Ceftriaxone Induced Toxic Epidermal Necrolysis

Toxic epidermal necrolysis is a life threatening immune complex mediated hypersensitivity reaction which mainly involves skin and mucous membrane^[1]. It is characterized by blisters that meld into one another to cover a substantial portion of the body (30% and more), and extensive peeling or sloughing off of the skin. Toxic epidermal necrolysis is a more extensive form of Steven Johnson syndrome i.e. when more than 30% of body surface area is involved. It is called as Steven Johnson syndrome when less than 10% body surface area is involved. The intermediate form with 10 to 30% body surface area involved is called as SJS/TEN^[2]. The incidence of toxic epidermal necrolysis is between 0.4 and 1.9 cases per million each year^[3]. Since the time toxic epidermal necrolysis was first discovered by Dr. Lyell, it remained a deadly disease with a mortality of around 30%^[18]. Majority of cases reported are due to idiosyncratic drug reactions, but it can also be due to infections or more rarely cancers^[4]. Certain genetic factors have been found to be associated with increased risk of toxic epidermal necrolysis. For example, certain HLA-B*1502^[15], HLA-A*3101^[16], and HLA-B*5801^[17] have been seen to be linked with TEN development when exposed to specific drugs. In the present case toxic epidermal necrolysis was caused by ceftriaxone therapy.

Case Presentation

A 65 year old patient presented with recurrent bilateral inguinal hernia and was admitted in the Department of General Surgery SKIMS, and subsequently operated after proper evaluation. During postoperative period he was administered i/v antibiotics and analgesics. Patient was administered ceftriaxone 1gm i/v bid. After receiving 2nd dose next morning on second postoperative day, patient developed some itching which he didn't complain to anybody. Subsequently after receiving 3rd dose at evening, itching increased in intensity, and he started developing

rashes. Patient was administered antihistaminic and all other medication was stopped, but till morning patient developed blisters with extensive peeling off of skin.

Patient was again repeatedly enquired for some previous drug history when he remembered that years back when he developed some chest infection, he was given Inj. Ceftriaxone by some local doctor at Anantnag. That time also he developed itching, so injection was stopped.

On examination (Fig.1 and Fig.2) superficial burn type blisters with some peeling off of skin was seen on whole back, chest, abdomen and both upper and lower limbs. Underlying area was reddish. There was also diffuse erythema noticed surrounding main lesions over these areas. Nikolsky sign was +ve. Mucosa was not involved. Causality assessment revealed its association with ceftriaxone. Ceftriaxone was immediately stopped, injection hydrocortisone 500mg started along with local treatment like wound debridement and application of saline soaked gauze. Patient responded well and after few days, prognosis was very well with lesions regressing in size, erythema diminishing and no pruritus (Fig.3). Patient is now regularly coming for follow up at surgical OPD and is cured of the lesions.

Fig.1: Blisters with extensive peeling of skin after receiving second dose of Ceftriaxone

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Fig.2: Front View of same patient

Fig. 3: Lesions regressing in size one week after stopping Ceftriaxone

DISCUSSION

Toxic epidermal necrolysis is a rare exfoliative disorder with reported mortality rates varying from 20 to 60 percent^[4]. The drugs frequently acting as causative agents are non-steroidal anti-inflammatory agents, chemotherapeutic agents, antibiotics and anticonvulsants^[4,5]. Among cephalosporin's, ceftazidime⁶, cefuroxime^[7], cephalexine^[7-10] and cephem^[11] have been implicated. Pathogenesis of toxic epidermal necrolysis is thought to be consequence of keratinocyte apoptosis which leads to widespread epidermal death^[12]. An important role of cytotoxic T lymphocytes is also known^[4]. Recent studies indicated that toxic epidermal necrolysis may be an MHC-class-1- restricted specific drug sensitivity resulting in clonal expansion of CD8+ cytotoxic lymphocytes with potential for cytotoxicity. The cytotoxicity is apparently

mediated by granzymes (serine proteinases that are components of cytotoxic cells and natural killer cell granules)^[13].

Clinical manifestations of toxic epidermal necrolysis include a prodromal phase with influenza like symptoms followed by intense erythema, urticarial plaques, and bullae which progress over days or two to a more generalized epidermal slough^[4]. Mucosal involvement is usually severe and precedes the skin involvement. This can involve GIT mucosa, thus impairing alimentation and higher risk of infections, thus a worse prognosis. Better prognosis in present case was due to absence of mucosal involvement. Further, progressive neutropenia and thrombocytopenia may develop leading to septic complications, multiorgan failure and death. Therapeutic guidelines are still lacking, but immediate withdrawal of causative agent together with supportive care, steroids and immunoglobulins^[14] have been implicated.

CONCLUSION

Toxic epidermal necrolysis is an exfoliative skin disorder which is usually life threatening. High clinical suspicion, prompt recognition, immediate withdrawal of suspected agent and initiation of supportive care, together with multidisciplinary collaboration are mandatory for these patients where optimal treatment guidelines are still unavailable.

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