Case Report

Steven-Johnson Syndrome (SJS) in a Multiple Myeloma patient treated with lenalidomide and low dose dexamethasone regimen: a rare Case Report

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Abstract

Lenalidomide is an immunomodulatory drug (IMiD), a derivative of thalidomide used in the treatment of multiple myeloma. Stevens-Johnson syndrome (SJS) is a rare but life-threatening cutaneous adverse reaction, at a rate of 1.1 to 7.1 cases per million person-years, mortality rate between 1% to 3% and 10% to 70% when it is associated with TIN. Very few cases of Lenalidomide induced SJS has been reported. We describe a case of Stevens-Johnson syndrome induced by induction therapy lenalidomide-low dose Dexamethasone regimen in a 56 year-old male who underwent induction therapy for multiple myeloma.

Keywords: Lenalidomide, Immunomodulatory Drugs, Multiple Myeloma, Adverse Cutaneous Reactions, Stevens-Johnson Syndrome

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Introduction

Cutaneous drug eruptions are one of the most frequent manifestations of adverse drug reactions. Adverse cutaneous drug reactions are found to affect 2-3% of hospitalized patients [1]. The reported percentage of potentially serious adverse drug reactions varies greatly and is estimated to be above 2% [1]. Some of the serious reactions include Stevens Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and the overlap category of SJS and TEN. SJS is a rare serious mucocutaneous disease with clinical features of illness and tenderness of skin and mucosa with systemic symptoms characterized by the presence of hemorrhagic erosions, erythema, flat, atypical target lesions and the epidermal detachment is < 10% of the total body surface area (BSA) presenting as blisters and areas of denuded skin. Two or more mucosal sites are usually affected. Stevens-Johnson syndrome (SJS) is a rare but life-threatening cutaneous adverse reaction. While SJS may sometimes be admixed with diagnoses of erythema multiforme (EM) minor or major, SJS and toxic epidermal necrolysis (TEN) are considered to be severity variants of the same disease with drug exposure the primary etiologic factor. It represents distinct entities within a spectrum of a single disease with common causes and mechanisms. Typically, it involves the skin and mucous membranes. While minor presentations may occur, significant involvement of the oral, nasal, eye, vaginal, urethral, gastrointestinal (GI), and lower respiratory tract mucous membranes may develop in the course of the illness. GI and respiratory involvement may progress to necrosis. The incidence of SJS has been estimated to be in the ranges of 1.1 to 7.1 cases per million person-years, and that of TEN at 0.4 to 1.2 per million person-years.[1] Despite their rare occurrence, increased recognition, and improved management, mortality among patients with SJS or TEN has been reported to be between 1% to 3% and 10% to 70%, respectively.[1] Diagnosis relies mainly on clinical signs together with the histological analysis of a skin biopsy showing typical full-thickness epidermal necrolysis due to extensive keratinocyte apoptosis. Differential diagnosis includes linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis (AGEP), disseminated fixed bullous drug eruption and staphyloccocal scalded skin syndrome (SSSS). Several drugs are at "high" risk of inducing TEN/SJS including: Allopurinol, Trimethoprim-sulfamethoxazole and other sulfonamide-antibiotics, aminopenicillins, cephalosporins, quinolones, carbamazepine, phenytoin, phenobarbital and NSAID's of the oxicam-type. Missed diagnosis of SJS is common, and recovery can take weeks to months, depending on the severity of the condition . We describe a case of multiple

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myeloma that developed SJS during primary induction treatment of Lenalidomie-dexamethasone regimen.

Case Report

We describe a case of Stevens-Johnson syndrome induced by lenalidomide-low dose Dexamethasone regimen in a 56 year-old male undergoing induction therapy for multiple myeloma. During the 3rd dose of induction therapy, he suddenly developed fever, swelling of tongue, sore mouth & throat, fatigue, cough, hypotension and burning eyes followed by a diffuse, whole body mixed red and purple coloured maculopapular rash with desquamation that speeded within a day, which was followed by prominent vesicular-bullous lesions on skin and mucus membrane of mouth, nose and genitals, crusting of lips, erythematous ulcers on soft palate that could not be distinguished from petechial haemorrhages for which he was admitted to Hospital. The laboratory parameters were : haemoglobin – 9.6g%, total count 13200/cumm, DLC- Neutrophils (72%), Lymphocytes (25%), Monocyte (1%), Eosinophil (2%), platelet count 1.52 L/cumm, ESR-27, RBS-142 mg%, serum creatinine-1.1mg/dl, blood urea 32 mg/dl, AST-25U/L, ALT-26U/L, ALP-122U/L, sodium-142meq/L, potassium 3 meq/L, calcium-7.1g %, total bilirubin-0.15mg %. The serum protein electrophoresis parameters were albumin 2.63g/dl, alpha-1 – 0.32g/dl, alpha-2 – 0.77g/dl, beta – 0.80g/dl, M-band – detected, M-spike – 6.44 g/dl, serum immunofixation electrophoresis parameters were – M-band – detected, IGG band – posive, IG band – not detected, IGA band – not detected, IGM band – not detected, kappa band – positive, lamda band – not detected and MRI of lumbar spine revealed osteoporotic compression collapse of D12 and L1 vertebrae. Lenalidomide was discontinued, and the patient was treated with intravenous dexamethasone 10 mg every 6 hours and topical corticosteroids. Over the next week, the patient's condition improved, but he had extensive exfoliative rash and pruritus that required antihistamine therapy. By hospital day 6, his rash got improved and pruritus resolved. He was discharged with a tapering dose of oral prednisone. Lenalidomide was switched to bortezomib for his induction therapy, and the patient did not experience any further cutaneous reactions. The results of a skin biopsy concluded that the findings were consistent with a drug hypersensitivity reaction, suspected to be Stevens-Johnson syndrome. Use of the Naranjo adverse drug reaction probability scale indicated a possible relationship (score of 3) between the patient's development of Stevens-Johnson syndrome and lenalidomide therapy.

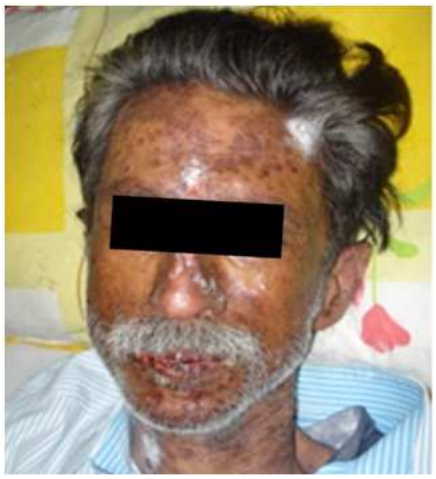


Fig 1: The patient with purpuric macules, oral erosion with hemorrhagic crusting

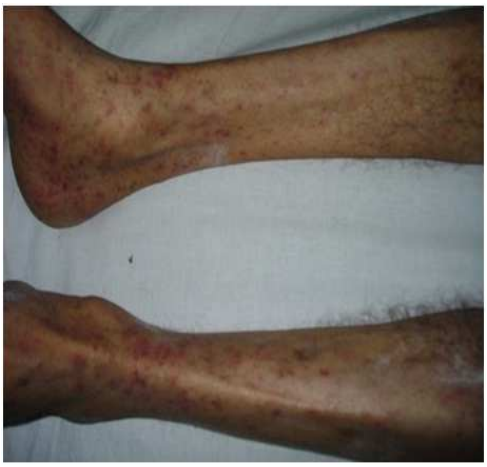
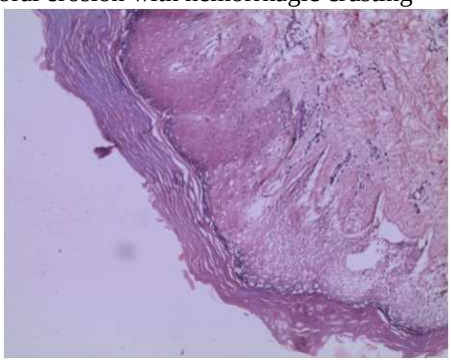


Fig 2: The patient with purpuric macules over the lower extremities



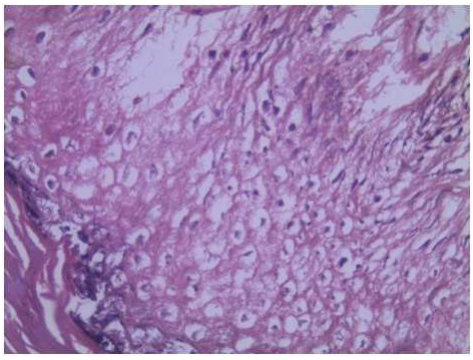


Fig 3: Histopathology of biopsy shows skin with part of viable and adjacent necrotic part suggesting secondary drug induced reactive dermatitis

Fig 4: Histopathology of skin lesion shows reactive areas at junction between epidermis and dermis suggesting reactive dermatitis.

Discussion

Stevens-Johnson syndrome (SJS) is a rare but life-threatening cutaneous adverse reaction. SJS may sometimes be admixed with diagnoses of erythema multiforme (EM) minor or major[1]. SJS and toxic epidermal necrolysis (TEN) are considered to be the severity variants of the same disease where exposure to certain drugs drug is the primary etiologic factor[2]. The incidence of SJS has been estimated at 1.1 to 7.1 cases per million person-years, and that of TEN at 0.4 to 1.2 per million person-years [1]. Mortality among patients with SJS or TEN has been reported to be between 1% to 3% and 10% to 70%, respectively [1]. Stevens---Johnson Syndrome has been described in patients with multiple myeloma who received lenalidomide therapy. To our knowledge, a few published case reports of severe Stevens-Johnson syndrome with lenalidomide have been reported. There are reports mentioning the correlation between SJS and lenalidomide treatment [3-5]. Thus, we believe this to be the rare case report of a patient who developed Stevens-Johnson syndrome while receiving lenalidomide for induction therapy for multiple myeloma. Clinicians should have a heightened awareness of the signs and symptoms of these severe skin reactions if their patients are receiving lenalidomide. The presentation is unexplained widespread skin pain, facial swelling, blisters on your skin and mucous membranes, hives, tongue swelling, a red or purplish skin rash that spreads and shedding of the skin. This case is reported to highlight the rarity of the possible severe side effects of lenalinomide as Stevens---Johnson Syndrome.

Conclusions

Dermatological side effects are a known complication due to lenalidomide use with a frequency ranging from 12% to 43%, with the highest rates similar to those due to thalido-mide use. Most eruptions occur during the first month of therapy and have been described as morbilliform, urticarial, dermatitic, acneiform, or undefined [6]. Physicians prescribing lenalidomide should monitor their patients for possible cutaneous adverse reactions, in particular if patients have a history of thalidomide skin eruption. Due to the increasing number of prescriptions of lenalidomide for the treatment of multiple myeloma the potential ability of lenalidomide to induce severe SJS must be taken into consideration

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