Case Report

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Toxic Epidermal Necrolysis in a Patient with Allopurinol, Colchicine and Alcohol Use

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Abstract

Introduction: Toxic epidermal necrolysis is a severe, acute, mucocutaneous, life-threatening hypersensitivity syndrome with high mortality and bullous lesions on the skin, eyes and mucous membranes. It often develops due to drugs. Sulfonamide group antibiotics and antiepileptic drugs are the most commonly responsible agents. Allopurinol is a common cause of toxic epidermal necrolysis as in most drug reactions. Colchicine is widely used in dermatology and rheumatology and is generally known as an agent with a broad safety profile.

Case report: Here we present a case of toxic epidermal necrolysis in our case with allopurinol, colchicine and alcohol use in order to draw attention to the increased risk of drug coexistence.

Conclusion: Again, we wanted to draw attention to the management of our case and the efficacy and safety of high-dose intravenous immunoglobulin therapy.

Keywords: Toxic epidermal necrolysis, allopurinol, colchicine, intravenous immunoglobulin.

Introduction

Toxic epidermal necrolysis (TEN) is a serious life-threatening hypersensitivity syndrome with high mortality and acute course of bullous lesions in the skin, eyes and mucous membranes[1]. The annual incidence of TEN, which often develops due to drugs, is approximately 0.4-1.2 per million[1]. Sulfonamide group antibiotics and antiepileptic drugs are the most frequently held responsible agents[2]. In some epidemiological studies, allopurinol has been held responsible for approximately 10% of all cases[3]. Allopurinol is a xanthine oxidase inhibitor, especially used in the treatment of gout and hyperuricemia. It causes cutaneous drug reactions quite frequently. Colchicine is widely used in gouty arthritis, familial mediterranean fever, Behçet's disease, erythema nodosum and neutrophilic dermatoses[4]. Here we wanted to present our case of toxic epidermal necrolysis and treatment management in the case of allopurinol, colchicine and alcohol use.

Case Report

A 33-year-old male patient was diagnosed with gouty arthritis from internal medicine department and treatment was started with allopurinol and colchicine 15 days ago. On the fifteenth day of the treatment, he was referred to our hospital with complaints of widespread redness, mouth ulcers and stinging eyes. The patient, who was evaluated in the emergency department, had a history of daily alcohol use in his medical background.

On his physical examination, the blood pressure was 140 / 80 mmHg, pulse was 128 / min, and body temperature was 36.7 °C. In dermatological examination there was erythematous maculopapular eruption in approximately 80% of his body which tended to merge bullous lesions and erode areas in more than 30% of his body (Figure 1). There was eye, oral and genital mucosa involvement (Figure 2).

Laboratory analysis revealed C-reactive protein (CRP) 165 mg / L, serum bicarbonate 19 mmol / L. The SCORe

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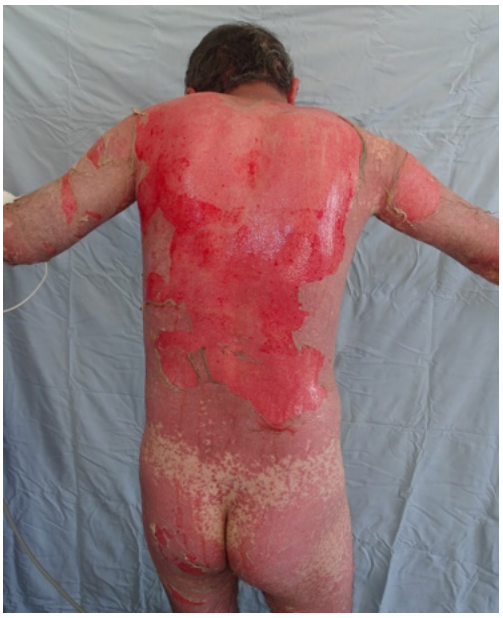

Figure 1: Erythematous maculopapular eruption and diffuse exfoliation, tending to merge in approximately 80% of the body

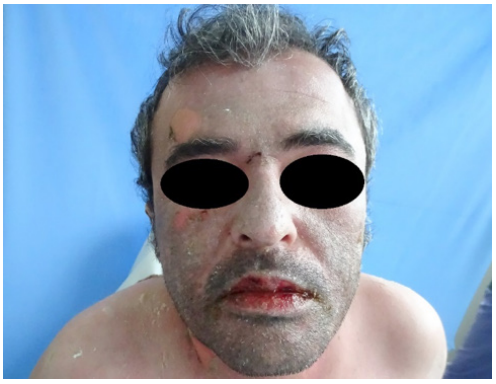

Figure 2: Oral mucosa and eye involvement

of Toxic Epidermal Necrosis (SCORTEN score) is a severity-of-illness scale. The SCORTEN score was evaluated as three due to pulse, serum bicarbonate and body surface areas. The patient, who had a definitive diagnosis of TEN, was hospitalized in the reanimation intensive care unit. Cutaneous biopsy was taken for differential diagnosis.

IV ceftriaxone 70 g / day (1 g / kg / day) was administered for 14 days with the recommendation of the infectious diseases department. 350 g (70 g / day, total 5 g / kg) intravenous immunoglobulin (IVIG) treatment was administered for five days. 1 mg / kg / day (70 mg) methylprednisolone treatment was started and was gradually tapered after (2 weeks) after the response was obtained. Levocetirizine 5 mg was given three times a day until the patient was discharged from the hospital. Local streoid, eau de borique %2, antibiotic cream and sterile dressings, which made by plastic surgeons, treatments were applied. Nutritional and electrolyte follow-up of the patient was done by the reanimation unit. No secondary infection or metabolic disorder developed in the case. In terms of eye and genital mucosa involvement, recommended local treatments were applied to our case, who was consulted with urology and ophthalmology.

The patient whose bullous lesions regressed with the treatments at the end of two weeks was taken to the dermatology service from the intensive care unit. The patient was discharged with almost complete regression of the lesions followed in the service for two weeks (Figure 3).

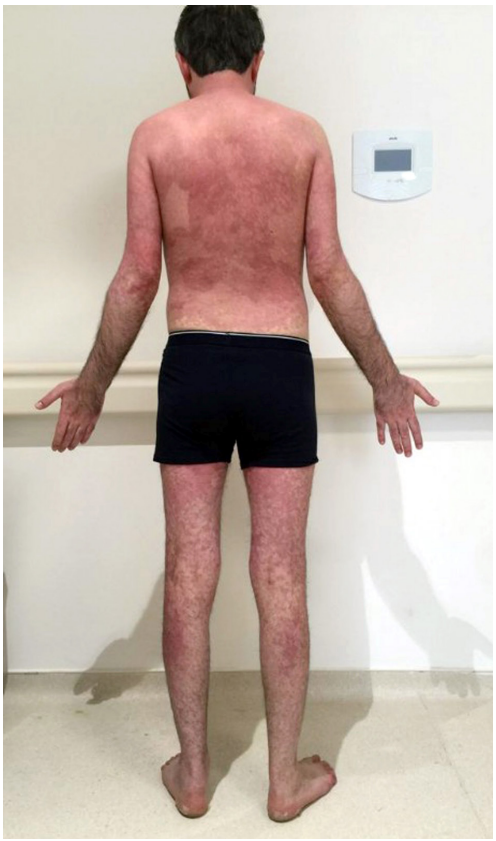

Figure 3: Almost complete regression in lesions after approximately four weeks

Discussion

The treatment of toxic epidermal necrolysis first begin with the detection and discontinuation of the etiological agent[1]. The patient should then be transferred to a hospital with a burn unit (or intensive care unit). It is necessary to do wound care, maintain the ambient temperature of 30–32 °C, and maintain fluid-electrolyte balance[2]. The SCORTEN score should be calculated on day 1 and 3 in terms of mortality and risk follow-up[3]. In addition to steroid therapy IVIG, tumor necrosis factor (TNF) inhibitors or cyclosporin should be considered as adjuvant therapy within first 24-48 hours[5,6]. We planned IVIG treatment for our case whose the Scorten score we calculated three and was in the high risk group because of his high CRP, infection parameters and high safety profile of IVIG.

IVIG, which is used in the treatment of toxic epidermal necrolysis, has been shown to contain antibodies that block

Fas in vitro and inhibits the formation of the Fas-FasL (Fas ligand) composition[7]. However, there are opinions that argue that the duration and extent of necrolysis and mortality rates in patients using IVIG are not different than expected. In a study (using IVIG treatment) in which 64 patients were evaluated retrospectively, mortality did not decrease. However, the low number of patients in this study and its retrospective nature were important limitations of the study[8].

It has been shown that there is no significant reduction in mortality in a large meta-analysis study in which 221 patients were evaluated, but it decreases mortality at doses above 2 g / kg IVIG treatment[9,10]. In our case, it was planned to give 210 g IVIG from 3 g / kg in 3 days, but since the lesions continued, the treatment was completed in 5 days and 350 g IVIG was given from a total of 5 g/kg. As mentioned in the literature, with the effect of using high IVIG doses, the patient's condition was improved within weeks and he was discharged in a healthy.

Allopurinol can cause reactions such as hypersensitivity reaction, Drug Reaction with Eosinophilia and Systemic Symptom (DRESS), Stevens-Johnson syndrome (SJS) and TEN. In a meta-analysis study, it was stated that allopurinol is the leading cause of SJS / TEN in many countries (11). In the same study, it was reported that HLA-B * 5801 tissue typing can be used to detect allopurinol-induced SJS / TEN worldwide, regardless of geographical ethnic differences. Thus, it is thought that the development of SJS / TEN can be prevented by controlling allopurinol prescription in people who carry this allele more frequently. However, this practice has not yet entered the clinical practice routine.

Colchicine, another drug used by our case, is a commonly used agent in dermatology and rheumatology, with a wide safety profile in terms of cutaneous reactions. In a meta-analysis related to SJS and TEN in 2019, there were only four cases in the literature due to colchicine[1]. It is known that agents that inactivate microtubules induce apoptosis. Colchicine has been shown to induce apoptosis in fibroblasts, osteosarcoma cells, myeloid leukemia cells, cerebellar granular cells and adenocarcinoma cells[12].

It is known that the use of alcohol together with drugs increases the development of TEN[1]. Our case was using colchicine and alcohol along with the use of allopurinol, which is known to cause TEN. We think that the combination of colchicine and alcohol besides allopurinol probably facilitates reaction development. Allopurinol, which is held very responsible for drug reactions, should be used very carefully. Other drug history and alcohol use should also be questioned in cases that are planned to be used.

Conclusion

TEN cases, one of the most serious of dermatological emergencies, should definitely receive a multidisciplinary care under the leadership of the dermatologist under intensive care conditions[6]. In this article, we wanted to draw attention to our toxic epidermal necrolysis case with allopurinol, colchicine and alcohol use and the possible side effects of allopurinol may increase with the combination of drugs and alcohol. Again we wanted to point out that high-dose IVIG, previously recommended in the literature at a dose of 2-4 g / kg (5 g / kg in our case), is a safe and effective option.

References

1. Chaby G, Ingen-Housz-Oro S, De Prost N, Wolkenstein P, Chosidow O, Fardet L. Idiopathic Stevens-Johnson syndrome and toxic epidermal necrolysis: Prevalence and patients' characteristics. J Am Acad Dermatol. 2019; 80(5):1453-1455.
2. Rodríguez-Martín S, Martín-Merino E, Lerma V, Rodríguez-Miguel A, González O, González-Herrada C, et al. Incidence of Stevens-Johnson syndrome/toxic epidermal necrolysis among new users of different individual drugs in a European population: a case-population study. Eur J Clin Pharmacol. 2019; 75(2):237-246.
3. Mockenhaupt M, Viboud C, Dunant A, Naldi L, Halevy S, Bavinck JNB, et al. Stevens–Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. J Investig Dermatol. 2008;128(1):35-44.
4. Dursun R, Temiz SA, Özer İ, Daye M, Ataseven A. Management of patients with Behçet's disease during the COVID-19 pandemic. Dermatol Ther. 2020;e14063. https://doi.org/10.1111/dth.14063 [Online ahead of print].
5. Schneider JA, Cohen PR. Stevens-Johnson syndrome and toxic epidermal necrolysis: a concise review with a comprehensive summary of therapeutic interventions emphasizing supportive measures. Adv Ther. 2017;34(6):1235-1244.
6. Temiz SA, Ozer I, Ataseven A. Dermatologic Emergencies. Selcuk Med J. 2020;36(2):157-167.
7. Alpsoy E, Dicle Ö, Karakas AA. Steven-Johnson sendromu ve toksik epidermal nekroliz/Steven-Johnson syndrome (SJS) and toxic epidermal necrolysis. Turkderm 2010;44(4):180-186.
8. Lee HY, Lim YL, Thirumoorthy T, Pang SM. The role of intravenous immunoglobulin in toxic epidermal necrolysis: a retrospective analysis of 64 patients managed in a specialized centre. Br J Dermatol. 2013;169(6):1304-1309.
9. Huang YC, Li YC, Chen TJ. The efficacy of intravenous immunoglobulin for the treatment of toxic epidermal necrolysis: a systematic review and meta-analysis. Br J Dermatol. 2012;167(2):424-432.
10. Barron SJ, Del Vecchio MT, Aronoff SC. Intravenous immunoglobulin in the treatment of S tevens–J ohnson syndrome and toxic epidermal necrolysis: a meta-analysis with meta-regression of observational studies. Int J Dermatol. 2015;54(1):108-115.
11. Yu KH, Yu CY, Fang YF. Diagnostic utility of HLA-B* 5801 screening in severe allopurinol hypersensitivity syndrome: an updated systematic review and meta-analysis. Int J Rheum Dis. 2017;20(9):1057-1071.
12. Sardana K, Sinha S, Sachdeva S. Colchicine in dermatology: Rediscovering an old drug with novel uses. Indian Dermatol Online J. 2020;11(5):693.