Case Report: Stevens-Johnson Syndrome from Ertapenem

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Abstract: Stevens-Johnson syndrome and toxic epidermal necrolysis are severe hypersensitivity related mucocutaneous reactions, characterized by extensive necrosis and detachment of the epidermis. Meropenem has been reported to cause stevens-johnson syndrome in a patient with similar reaction to cefotaxime. Penicillin and Carbapenem class of drugs share common beta-lactam ring in their molecular structure and are associated with a small risk for allergic cross-hypersensitivity. There is no clear consensus regarding the use of carbapenem class of drugs in patients with documented severe hypersensitivity reaction to penicillin group of drugs. We present a fatal case report of Stevens-Johnson syndrome from Ertapenem in a patient with previous similar reaction to Amoxicillin. We also discuss about potentially avoiding the use of carbapenem drugs in patients with severe hypersensitivity reactions to penicillin.

Keywords: Stevens-Johnson syndrome, Ertapenem, Carbapenem, Ampicillin.

INTRODUCTION

75 year old asian male with past history of IgG Kappa multiple myeloma, thrombocytopenia, stroke, chronic kidney disease presented to the ED with complaints of non-traumatic fall. He had also history of fever, chills, foul smelling urine and confusion for 1 day. Review of systems was significant for chronic weakness and reduced appetite. Patient looked lethargic on presentation and examination showed diffuse nonpruritic petechial rash in face and legs.

Initial labs showed WBC of 2.5 10(3)/mcL with absolute neutrophil count of 440 10(3)/mcL, Hemoglobin of 7.3 g/dL, platelets of 30 10(3)/mcL. Complete metabolic profile showed creatinine of 3.79 mg/dL(baseline 1.8 mg/dL). Urine analysis showed WBC of 50-200/HPF, esterase 2+, nitrite and bacteria positive. Initial procalcitonin was 46.55 ng/mL, which increased to 107.42 ng/mL in 3 days. Chest Xray did not show any opacities. Nasal methicillin resistant staphylococcus aureus (MRSA) screen was positive and HIV ELISA was negative. Initial concern was for neutropenic fever from urinary tract infection in an immunocompromised patient. He has had previous Stevens-Johnson syndrome (SJS) reaction to ampicillin and was also allergic to penicillin causing hives. He was given one dose of Ertapenem and Vancomycin.

He developed a new skin rash the following day and was diffusely erythematous throughout the body. Both the antibiotics were stopped due to concern for SJS and gentamycin was started. Initial urine culture was positive for *E. coli* resistant to cefoxitin and levofloxacin but subsequent urine cultures were negative. Clinical course was complicated because of obtundation, decerebrate posture requiring intubation and ventilator support. Computed tomography (CT) and Magnetic resonance imaging (MRI) of brain was negative. His clinical status did not improve with continuing fevers, skin rash desquamating to purplish patches in few regions of body, facial swelling and he eventually deceased after comfort care was chosen by his power of attorney.

DISCUSSION

To our best of knowledge, this is the first reported case of SJS secondary to Ertapenem exposure. Penicillins have been extensively reported to cause SJS reactions [1]. Penicillin and Carbapenem class of drugs share common beta-lactam ring in their molecular structure and are associated with a small risk for allergic cross-hypersensitivity. One of the earliest Studies on this topic by Saxon A *et al*. reported that incidence of cross-reactivity between penicillin and carbapenems as being 47% [2] but these were extrapolated from skin testing of carbapenem drugs in penicillin allergic patients whose clinical significance cannot be determined. Prescott WA Jr *et al.* reported that the incidence of hypersensitivity of allergic reactions to carbapenems is 11% in penicillin allergic patients [3]. In a large study by Sodhi M *et al.*, incidence of hypersensitivity cross reactivity was determined to be 9.2% [4]. However a prospective study reported that it is safe to use meropenem in patients with history of allergic reactions to penicillin [5]. The main limitations of these observations are that these studies have not separately addressed the incidence of severe cross-hypersensitivity reactions such as SJS and toxic epidermal necrolysis (TEN)

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which can often be fatal. One previous case report reported TEN to meropenem in a patient with documented TEN to cefotaxime [6].

SJS occurs in 1-2 cases per million person years [7,8]. Common drugs causing SJS include allopurinol, antibiotics (Suflonamides, penicillins and cephalosporins), carbamazepine, lamotrigine [1]. Risk factors for SJS include HIV, immunologic diseases (multiple myeloma in my patient) and viral infections. Pathogenesis is poorly understood with some studies reporting possible cell-mediated cytotoxic reaction against keratinocytes leading to massive apoptosis [9]. Typical presentation is a prodrome of fever followed by erythroderma, facial edema and mucosal erosions and bleeding. Although skin biopsy can be used to confirm the condition, clinical diagnosis in the setting of trigger factor is mostly used for diagnosis. Differential diagnoses include erythema multiforme, erythroderma, toxic shock syndrome and staphylococcal scalded skin syndrome. Definitive treatment is to stop the offending drug and give supportive wound care, fluid replacement, and provide sterile environment along with adjunctive therapies such as systemic corticosteroids, intravenous immunoglobulin and cyclosporine. Overall mortality is 10 percent and most of them are secondary to sepsis, acute respiratory distress syndrome and multi-organ failure [1].

In conclusion, the main objective of our clinical observation is to emphasize the need to avoid all beta lactam containing antibiotics in a patient with documented severe hypersensitivity reactions such as SJS, TEN to any beta lactam antibiotic. Randomized studies are needed to determine the true incidence of severe cross-hypersensitivity between penicillin and carbapenem class of drugs.

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