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RESEARCH ARTICLE

ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS SECONDARY TO IMATINIB IN A PATIENT WITH GASTROINTESTINAL STROMAL TUMOR

Youness Elkhachine[1], Mohammed Sinaa[2], Aziz Bazine[3], Abdessamad Sakkah[1], Abderazzak Jakar[1] and Jalal Elbenaye[1]

1. Department of Dermatology, Moulay Ismaïl Military Hospital, Meknes, Morocco.
2. Department of Cytopathology, Moulay Ismaïl Military Hospital, Meknes, Morocco.
3. Department of Oncology, Moulay Ismaïl Military Hospital, Meknes, Morocco.

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Abstract

Background: Imatinib is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukemias and gastrointestinal stromal tumors.

Main Observation: We describe the case of a 64-year-old patient, who had been on imatinib 400 mg / day for a gastrointestinal stromal tumor. He developed one week later a diffuse pustular erythematous pruritic rash associated with an erosive cheilitis. The histological study confirmed the diagnosis of acute generalized exanthematous pustulosis (AGEP). Pharmacovigilance survey concluded that there is a causal link between imatinib and the occurrence of this cutaneous reaction. The causality assessment according to the updated French method was "i5" and "B3" for the intrinsic and extrinsic causality scores respectively. The evolution after discontinuation of this drug was favorable. The patient was then put on sunitinib with a complete therapeutic response and better tolerance.

Conclusion: AGEP secondary to imatinib remains a rare but proven side effect. The outcome is generally favorable but requires the use of other molecules such as sunitinib.

Introduction:-

Imatinib is a tyrosine kinase inhibitor widely used in the treatment of several cancer conditions, particularly chronic myeloid leukemia and gastrointestinal stromal tumors (GIST). This molecule is generally well tolerated, however, adverse reactions may occur, particularly cutaneous and mucosal ones. We report a case of acute generalized exanthematous pustulosis after the introduction of imatinib.

Case report:

A 64-year-old patient was put under imatinib (400 mg/day) for a GIST. Seven days later he developed a pustular erythematous pruritic rash affecting the trunk and extremities. The pustules were superficial, small (< 2 mm), non-follicular, lactescent and confluent in places (Figure 1). Erosive cheilitis was also found. The patient has a preserved general condition with no fever. The lymph nodes were free. Interrogation did not find any other drug intakes. We didn't find any history of psoriasis, recent infection or mercury exposure. Laboratory studies revealed neutrophilic leukocytosis, and bacteriological study of the pustules was negative. The histology confirmed the diagnosis of acute

Corresponding Author:- Youness Elkhachine
Address:- Department of Dermatology, Moulay Ismaïl Military Hospital, Meknes, Morocco.

generalized exanthematous pustulosis (Figure 2). Pharmacovigilance survey concluded that there is a causal link between imatinib and the occurrence of this cutaneous reaction. The evolution after discontinuation of this drug was favorable (Figure 3). The patient was then put on sunitinib with a complete therapeutic response and better tolerance.

Discussion:-

Imatinib is a specific tyrosine kinase inhibitor targeting BCR-ABL, KIT and the platelet derived growth factor (PDGF) receptor. It is indicated for the treatment of chronic myeloid leukemia and gastrointestinal stromal tumours. It is also used in other hematological diseases, in Darier Ferrand dermatofibrosarcoma and in melanoma with KIT mutation [1].

Cutaneous and mucosal side effects are more common during imatinib therapy. The incidence varies between 7% and 88.9%. These adverse reactions occur generally at a dose ≥ 600 mg / day. Low molecular weight of imatinib suggests that these effects are the result of a pharmacological rather than immunological process [2].

Maculopapular rashes are the most common. They were described in 67% of cases by Valeyrie et al. in a prospective study of 54 patients [3]. Bilateral and facial periorbital oedemas are also frequently described (up to 70% of patients depending on the series). They can be severe, early and may involve other parts of the body [1]. Other skin reactions may include lichenoid lesions, psoriasiform rashes, pityriasis rosa-like. Pigmentation disorders are also reported with localized or diffuse hypopigmentation or, less frequently, hyperpigmentation [4]. Imatinib may also cause dry skin, photosensitivity, urticaria or acneiform lesions, and more rarely mucinosis, porphyria, erythema nodosum or sweet syndrome [1]. More serious events were reported. These may include DRESS syndrome (Drug rash with Eosinophilia and Systemic Symptoms), Stevens-Johnsons syndrome or acute generalized exanthematous pustulosis (AGEP) [5].

AGEP is a rare event during imatinib therapy. Only a few cases have been reported [6, 7, 8]. The mean time to onset ranges from 01 to 03 months and the dose is usually greater than 600 mg/day. Only one case was mentioned after 400 mg/day dose [6].

In our case, the diagnosis of AGEP secondary to imatinib was evoked in front of the chronology of the eruption, clinical and histopathological appearance and the outcome after discontinuation. The causality assessment according to the updated French method was “i5” for intrinsic causality score (C2 for the chronological score and S3 for the semiological score) and “B3” for the extrinsic causality score [9].

Given the serious nature of this side effect, reintroduction test was not possible. Updated French method, allowed us to evoke the causal link between imatinib and the occurrence of this cutaneous reaction. This method remains a very useful mean which help to confirm diagnosis and contribute to the quality and the relevance of the data stored in pharmacovigilance databases [9].

Conclusion:-

AGEP secondary to imatinib remains a rare but proven side effect. The outcome is generally favorable but requires the use of other molecules such as sunitinib.

Conflicts of Interest:

Authors declare no conflict of interest.

Figures:

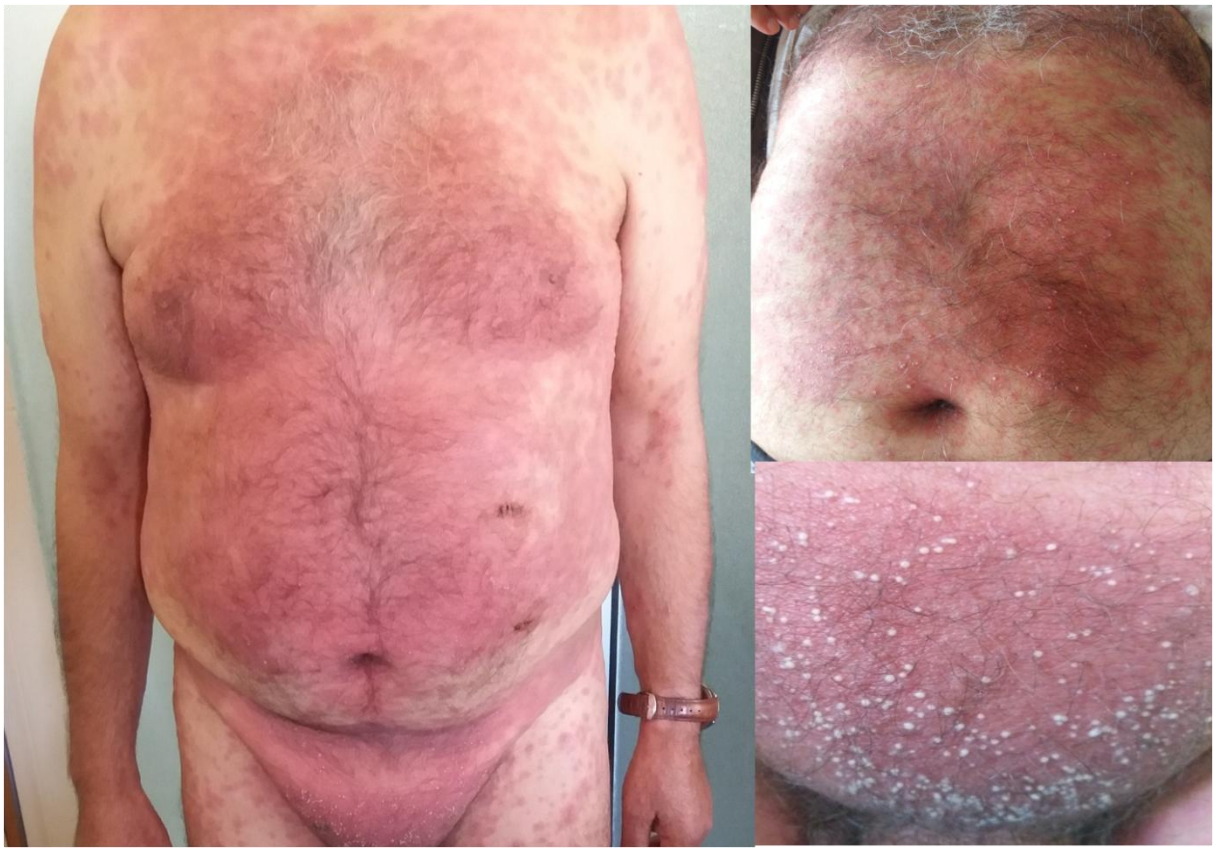

Figure 1:- Erythematous pustular rash affecting the trunk and extremities.

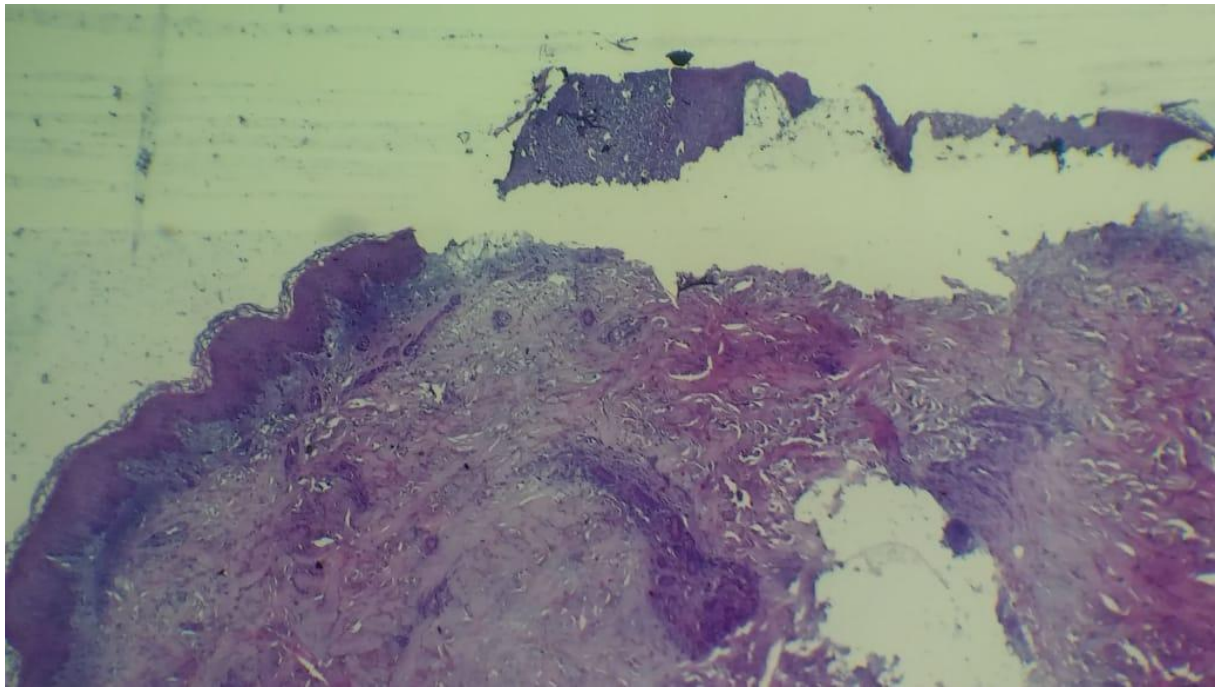

Figure 2:- Spongiform pustules containing clusters of neutrophilic polynuclear cells associated with apoptotic keratinocytes (HE × 100).

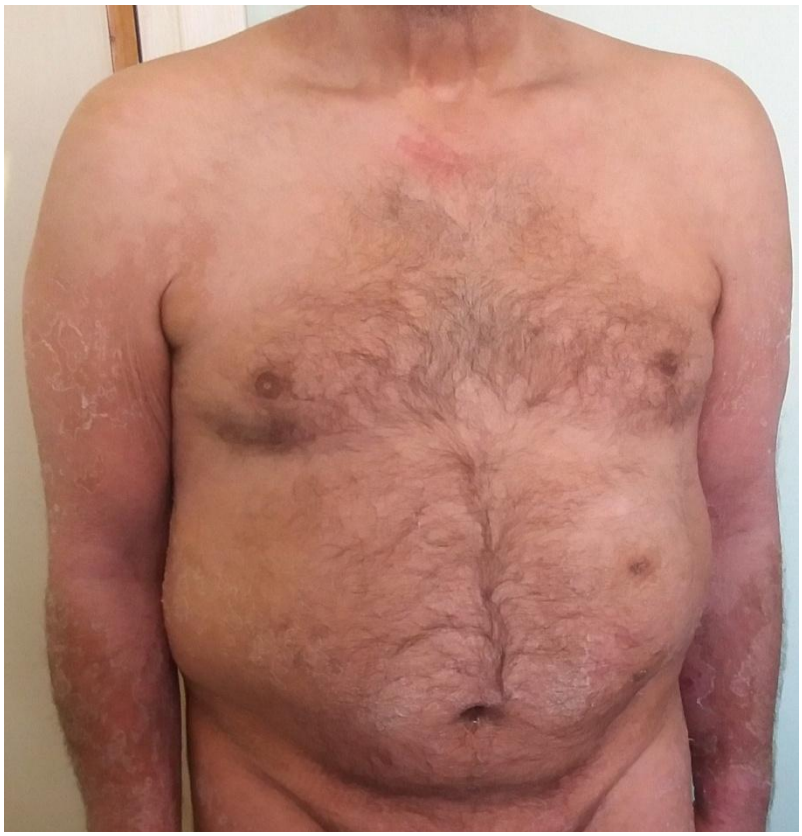

Figure 3:- Spontaneous favorable evolution after 15 days of imatinib discontinuation with diffuse desquamation.

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