome. Numerous systemic diseases, food allergies, drugs, and infectious causes like bacterial, fungal, and viral along with malignancies, particularly lymphomas and leukemia, have been implicated in causing EAC indicating a
multifactorial etiology. EAC may also be idiopathic, and it is important that a thorough clinical examination and relevant investigations should be undertaken to rule out the causes of these lesions. Clinically, EAC may be seen as superficial plaques or deep indurated plaques in which case the superficial pruritic lesions are often times associated with a trailing scale along the centrifugal expanding edges of the lesions, not commonly seen in the case of deep plaques. Histologically, these lesions are reported as perivascular lymphohistiocytic infiltrates involving the dermis with papillary dermis edema, with or without epidermal changes.

PEACE syndrome can also be a sign of reactivation of the underlying cancer when previous history of remission of malignancy is present. Our patient presented with skin lesions and was timely diagnosed due to prompt recognition of EAC lesions followed by a detailed clinical examination and diagnostic workup.

Conclusion

A primary care physician encountering patients presenting with skin lesions in day-to-day practice needs to conduct a detailed clinical examination and diagnostic workup for timely diagnosis and proper management. If needed consultation with a specialist can also be taken. Thus, it is concluded that the established cutaneous manifestation of diseases should be kept in mind as differential diagnosis before arriving at diagnostic conclusions.

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 patient(s) understands that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

References

1. Nakatani K, Kurose T, Hyo T, Watanabe K, Yabe D, Kawamoto T, et al. Drug-induced generalized skin eruption in a diabetes mellitus patient receiving a dipeptidyl peptidase-4 inhibitor plus metformin. Diabetes Ther 2012;3:14.
2. Gupta M, Gupta A. Fixed drug eruption to sitagliptin. J Diabetes Metab Disord 2015;14:18.
3. Maharjan K, Adhikari S, Amatya A, Kayastha G, Basnyat B. Erythema annulare centrifugum in a patient with chronic myeloid leukaemia on ponatinib. J R Coll Physicians Edinb 2020;50:54-5.
4. McDaniel B, Cook C. Erythema Annulare Centrifugum. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482494/. [last accessed 2020 Aug 29].
5. Chodkiewicz HM, Cohen PR. Paraneoplastic erythema annulare centrifugum eruption: PEACE. Am J Clin Dermatol 2012;13:239-46.
6. Kim DH, Lee JH, Lee JY, Park YM. Erythema annulare centrifugum: Analysis of associated diseases and clinical outcomes according to histopathologic classification. Ann Dermatol 2016;28:257-9.
7. Mu EW, Sanchez M, Mir A, Meehan SA, Pomeranz MK. Paraneoplastic erythema annulare centrifugum eruption (PEACE). Dermatol Online J 2015;21:13030/qt6053h29n.