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Lyell Syndrome Due to the Combination of Two Antiepileptic Drugs in a Child

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Summary

Introduction: Toxidermia in children is very rare, Lyell syndrome even more so, with a mortality rate estimated at 7.5%. We report the observation of a little girl presenting Lyell syndrome following antiepileptic drugs.

Observation: This is a 13-year-old girl, treated for epilepsy, who presented 12 days after taking Valproic Acid combined with Clobazam: a generalized feverish rash with mucous membrane involvement. Dermatological examination revealed flabby bubbles, the affected body surface area was estimated at 60%. Mucous membrane damage such as cheilitis, conjunctivitis, edema and eyelid detachment and genital erosions. Skin histology revealed intra-epidermal detachment with marked keratinocyte necrosis. The pharmacovigilance declaration incriminated the 2 molecules with the same imputability score I5B4. The diagnosis of Lyell syndrome with antiepileptic drugs was made based on anamnestic, clinical and histological evidence. After a 15-day stay in our training and symptomatic treatment, the outcome was favorable but with serious ocular after-effects such as synechiae and hyperpigmented scars.

Conclusion: Physicians should be vigilant and inform the patient and their family of the possible development of serious drug addiction when treatment with benzodiazepines is combined with valproic acid. Combination therapy should be avoided as long as possible because it increases the frequency of adverse effects.

Keywords: Drug addiction; Lyell syndrome; Antiepileptics

Introduction

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are diseases on the spectrum of serious cutaneous adverse reactions affecting the skin and mucous membranes [1]. Both are rare, with SJS and TEN affecting approximately 1 or 2/1,000,000 per year, and are considered medical emergencies because they are potentially fatal [2]. carbamazepine and phenobarbital, sulfonamide anti-infectives, are strongly associated with SJS/TEN in children. Valproic acid, acetaminophen, and nonsteroidal anti-inflammatory drugs as a group may also increase the risk of SJS/TEN [3]. The combination of several antiepileptic drugs can cause pharmacokinetic or pharmacodynamic interactions, potentially generating more pronounced adverse effects than those observed when taking a single antiepileptic drug [4]. We report the observation of a little girl presenting Lyell syndrome following the combination of benzodiazepines and valproic acid.

Observation

This is a girl, aged 13, 3rd of a family of 4. Who began to present clinical tonic crises 9 months ago, prompting her consultation with a doctor who was put on Valproic Acid? associated withClobazam12 days later the patient developed a generalized feverish rash with mucous membrane involvement. all evolving in a febrile context and deterioration in general condition. the initial clinical examination revealed a conscious patient in AEG with the dermatological examination presence of multiple roundels and pseudo-roundels, bubbles and erythematous and purpuric papules confluent in places in large plaques affecting the face, the 4 limbs and the trunk with plamo-plantar damage presence of detachment at the level of the trunk SC < 10% nikolsky was negative without signs signs of bacterial superinfection with damage to all the mucous membranes made of poorly limited erosion on a clean surface in places topped with a whitish coating on the oral, nostril, genital level, and conjunctival hyperemia associated with significant eyelid edema. the diagnosis of Steven Johson type drug addiction or erythema multiforme major was initially mentioned, the action to be taken was to stop all medications, conditioning, declaration to pharmacovigilance, to hospitalize the patient in pediatrics then transferred to our training for treatment, the evolution was marked 2 days later by extension of the detachment with a skin surface affected more than 60%. Skin histology revealed an intra-epidermal detachment with marked keratinocyte ne-

crosis. The pharmacovigilance declaration incriminated the 2 molecules with the same imputability score I5B4. The diagnosis of Lyell syndrome with antiepileptic drugs was made based on anamnestic, clinical and histological evidence. The patient underwent a biological assessment which revealed normochromic normocytic anemia, acute renal failure and a correct ionogram, a skin sample which revealed a superinfection with Acineto bacter baumani the patient was put on parenteral antibiotic therapy symptomatic treatment consisting of daily bath topical treatment, vaseline compresses, mouthwashes and twice-daily eye care with anti-inflammatory eye drops and antibiotics associated with the installation of eye rings. The evolution was favorable after a 15-day stay but with serious ocular after-effects such as ocular synechiae, and hyperpigmented scars.

Discussion

Serious drug reactions are severe drug accidents linked to the recent introduction of a drug known to induce it. They constitute an emergency involving the vital and functional prognosis of the patient [5]. Toxic epidermal necrolysis also called Lyell syndrome described for the first time in 1956 by the Scottish dermatologist Alan Lyell [6]. It is an entity among these accidents, it is characterized by the brutal destruction of the superficial layer of the skin and the mucous membranes. It is one of the toxic bullous dermatoses which are classified according to severity: surface affected less than 10% of the body surface Stevens-Johnson syndrome; surface area affected between 10% and 29% of body surface area: transitional forms; surface affected greater than 30% of the body surface: Lyell syndrome

Figure 1: Presence of multiple roundels and pseudo-roundels, bubbles and erythematous and purpuric papules confluent in places in large plaques.

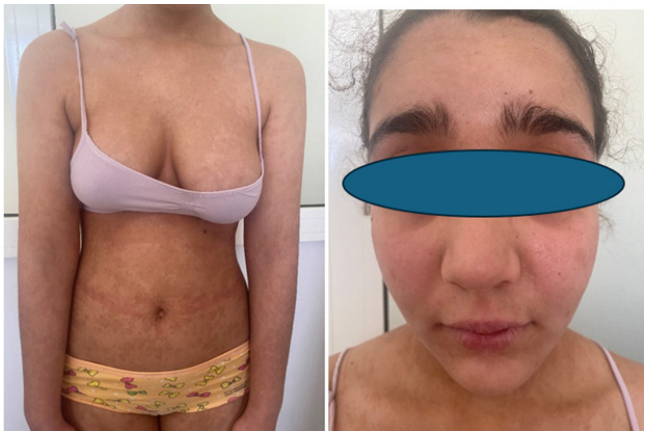

Figure 2: Control photo 2 months after hospital discharge showing post-inflammatory hyperpigmentation.

or toxic epidermal necrolysis [7]. The first symptoms of TEN and SJS can be fever, itchy eyes, pain when swallowing, each of which can precede the skin manifestations by 1 to 3 days [8] this is the case of our patient who presented prodromes had fever and asthenia 3 days before the symptoms. According to the literature[9], our case also presented ulcerations of the oral mucosa, hemorrhagic crusts on the lips and nose, conjunctivabilateral hyperemic, papules and erythematous bubbles mainly localized on the face, neck, trunk and genitals, and on the upper and lower limbs with a skin surface area of 60%.

Unfortunately, there is no specific treatment for TEN that has demonstrated effectiveness in controlled studies [9]. Its treatment is similar to the treatment of severe burns and it is reported that early transfer to a burn center is important for a favorable outcome. In addition to symptomatic treatment, immunosuppressants can be used such as corticosteroids [10] in our patient we did not use corticosteroid courses due to the infection she presented. Although intravenous immunoglobulin (IVIG) is also used for the treatment of SJS/TEN, the largest trial involving 281 patients showed no benefit to using IVIG, so we did not use it during our patient's treatment [11]. plasmapheresis which demonstrated its effectiveness in several series of cases [12] it was not used in our patient due to lack of albumin in the hospital. Despite the installation of eye rings and anti-inflammatory eye drops our patient presented after-effects ocular types synechiae and this is perhaps explained by the importance of the affected skin surface as has been shown in certain studies [5].

Conclusion

We reported a case in which a drug interaction between valproate and benzodiazepine contributed to the development of TEN. Physicians should be vigilant and inform the patient and family about the possible development of SJS/TEN when treatment with clobazam is combined with valproic acid. Finally, we believe that combination therapy should be avoided as long as possible in patients receiving antiepileptic drugs because it increases the frequency of adverse effects.

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Conflict of Interest: The authors declare that they have no conflicts of interest.

References

1. Mockenhaupt M. The current understanding of Stevens-Johnson syndrome and toxic epidermal necrolysis. Rev Expert Clin Immunol, 2011; 7: 803–813.
2. Yapici AK, Fidanci MK, Kilic S, et al. Stevens-Johnson Syndrome triggered by a combination of clobazam, lamotrigine and valproic acid in a 7-year-old child. Ann Burns Fire Disasters, 2014; 27(3): 121–125.
3. Sangwan SK, Sharma N, Agarwal T, Khanna N, Pandey RM, Sharma A, et al. Chronic ocular sequelae in Stevens-Johnson syndrome: a genetic association study. Mol Vis, 2022.
4. Hikino K, Abe Y, Sakashita K, Ozeki T, Mushiroda T. Characteristics of adverse drug reactions associated with antiepileptics at a tertiary children's hospital in Japan: A retrospective observational cohort study. Epilepsy Research, 2021.
5. Mouafik S-B, Hocar O, Akhdari N, Amal S, Belghmaidi S, Ennassiri W, et al. Ophthalmic manifestations after Lyell and Stevens-Johnson syndromes. Ann Dermatol venerol, 2015.
6. Pamnani S, Bakshi SS, Acharya S. Toxic Epidermal Necrolysis: A Case Report on a Drug-Induced Phenom-

enon. Cureus, 2022.
7. Martin T, Li H. Severe cutaneous adverse drug reactions: A review on epidemiology, etiology, clinical manifestation and pathogenesis. Chin Med J, 2008.
8. Feldmeyer L, French L-E. Toxic epidermal necrolysis (Lyell syndrome). Dermatology and sexually transmitted infections © 2017, Elsevier Masson SAS.
9. Harr T, French LE. Stevens-Johnson syndrome and toxic epidermal necrolysis. Chem Immunol Allergy, 2012.
10. Hasegawa A, Abe R. Recent advances in managing and understanding Stevens-Johnson syndrome and toxic epidermal necrolysis. F1000Res, 2020.
11. S chneck J, Fagot JP, Sekula P, Sassolas B, Roujeau JC, Mockenhaupt M. Effects of treatments on the mortality of Stevens-Johnson syndrome and toxic epidermal necrolysis: A retrospective study on patients included in the prospective EuroSCAR Study. J Am Acad Dermatol, 2008.
12. Kamanabroo D, Schmitz-Landgraf W, Czarnetzki BM: Plasmapheresis in drug-induced severe toxic epidermal necrolysis. Arch Dermatol, 1985.