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Case report

Ponatinib and erythema annulare centrifugum: a rare cutaneous reaction in a patient with chronic myeloid leukemia

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Abstract

Erythema Annulare Centrifugum (EAC) is a rare form of reactive erythema, often idiopathic but sometimes associated with a paraneoplastic etiology or certain medications. This case report describes a 69-year-old patient with chronic myeloid leukemia (CML) who developed clinically confirmed EAC within a month of initiating Ponatinib. The case highlights the diagnostic challenge of distinguishing skin eruptions related to a paraneoplastic process from drug-induced reactions. Despite the emergence of EAC, Ponatinib was continued due to the patient's favorable clinical and biochemical response to CML treatment. This case emphasises the importance of balancing dermatological adverse effects with oncological benefits in therapeutic decision-making.

Key words: erythema annulare centrifugum, chronic myeloid leukemia, ponatinib

Introduction

EAC is a rare entity of reactive erythema characterised by annular-shaped erythematous plaques with a trailing scale. It is associated with various etiologies but often idiopathic. EAC is thought to be caused by hypersensitivity due to interactions between inflammatory cells, mediators, and foreign antigen substances[1,3,7]. When EAC occurs as a paraneoplastic phenomenon, it is referred to as paraneoplastic erythema annulare centrifugum eruptions (PEACE)[2]. Certain drugs are also aetiological factors.

Herein we report an elderly patient with CML currently undergoing treatment with Ponatinib, recently diagnosed with EAC. This report explores possibilities of PEACE or EAC as an adverse effect of Ponatinib.

Case presentation

A 69-year-old known patient with CML for 8 years presented with asymptomatic slowly progressive dry scaling skin lesions in bilateral armpits and groins for five months duration. There was no history of previously diagnosed skin disease. He was not on any other drugs apart from Ponatinib at present.

Previously he was on several Tyrosine kinase inhibitors (TKI)s. Imatinib and Nilotinib were the initial drugs respectively which the patient became resistant after some time. Due to the intolerance, Dasatinib was changed into Ponatinib. At the initiation of Ponatinib therapy BCR-ABL1/ABL1 quantification was 33% IS. Over the period of 10 months the quantification has improved up to 10.5% IS. The latest FBC reveals 5.9×10^9/L. He is currently tolerating Ponatinib well with good clinical outcome. These skin lesions appeared within a month of starting Ponatinib 45mg daily.

On examination, erythematous annular plaques with trailing scales with central clearing were observed in bilateral armpits and groins extending to the lateral chest (Figure 1) and thighs, forming lesions that are 6-10 cm in diameter.

Fungal scrapings were negative. The diagnosis of EAC was made clinically. He was treated with topical steroids with topical emollients. After progressing over 5 months, now the lesions remain static.

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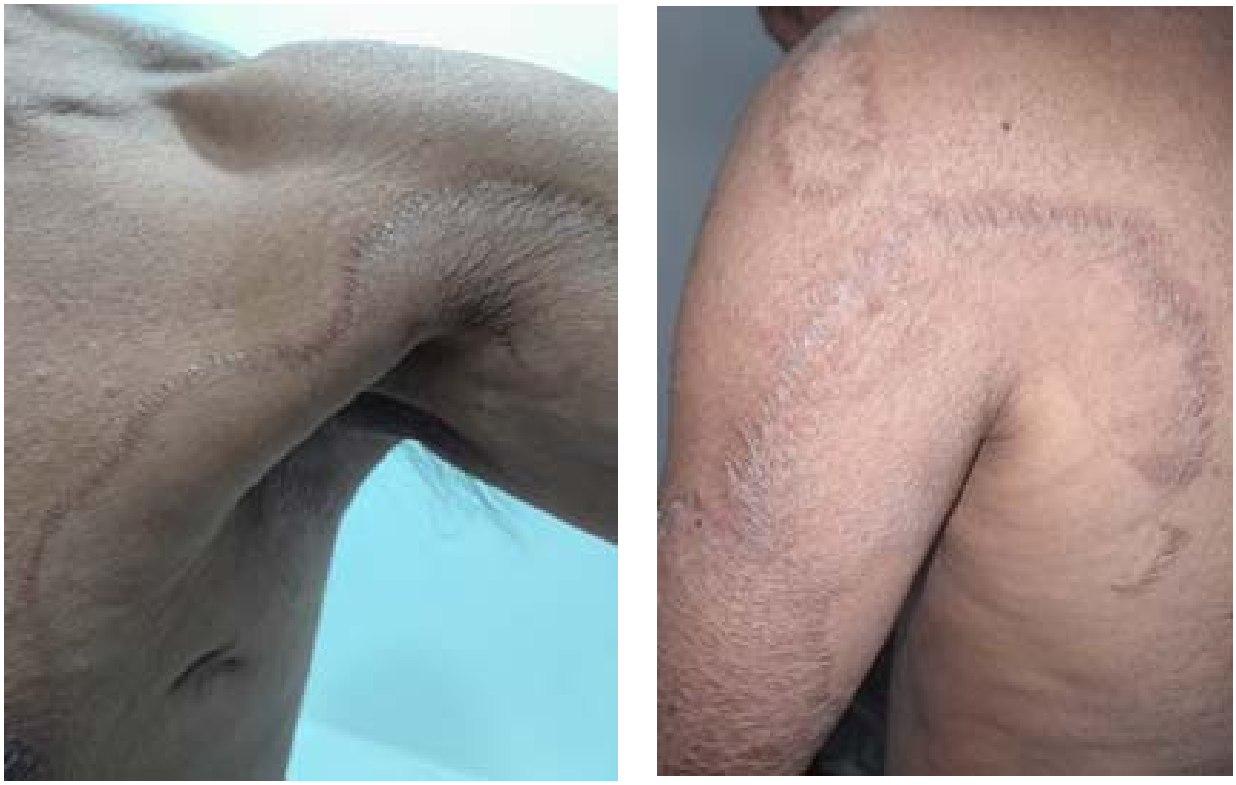

Figure 1. *Erythematous annular shaped plaques with trailing scales in armpits with central clearing.*

Discussion

The term EAC was introduced by Jean Darier in 1916 to describe an annular indurated erythematous lesion without scales. It was histologically characterised by a superficial and deep lymphohistiocytic infiltrate and normal epidermis. There are two types of EAC, a superficial type showing scales, and the deep type as described by Darier. Dermatologists use the term EAC to denote both forms. Trunk, thighs and arms are the most involved sites[1,7,8].

Though previous literature suggests EAC is mostly idiopathic, a retrospective observational study has identified associated etiological conditions in 52.3%. Etiological conditions include infections, malignant conditions, drugs and autoimmunity[7,8]. In our patient there were no other etiological factors to be found upon clinical history, examination and with relevant investigations; other than that he is a known patient with CML who was recently started on Ponatinib drug therapy.

When we consider PEACE, lymphoproliferative malignancies were the most common cause where 63% of patients in a study regarding PEACE were associated with lymphoproliferative diseases, specifically lymphoma and leukemia. Studies suggest that these cutaneous symptoms are caused due to cytokines or other tumor-associated factors[2,9]. CML is caused by BCR-ABL1 oncogene that activates tyrosine kinase pathway constitutively, resulting in proliferation of the mutant Hemopoietic Stem Cells (HSC) leading to displacement of normal HSCs. The treatment of CML has been revolutionised by the emergence of TKIs, which has enabled most patients to achieve long-term survival. Ponatinib is a third-generation BCR: ABL1 TKI[4,6].

The administration of certain medications like non-steroidal anti-inflammatory drugs, pegylated interferon alfa-2a plus ribavirin combination therapy, rituximab etc. can trigger the occurrence of erythema annulare centrifugum, which often resolves upon discontinuation of the drug. Ponatinib is a potent therapeutic option in patients with CML as second- or later-line treatment for patients who are resistant or intolerant to other TKIs as it demonstrates high cytogenetic and molecular response rates in newly diagnosed chronic-phase CML. Ponatinib is the only approved TKI with clinically relevant activity against the T315I mutation to date. Ponatinib potently acts on numerous other kinases as well. A study based on Ponatinib in refractory CML revealed that common adverse events were rash, myelosuppression, and

constitutional symptoms. 26 out of 81 patients developed skin disorders, including rash and dry skin, being the most common nonhematologic adverse events associated with ponatinib therapy. But specific subtypes of the rashes are infrequently reported [5,6,7,10].

A previous case report of a known patient with CML for 14 years, has shown EAC was diagnosed 10 months after switching to ponatinib from imatinib, reasoning that EAC was caused by Ponatinib[11].

In our patient it can be challenging to determine whether the EAC is a manifestation of CML itself or a side effect of ponatinib. Improvement in BCR; ABL1 quantification and full blood count results after the initiation of Ponatinib favours Ponatinib induced EAC over PEACE.

However, EAC is generally a self-limiting disease and has a benign progression. The exact duration and resolution can vary depending on the underlying cause, if present, and individual factors. Skin lesions may persist as long as the triggering factor remains active. Therefore, the main goal of current treatment options is based on treating the underlying condition and alleviating subjective symptoms[3,7].

Conclusion

While cutaneous eruptions can be alarming to both the patient and the clinician, asymptomatic and non-progressive lesions should be carefully evaluated in the context of ongoing treatment benefits. In this scenario the significant improvement in the BCR: ABL1 quantification following initiation of Ponatinib, suggests that the therapeutic advantages outweigh the mild skin reaction. Therefore, continuing Ponatinib with close monitoring and supportive care is considered to be a reasonable approach.

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