DE GRUYTER OPEN
10.1515/AMB-2017-0007

CASE REPORTS

CLINICAL CASE OF TOXIC EPIDERMAL NECROLYSIS

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Abstract. *Toxic epidermal necrolysis or Lyell's syndrome is a severe life-threatening adverse drug reaction with a high mortality rate. The drugs most commonly involved are: antibiotics; anticonvulsants; antiretroviral drugs; nonsteroidal anti-inflammatory drugs, allopurinol. Case report: A 68-year-old female, presented with complaints of fever and extensive rashes on the skin of the face, the neck and the trunk, severe itching of the skin, ulcerations and erythema of the conjunctiva and the oral cavity and difficulty in swallowing. She has a period of two or three days of general discomfort and fatigue, rash, fever up to 38°C, sore throat, arthralgia, myalgia, loss of appetite and have been treated with antipyretics, antibiotic – ampicillin, antihistamines, vitamins. Her state worsened during the next 3 days, therefore she was hospitalized in the Toxicology clinic of University Hospital "N. I. Pirogov". Multiple maculopapular and bullous eruptions, plaques were present all over the body, blisters that cover a substantial portion of the body. The entire skin covering the body surface was denuded and peeled off with minor manipulation – the Nikolsky's sign. Intraorally, multiple oral ulcers of the buccal mucosa, tongue, palate, labial mucosa, and soft palate were seen. Hemorrhagic erosions were also seen on both the upper and lower lips. Conjunctivitis and ulceration of genitalia were also noted. The lesions got slowly better with serum therapy, fluid and electrolyte replacement, systemic corticosteroids, antihistamines, antibiotic, vitamins, H2 blockers, topical care of mucosal changes. Evolution was satisfactory with epidermization and the patient was discharged from the hospital after 1 month.*

Key words: *Toxic epidermal necrolysis, Lyell's syndrome*

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INTRODUCTION

Toxic epidermal necrolysis (TEN) or Lyell's syndrome is a severe life-threatening adverse drug reaction, characterized by bullous and erosive lesions involving oral, ocular, and genital mucosa and vast areas of the skin with extensive dermo-epidermal detachments.

Various etiologies have been proposed, but drugs have been mainly characterized as the offending agents. The drugs most commonly involved are: antibiotics; anticonvulsants; antiretroviral drugs; nonsteroidal anti-inflammatory drugs, allopurinol. An immunologic response to immune complexes formed by metabolites of the causal drug and the common tissue antigens is thought to be responsible for this disorder. Recovery is usually slow and may take up 3–6 weeks. As a rule, skin lesions heal without scarring, whereas mucosal scarring and strictures are frequent late complications [1, 2, 11].

Worldwide incidence is 1-2 cases per million population per year [4]. It can affect all age groups but is

more common in elderly people, perhaps due to the increased numbers of drugs that they are administered to. Mortality due to TEN is most often cited as 30-50% [1, 3-5]. Sepsis and multi-organ failure are the main causes of death.

A case of TEN, treated in the Toxicology clinic and Burn Centre, Emergency University Hospital "Pirogov" was presented.

CASE REPORT

A 68-year-old female, presented with complaints of fever and extensive rashes on the skin of the face, the neck and the trunk, severe itching of the skin, ulcerations, and erythema of the conjunctiva and the oral cavity and difficulty in swallowing. She has a period of two or three days of general discomfort and fatigue, rash, fever up to 38°C, sore throat, arthralgia, myalgia, loss of appetite and have been treated with antipyretics, antibiotic – ampicillin, antihistamines, and vitamins.

There was no history of previous hypersensitivity reaction to drugs.

Her state worsened during the next 3 days, therefore she was hospitalized in the Toxicology clinic. On general examination, she was well-oriented and conscious. Initial vital signs were: heart rate 88 beats per minute, blood pressure 145/89 mmHg, and respiratory rate 26 breaths per minute. Multiple maculopapular and bullous eruptions, plaques were present all over the body, blisters that cover a substantial portion of the body. The entire skin covering the body surface was denuded and peeled off with minor manipulation – the Nikolsky's sign. Intraorally, multiple oral ulcers of the buccal mucosa, tongue, palate, labial mucosa, and soft palate were seen. Hemorrhagic erosions were also seen on both the upper and lower lips. Conjunctivitis and ulceration of genitalia were also noted.

Based on the history and clinical presentation, a diagnosis of TEN was given.

The routine laboratory investigations were within normal limits.

A chest radiograph of the patient did not show any active lesion.

Immunoassays revealed an expressed lymphopenia affecting all lymphocyte subpopulations, with the exception of NK cells, and high levels of IgG. The patient was positioned in air-fluidised beds in burn unit and managed symptomatically by administering intravenous fluid and electrolyte replacement, systemic corticosteroids, antihistamines, antibiotic – klacid, human plasma, vitamins, H2 blockers, topical wound care with chlorhexidine acetate (Bactigras), topical treatment of mucosal changes – vaginal globules, ophthalmic preparations. Evolution was satisfactory with epidermization and she was discharged from the hospital after 1 month (Fig. 1, 2, 3).

Fig. 1

Fig. 2

Fig. 3

DISCUSSION

Toxic epidermal necrolysis is a severe acute skin disorder, described for the first time in 1956 by Alan

Lyell. TEN is thought to be an immunological disorder and to be one of the families of three skin disorders. TEN is considered to be the more serious, followed by Stevens-Johnson syndrome (SJS) and erythema multiforme, in order of severity of the disease.

Definitions vary and another classification system works on the fact that SJS and TEN are related conditions which can be differentiated by the degree of skin involvement. Less of the epidermis sloughs off in SJS, whereas TEN may be defined as involving > 30% of the total body surface area [4, 5].

An allergic reaction to a drug is most often among adults. The exact cause of the violent skin reaction is unknown. There appears to be an immune response leading to the rejection of the skin and mucous membrane. There is thought to be an immune complex-mediated hypersensitivity reaction to the presence of toxic drug metabolites which accumulate in the skin. This reaction results in the destruction of keratinocytes. Specifically, cytotoxic T lymphocytes cause keratinocyte damage and subsequent necrosis, mediated by granzyme B. Cytotoxic molecules, including FasL and granulysin, have been also implicated in causing the widespread keratinocyte apoptosis [8, 11].

Most cases involve the use of medications such as antibacterial sulfonamides, non-steroidal, anti-inflammatory drugs, anticonvulsants, some antibiotics. However, other etiologies, including infection, malignancy, and vaccinations, may exist [11].

The onset can occur at any age. TEN affects many parts of the body, but it affects mostly and severely the mucous membranes, such as in the mouth, eyes, and vagina. The severe findings of TEN are often preceded by 1 to 2 weeks of flu-like symptoms.

These symptoms may mimic those of a common upper respiratory tract infection.

The disease consists of a prodrome of malaise, lethargy, and fever, followed by erythema and massive bullae formation.

Pathologically, there is epidermal necrosis and vesication at the dermal-epidermal junction, but the dermis is relatively normal. The mucous membranes are usually included in the destructive process. Mucous membrane involvement occurs early in 90% of cases and commonly precedes other symptoms [8]. The conjunctival, buccal, nasal, pharyngeal, tracheobronchial, perineal, vaginal, urethral and anal mucosae may all be involved.

When the rash appears it may be over large and varied parts of the body, and it is usually warm and appears red. In hours, the skin becomes painful and the epidermis can be easily peeled away from the underlying dermis. Bullous and erosive lesions involve oral, ocular, and genital mucosae; and vast areas of the skin with extensive dermoepidermal detachments [3, 6, 9].

The patients have to be seen by a multidisciplinary team and must receive intensive supportive care. This includes early fluid and electrolyte replacement, aggressive nutritional supplementation, systemic corticosteroids, antihistamines, intravenous antibiotic therapy, oxygen therapy through a cannula, or assisted ventilation according to the patient's clinical condition and blood gas analysis, administration of inactivated human plasma, intravenous immunoglobulin, prevention of stress ulcers with H2 blockers, hydrotherapy under intravenous sedation and with the application of a chlorhexidine solution, local treatment of mucosal changes, prevention of ocular problems through daily observation by an ophthalmologist, who will prescribe appropriate ophthalmic medication (antiseptic solutions, topical antibiotics) and monitoring of vital functions [4, 7, 12].

As a rule, skin lesions heal without scarring, whereas mucosal scarring and strictures are frequent late complications. Late eye complications, potentially leading to blindness, occur in up to 50% of cases. Sepsis and multi-organ failure are the main causes of death. Hospital stay varies between 13 and 30 days without mortality. Recovery is usually slow and may take 3-6 weeks [10].

In our patient, the cutaneous tissue and the oral mucosa showed a sustained and relatively quick re-epithelialization, which allowed the patient to be discharged home after 30 days of hospitalization.

CONCLUSION

Severe adverse drug reactions as toxic epidermal necrolysis, is a rare, but very serious dermatological lesion, characterized by the sudden onset of high fever, with signs of systemic toxicity and intense mucocutaneous lesions.

The main treatment is the immediate suspension of the culprit drug and the patient's hospitalization in a service that can provide intensive care and minimize the risk of infection.

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