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Original Research Paper

Dermatology

ACUTE GENERALIZED EXANTHEMATOUS PUSTULOSIS(AGEP): A RARE MANIFESTATION OF AN ADVERSE DRUG REACTION INDUCED BY MEROPENEM, PIPERACILLIN AND TAZOBACTAM.

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ABSTRACT We report a 59-year-old female diabetic and hypertensive who developed AGEP, 24 hours after commencing antibiotics for urinary tract infection. The associated drugs were Meropenem, Piperacillin and Tazobactam with a possible combined effect of these three drugs that resulted in systemic involvement requiring intensive monitoring and prompt treatment. **Conclusion** The objective of reporting this case is to focus on the history that AGEP following injection meropenem and Piptaz led to systemic complications and dermatologists must be aware of such rare adverse effect. Accurate diagnosis and prompt treatment in adjunct with can reduce the mortality as in our case.

KEYWORDS : Acute Generalized Exanthematous Pustulosis, Meropenem, Adverse Reaction, AGEP

INTRODUCTION

Acute generalized Exanthematous pustulosis (AGEP) is a severe cutaneous adverse reaction, attributed to drugs in the majority (>90%) of the cases and may be associated with acute viral infections and mercury in some.[1]It is classified among the severe cutaneous drug reactions and is associated with systemic symptoms and organ manifestation in 17% of the cases; it has an incidence lying between 1 and 5 cases per million per year.[2,4] AGEP is a type IV (T-cell mediated) hypersensitivity reaction. The T-cell mediated response in AGEP results in neutrophilic inflammation.[3]

Case Report

We report a case of a 59 years old female patient known diabetic and hypertensive who developed complaints of itching all over the body after 24 hours of taking injection Meropenem, itching was associated with rash all over the body not involving oral mucosa. Initially, the patient had complaints of fever with chills, dysuria and urinary incontinence for 1 week for which she was started on injection Cefoperazone + Sulbactam on day 1 followed by injection Meropenem as patient's condition didn't improve. Patient had no history of similar complaints in the past. On examination: Patient was febrile and general condition stable.

Dermatological Examination:

Patient had bilateral symmetrical erythematous confluent patches on face and bilateral extremities with small, discrete, non-follicular pustules followed by desquamation of skin was present after day 3. Investigations revealed: CBC - leukocytosis, ESR was raised, CUE had >60 pus cells and bacteria - positive, Serum Uric acid-raised, LFT - Hypoalbuminemia was present and the culture from pustules was sterile. Skin biopsy was performed which later showed diffuse spongiosis, as well as numerous sub corneal pustules predominantly consisting of neutrophils, with some associated lymphocytes.

On day 3, Injection piperacillin and tazobactam was started. On Day 5, patient developed severe shortness of breath, grade IV type. On examination she was not responding, drowsy, tachypneic with BP - 220/120, hyperglycemia and was shifted to ICU for endotracheal intubation. Injection Labetalol 20 mg iv stat followed by infusion 10mg/hr. was given. Patient was maintaining saturation on 6 liters of oxygen. Also, HAI 10U i.v stat followed by infusion at 10 ml /hr. was given. After establishing the diagnosis of AGEP, we discontinued Meropenem and Piptaz injection. Patient was started on Inj. Methylprednisolone 1g i.v OD, Inj Linezolid 600 mg i.v BD and Inj Pheniramine Maleate. Patient was maintained on fluid and electrolytes. Topical Mupirocin cream, topical moisturizing lotion, body wash, regular dressings, oral betadine gargles and high albumin diet were advised. Patient was extubated after 2 days and monitored in the ICU. After 10 days of hospitalization, patient was hemodynamically stable, her lesions improved and was discharged on oral antibiotics and topical emollients.

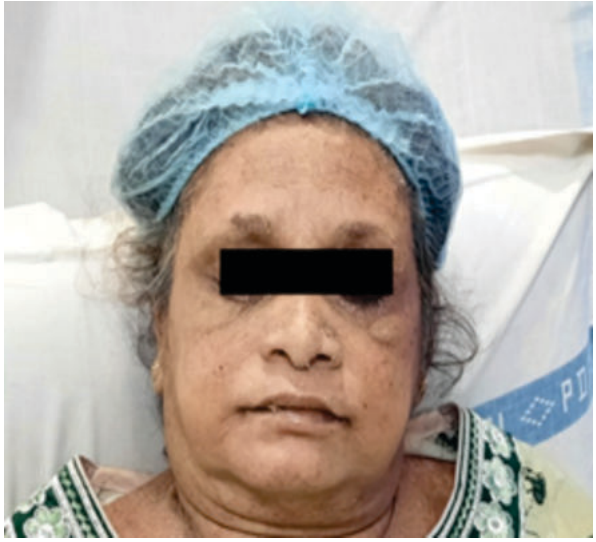

Figure 1a) multiple pustules over neck, scaling over nose and forehead

Figure 1b) multiple pustules on wrist region with erythematous confluent patches over right forearm and palm

Figure 1c) Multiple non follicular discrete pustules with erythematous rash over right forearm and arm on lateral side

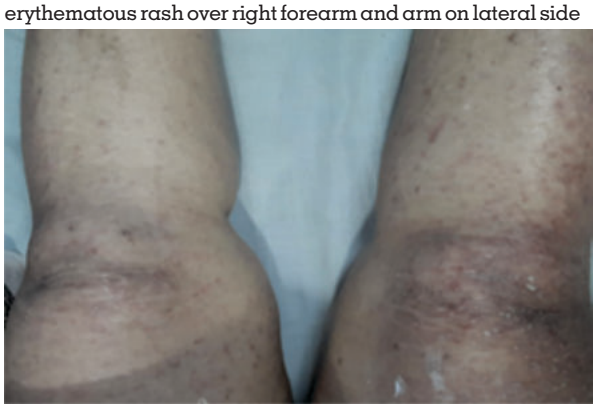

Figure 1d) multiple pustules over bilateral knees with an erythematous rash is seen

Figure 2a) Day 4 of admission, desquamation of skin over face and neck was present

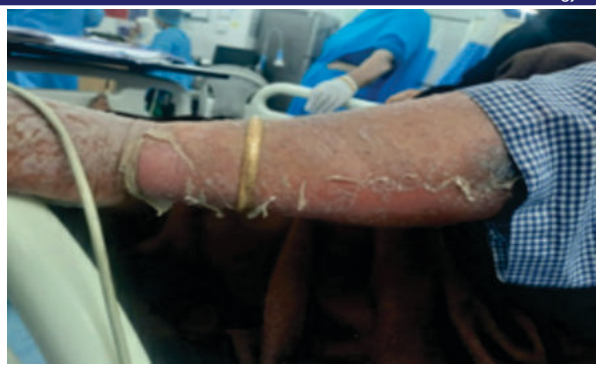

Figure 2b) Desquamation of skin of left forearm on day 4

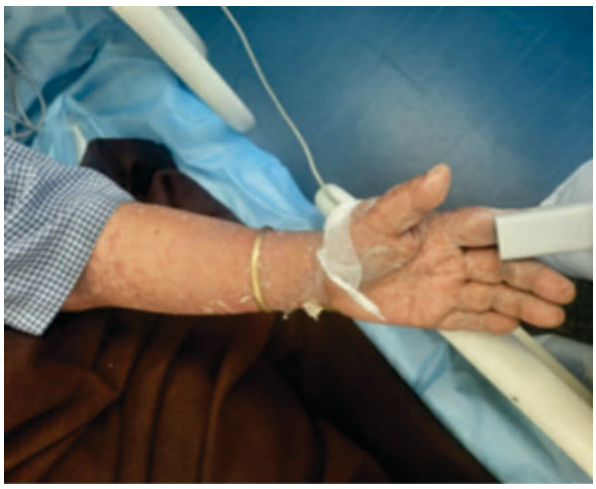

Figure 2c) Desquamation of skin over left forearm with reduced rash on day 4

Figure 2d) Desquamation of skin on day 4 over left forearm

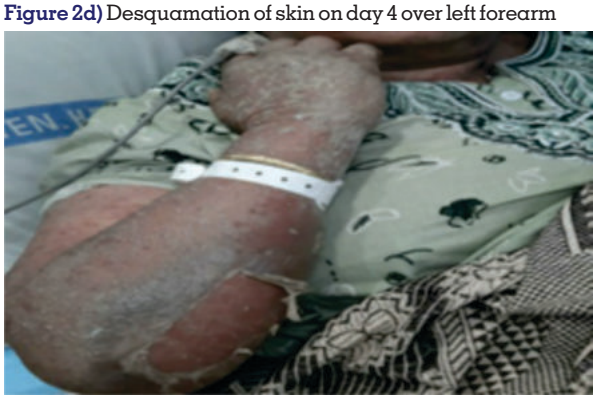

Figure 2e) showing desquamation of skin over right forearm and arm on day 4

DISCUSSION

Acute Generalized Exanthematous Pustulosis (AGEP) is a rare severe cutaneous reaction pattern which, in majority of the cases, is related to medication.[4] It is characterized by the

rapid development of non-follicular, sterile pustules on an erythematous base and is generally occurring within 48 hour of ingesting the suspected medication, of fever and pustulosis with leukocytosis. Most cases have a spontaneous resolution and only a single episode [1]. In our case, skin rash started on face with small discrete pustules within 24 hours of injection meropenem. Most of the authors suggest that AGEP,[5] is most commonly associated with the following drugs: pristinamycin, ampicillin, amoxicillin, quinolones, hydroxychloroquine, sulfonamides, terbinafine, diltiazem, ketoconazole, and fluconazole.[6] Drugs with weaker associations include macrolides, oxicam nonsteroidal anti-inflammatory drugs, and antiepileptic drugs.[6] This case reports AGEP with the systemic complications commencing after injection meropenem, piperacillin and tazobactam which is unusual and is less reported adverse reaction.

The disease is self-limiting, fever and pustules lasting for 7 to 10 days, followed by desquamation.[5] Systemic involvements are uncommon in AGEP. In a study of 58 patients, 17% of cases had internal organ involvement.[7] In our present case, leukocytosis, raised ESR, hypoalbuminemia was observed. On day 5 of hospitalization our patient worsened and required mechanical ventilatory support.

The main histopathological findings in AGEP are spongiform superficial pustule, papillary edema, polymorphous perivascular infiltrate with eosinophils and leukocytoclastic vasculitis with fibrinoid deposits.[5]The principal differential diagnoses of AGEP consist of pustular psoriasis, Sweet's syndrome, pustular erythema multiforme, TEN, drug rash with eosinophilia and systemic symptoms (DRESS), sub corneal pustulosis (Sneddon-Wilkinson syndrome), pustular vasculitis, and bullous impetigo.[8] In this case diagnosis of AGEP was made based on clinical and histopathological findings.

Treatment primarily involves withdrawal of the causative medicine. We stopped meropenem, piperacillin and tazobactam in this case. Supportive care in hospital (including fluid and electrolyte replacement) is often required during the acute illness. [9,10] Moisturizers, topical corticosteroids, oral antihistamines and analgesics may be required for symptomatic relief. [9,10] Systemic corticosteroids may be used to control inflammation in the acute phase,[9] as in our case which led to resolution of rash and systemic symptoms.

CONCLUSION

The objective of reporting this case is to focus/ highlight the history that AGEP following injection Meropenem and Piptaz led to systemic complications and dermatologists must be aware of such rare adverse effects. Accurate swift diagnosis and prompt treatment in adjunct can reduce the mortality, as seen in our case.

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