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Case report

Diclofenac sodium induced Stevens–Johnson syndrome in a hospitalized patient during treatment of splenic injury and mandibular fracture

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ABSTRACT

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare life threatening severe cutaneous adverse reactions, primarily caused by drugs and infection. Most of the cases of SJS are predominantly drug related. Drugs including antibacterial sulfonamides, non-steroidal anti-inflammatory drugs (NSAIDs) and anti-epileptic drugs have been identified to cause SJS/TEN. We report a case of 35 year old male, road accident victim, who suffered from mandibular fracture and a splenic injury, admitted to our hospital. Following the splenic embolization in Radiology Department he was administered cefazolin sodium and diclofenac sodium. The patient developed skin lesions characteristic of SJS, which was confirmed by skin biopsy. From the course of the skin lesions and its relation to diclofenac sodium administration and discontinuation, the drug was suspected to have caused SJS. The cefazolin sodium and diclofenac sodium were stopped one after another. Patient was successfully treated with prednisolone and was issued with drug card to prevent further attack of SJS by the same drug. We report the present case, in order to raise awareness that frequently prescribed NSAIDs diclofenac sodium has potential to cause rare skin disorder like SJS and prepare physician for the early intervention of any such future incidence.

1. Introduction

Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare life-threatening immune-mediated severe cutaneous adverse reaction predominantly involving skin and mucous membrane. The disease involves apoptosis of keratinocytes which causes the separation of epidermis from the dermis [1–3]. In 1922, Stevens and Johnson [4] first identified SJS, as an unusual skin disorder while treating two young boys of aged 7 and 8 years, respectively, and they described SJS as "extraordinary, generalized eruption with continued fever, inflamed buccal mucosa and severe purulent conjunctivitis." Although there were initial arguments whether SJS is altogether a distinct disease or a severe form of erythema multiforme (EM) [5], but later evidences confirmed SJS as a distinct cutaneous adverse reaction, different from EM [6]. Most widely accepted classification was first proposed by Bastuji-Garin et al. [7] and the classification is based on the extent of epidermal (skin) detachment; less than 10% body surface area (BSA) detachment for SJS and more than 30% BSA detachment for TEN while 10–30% BSA detachment for overlapping SJS/TEN [8]. SJS and TEN are rare conditions with an estimated incidence rate of 1–6 and 0.4–1.2 cases per million person-years. Both SJS and TEN are associated with high morbidity and potential mortality. SJS, constituting the milder form of skin detachment has a mortality rate of less than 5%, while TEN with extensive skin detachment is associated with a higher mortality rate of 30–40% [9,10]. The three major causes which trigger SJS/TEN include infection, adverse drug reaction (ADR) and a combination of ADR and infection but rarely cancer [11]. More than 100 drugs were identified which cause SJS/TEN [1,10]. In a multi-center retrospective study, Barvaliya et al. [12] showed that around 95% of SJS cases were drug-induced. According to a report on severe ADRs by the Ministry of Health, Labor and Welfare (MHLW), Japan, 3.4 patients per million person-years were diagnosed (2006–2008) with SJS/TEN and allopurinol and carbamazepine were identified as the two major causing agents in those cases [13]. The specific gene markers, HLA-B*1511 and HLA-B*5801 have been identified as risk factors for carbamazepine and allopurinol induced SJS, respectively, in Japanese patients [14,15].

Diclofenac sodium, a non-steroidal anti-inflammatory drug (NSAID), frequently prescribed as pain reliever after minor oral surgical procedure like tooth extraction in dental practice has also been known to cause rare cases of Stevens–Johnson syndrome [16].

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

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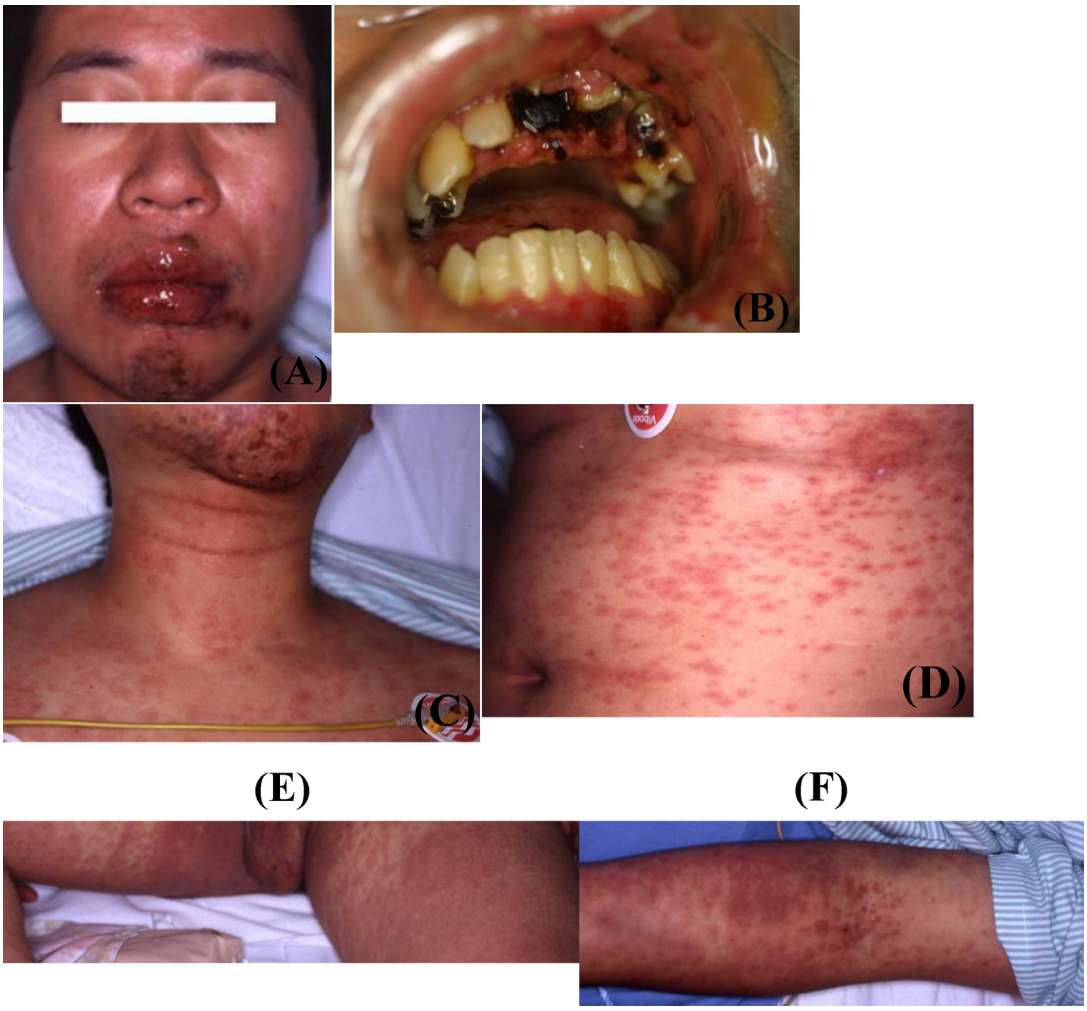

Fig. 1. The photograph of the affected areas. (A) Frontal view of the face; (B) oral; (C) neck; (D) abdomen; (E) thigh; and (F) upper extremities.

We report here, a case of diclofenac sodium induced SJS occurring during the treatment of splenic injury and mandibular fracture in hospitalized patient, so as to bring awareness among the physicians that, a common analgesic like diclofenac sodium has the potential ability to cause Stevens–Johnson syndrome.

2. Case report

A 35-year-old male, injured in a road-accident was brought to our hospital and hospitalized. The patient presented with multiple contusions in the lips and mental region, with dislocation of the upper anterior tooth and trismus. A computed tomography (CT) scan revealed multiple fractures: fractures of right articular process, the maxillary alveolar bone and the midline region of the mandible. Since the luxated tooth seemed repositionable, it was reset and secured. He also had a splenic injury, so, splenic embolization was performed in the Radiology Department. Post procedure, cefazolin sodium (4 g/day) and diclofenac sodium (150 mg/day) were prescribed to control infection and pain. Three days later, the patient developed a high fever (38–40 °C) with erythematous macules and plaques all over his body, including erosion of oral mucosa (Fig. 1). Drug reaction SJS was suspected and cefazolin sodium was discontinued. The diclofenac sodium was continued for pain. The patient continued to develop new lesions all over his body including the genital area (Fig. 1E) even after the discontinuation of cefazolin sodium and the appearance of new lesions continued in the same pace till sixth day; so, diclofenac sodium was finally suspected to have caused SJS and drug was stopped. The referral was sent to dermatology department for opinion; they also suggested the clinical diagnosis of SJS. The patient had no history of prior systemic illness, drug intake, malignancy or drug allergy and the patient's family history was also non-contributory.

The hematological investigation on the sixth day revealed the following results: total white blood cell (WBC) count 4500 cells/cumm, C-reactive protein (CRP) 12.35 mg/dl, aspartate aminotransferase (SGOT) 233 IU/l, alanine aminotransferase (SGPT) 271 IU/l, gamma-glutamyltranspeptidase (gamma-GTP) 273 IU/l and blood culture did not grow any organism. Biopsy was taken from the erythematous plaque on the body. The skin biopsy revealed the impending cleft in epidermis with necrosis of the epidermal keratinocytes. There were cellular infiltrations around the vessels in the upper dermis with edema of the dermis. The epidermis and the dermo-epidermal junction showed liquefactive degeneration. There was inflammatory infiltrate in the basal layer region (Fig. 2). These findings confirmed the clinical diagnosis of SJS.

The patient was started on injectable prednisolone IV (80 mg/day) for the SJS. The lesion had significant improvement on the 10th day, except for the mucosal lesions, which was slow to respond. The skin lesion healed leaving hypopigmentation on the