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CASE REPORT / OLGU SUNUMU

Successful management of a patient with toxic epidermal necrolysis by high dose intravenous immunoglobulin

Toksik epidermal nekrolizisli bir hastanın yüksek doz intravenöz immünglobulin ile başarılı tedavisi

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ABSTRACT

Toxic epidermal necrolysis (TEN) is a disease that mostly caused by drug use and characterized by acute onset and rapidly progressive necrosis of the epidermis. In severe cases, mortality rate change between 20% and 60%. Although there is no definite treatment, some authors have reported the effectiveness of intravenous immunoglobulin (IVIG). Here, we presented a 9-year-old male patient with TEN. Skin rashes of patient began after three days of using ibuprofen, metronidazole, clarithromycin, and procaine penicillin. Skin lesions resembling second-degree burns covered 50% of the patient's body surface area. After giving high-dose IVIG, the patient's lesions improved. This case is an example of effect of high dose IVIG in the treatment of TEN. *J Clin Exp Invest 2013; 4 (4): 503-505*

Key words: Toxic epidermal necrolysis, intravenous immunoglobulins, child

ÖZET

Toksik epidermal nekrolizis (TEN) sıklıkla ilaç kullanımı sonucu gelişen, akut başlangıçlı, çok hızlı ilerleyen, epidermis nekrozu ile karakterize bir hastalıktır. Şiddetli seyreden olgularda mortalite oranı %20-60 arasında değişir. Kesin tedavisi olmamasına rağmen intravenöz immünglobulin (İVİG) tedavisinin etkili olduğunu belirten yayınlar mevcuttur. Bu çalışmada; ibuprofen, metronidazol, klaritromisin ve prokain penisilin kullandıktan üç gün sonra deri döküntüleri başlayan ve %50 oranında ikinci derecede yanık düzeyinde lezyonlar ile TEN tablosu gelişen 9 yaşında erkek hasta sunulmuştur. Hastaya verilen yüksek doz İVİG tedavisi ile düzelme sağlandı. Bu olgu TEN tedavisinde etkinliği tartışmalı olan İVİG tedavisine olumlu yanıt alınabileceğine bir örnektir.

Anahtar kelimeler: Toksik epidermal nekrolizis, intravenöz immünglobulinler, çocuk

INTRODUCTION

Toxic epidermal necrolysis (TEN) is an acute onset, and rapidly progressive disease of the skin, and mucous membranes characterized by necrosis of the epidermis. It may occur due to many causes such as drugs and infections. Mortality rate ranged from 20% to 60% [1]. The most common etiologic agents are drugs such as antibiotics, anticonvulsants, nevirapine, abacavir, and non-steroidal anti-inflammatories. Measles, chickenpox, herpes zoster, herpes simplex, *Escherichia coli*, *Mycoplasma pneumoniae*, aspergillosis, vaccines and malignant diseases are other etiologic causes [2]. There is still no definitive treatment proven effective in cases of TEN. Some previous studies reported that corticosteroids may improve the prognosis of TEN. The increasing risk of secondary bacterial infection by this treatment leaded to alternative drugs and methods. For this purpose, plasmapheresis, cyclosporine, thalidomide, pentoxifylline, cyclophosphamide, and granulocyte colony-stimulating factor were tested. Recent reports draws attention to successful results by intravenous immunoglobulin (IVIG) therapy. In this study, we presented a severe TEN case that dramatically gave response to high-dose IVIG therapy.

CASE REPORT

A Nine-years-old male patient with common purple-brown skin rashes and peeling skin complaints admitted to our hospital after three day of using ibuprofen, metronidazole, clarithromycin, and procaine penicillin for the treatment of upper respiratory tract infection and gastroenteritis. On physical examination, there were poor general condition, impairment of consciousness, 39ºC body temperature, 140 heartbeat per minute, hyperemic oropharynx, hem-

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orrhagic lesions in the mouth, bilateral edematous eyelids, hyperemic conjunctivae, and coarse crackles on lung oscultation. In addition, there were bullous lesions, peelings locally subcutaneous hemorrhages on face, lips and all over the body (Figure 1).

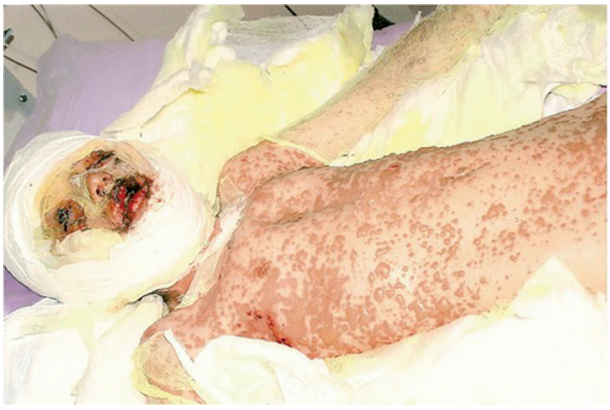

Figure 1. An image of case at hospitalization

On the laboratory examination, there were hypoalbuminemia 2.5 g/dL (normal limits, NL: 3.5-5.0 g/dL), hypocalcemia (7.1 mg/dL, NL: 8.4-10.2 mg/dL), hyperglycemia (202 mg/dL, NL: 70-109 mg/dL), hyperamylasemia (650 U/L, NL: 25 to 125 U/L), high C-reactive protein (18.5 mg/dL, NL: 0 to 8 mg/dL), normal level of total IgE: 312 IU/mL, high level of D-dimer (484 mg/L, NL: <279 mg/L), leucopenia (3,800/mm^3; NL: 4.4 to 11.3/mm^3). There were 70% neutrophils and 30% lymphocyte on peripheral blood smear. Liver and kidney function tests, and electrolytes were within normal limits. Laboratory examinations on the fifth day of hospitalization showed; albumin 2.3 mg/dL, total amylase 451 U/L (NL: 25 to 125 U/L), pancreatic amylase 63 U/L (NL: 8 to 53 U/L), LDH 418 U/L (NL: 200 to 450 U/L), PTZ: 16.5 sec (NL: 9.5 to 13 sec), INR 1.35 sec (NL: 0.88 to 1.2 sec), APTT 21.5 sec (NL: 25 to 35 sec), and erythrocyte sedimentation rate 67 mm/h. Skin, blood, urine and wound cultures were negative. Gruber Widal (for salmonellosis) and Wright (for brucellosis) tests and cytomegalovirus, toxoplasmosis and malaria tests were negative. There were no abnormal findings in the bone marrow examination except increasing myeloid series due to infection.

Patients were admitted to the intensive care unit. Primarily all old medications were stopped. Patient's wounds were dressed daily. Dental care was performed for oral lesions. Intravenous immunoglobulin (2 g/kg/day) was administered to patient for a period of four days. Vancomycin (45 mg/kg/d) was added therapy for persistent fever. On the tenth day of hospitalization, patient's lesions regressed a little bit. The twenty-fifth day of hospitalization patient was discharged when lesions and clinical findings recovered (Figure 2). At the first control examination following two weeks of discharge, there was no sign of disease except for some scleral adhesions and hypopigmented areas of previous skin lesions.

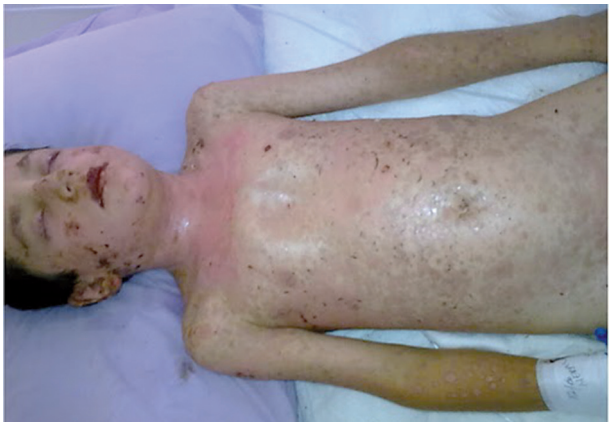

Figure 2. An image of case at discharge from hospital

DISCUSSION

Toxic epidermal necrolysis is an emergency life-threatening dermatologic disease that characterized by necrosis of two or more mucosal surface's epidermis of more than 30% of the skin. The incidences of it have been reported between 0.5 and 1.89/1.000.000. The drugs consisted 80-90% causes.

Previous studies have reported that corticosteroids improved prognosis of TEN. However, because steroids increase the risk of secondary bacterial infection, IVIG has been used as an alternative therapy. Recently, it has been reported that IVIG therapy gave successful results. Because high dose IVIG has anti-inflammatory activity, IVIG is preferred instead of corticosteroids in the children, in the elderly patients and immunocompromised patients [3].

There is a consensus that keratinocyte cell death in TEN is a result of apoptosis. It has been shown that IVIG has in vitro antibodies that blocking Fas and block apoptosis by preventing the formation of Fas-Fas ligand compound [4]. There is no consensus on standard protocols for use, dosage and regimens of IVIG in TEN due to lack of sufficient controlled trials. Effective drug doses range from 0.2 to 2 g/kg/day [5]. In a study, it has been reported that administration of IVIG (0.6 to 0.7 g/kg/day) for four days, stopped the epidermal differentiation at 4.8 days of initiation of therapy [6]. Başkan et al.

[7] administered 0.6 to 0.7 g/kg/day IVIG, and plasmapheresis during 4-5 days to cases that could not treated by pulse steroids. No complications were reported due to IVIG therapy. They reported that IVIG stopped the formation of bullous and epidermal detachment [7]. In addition, Tukenmez et al. [8] reported IVIG therapy with positive results in two cases with TEN. In a multicenter study, Prins et al. found that in the early period high-dose IVIG infusion was safe, well-tolerated and an effective treatment modality in cases with TEN [9]. Mittmann et al. [10] reviewed a total of 17 articles about the effectiveness of IVIG in cases with Steven Johnson syndrome or TEN, and reported that IVIG was helpful in these cases. Our case supported previous reports.

In conclusion, although there is no certain treatment option for TEN, IVIG therapy may be an effective and safe alternative therapy for pediatric cases with TEN.

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