Post-medication Stevens–Johnson syndrome in a girl hospitalized for a norovirus and rotavirus infection

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Abstract

Stevens–Johnson syndrome (SJS) is a cutaneous mucosal disorder characterized by extended necrosis and detachment of the epidermis affecting <10% of the body surface, caused by drugs or infections. The authors report a case of a girl with Depakine resistant epilepsy, who develops a SJS in the third week of introducing lamotrigine. The girl also presents an acute diarrheal disease with double viral etiology – rotavirus and norovirus. The clinical image comprises polymorphic erythematous maculopapular exanthema with vesicular and bullous elements, with ulcerations and desquamations at the level of the eyelids, mouth, anogenital area and tegument denuding at the level of the abdomen and limbs. The SCORTEN score (SCORe of Tox ic Epidermal Necrosis) for establishing the seriousness is 1. The evolution of the disease is slowly favorable under conservative treatment, which does not involve the use of corticotherapy or intravenous immunoglobulins. Although there is a low incidence of this syndrome in pediatrics, it may occur as complication of using some drugs – mostly anti-epileptics or antibiotics, corroborated or not with an infectious process.

Keywords: Stevens–Johnson syndrome, norovirus, rotavirus.

Introduction

The Stevens–Johnson (SJS) syndrome is a severe and rare cutaneous-mucous condition. The causes vary from medication (over 100 drugs comprised) to infection. The most common medicines involved are lamotrigine, carbamazepine, sodium valproate, sulfonamides, antibiotics, allopurinol, phenytoin and pyrimethamine. Lamotrigine in combination with sodium valproate increases the risk of SJS. Clinically, it is expressed by a flu-like image; followed by an oral and conjunctive mucosa infection. This is further followed by ulcerations and erosions of the mouth, nose, eyes and genital mucosa, associated with desquamation. The treatment requires specialized care, with mandatory hospitalization, consisting of hydroelectrolytic rebalancing, analgesics, erosions care, intravenous steroids or immunoglobulins (the last two are debatable) [1–6].

The case is of a 5-year-old girl with epilepsy, undergoing chronic sodium valproate therapy with an unfavorable evolution that required the introduction of a second anti-epileptic, lamotrigine. Since week 3 of lamotrigine introduction, there were significant cutaneous mucosal elements for SJS, coincidental with a double etiology – norovirus and rotavirus.

Case presentation

CM, a 5-year-old girl, 27 kg weight, was admitted on 09.07.2015 in the Department of Pediatrics, Emergency County Hospital, Arad (Romania), with the following symptoms: food refusal, periumbilical pain, vomiting, two watery stools and a maculopapular vesicular rash. Since the age of 3, the girl has had epilepsy with focal motor seizures refractory to prior treatment with Depakine (sodium valproate, 600 mg daily dosage). The neurologist indicates the association of lamotrigine in progressively increased dosages (week 1 – 2×25 mg/day, week 3 – 2×50 mg/day).

Two days prior to hospitalization, the girl had 2–3 episodes of vomiting/day, abdominal pain and 2–3 watery stools/day. On the day of admission, the girl presented with fever, itchiness, discrete polymorphous maculopapular vesicular exanthema and difficulty in swallowing. Therefore, admission is recommended to evaluate the complex symptomatology.

Clinical: weight 27 kg, height 121 cm, conjunctival hyperemia, face pain, pluriorificial, mouth and cheeks exanthema with vesicular-bullous elements (with serous citrine or cloudy content), sialorrhea, dry and cracked lips with fuliginosities, mouth ulcers, congested pharynx and some vesicular elements on the vaginal and perianal mucosa (Figures 1 and 2).

On day two of admission, the elements started to extend to the trunk and limbs, intensify on the face and evolve towards giant vesicles on the cheeks. Fuliginosities appeared on the edge of the eyelids and on the genital and anal mucosa. Vesicles on the palms and soles (Figure 3) and perioral hemorrhagic crusts with discrete bleeding during speech or feeding also appeared.
The abdominal pains decreased in intensity and the vomiting subsided. The apparition of the conjunctival, genital and anal cutaneous mucosal lesions of the vesicular-bullous type, affecting about 10% of the body, linked to the administration of lamotrigine on the 19th day, raised the suspicion of a Stevens–Johnson syndrome.

The Elisa Ridascreen Third Generation test of the feces shows the presence of norovirus and rotavirus; the co-infection is probably coincidental with the development of the Stevens–Johnson syndrome.

The SCORTEN score (SCORe of Toxic Epidermal Necrosis) in this case was 1 – the detachment affected approximately 10% of body surface area, in the absence of other risk factors: child, no associated neoplasia, normal cardiac frequency and normal level of serum sodium bicarbonate and glucose.

During the hospitalization, therapy with lamotrigine was interrupted. A hygienic dietetic treatment of the digestive episode was introduced; hydroelectrolyte and acid-basic disorders equilibration (according to the ionogram and Astrup parameter) and topical treatment were applied. A thorough cleaning of the cutaneous lesions was also performed and a local anesthetic given.

Corticotherapy (considered controversial) was avoided because of the digestive viral co-infection.

Topical corticosteroids (Diprogenta) were used instead on the face, trunk and limbs. Herbal preparations based on common marigold extract were applied around the mouth, on the genital and anal mucosa and also large dosages of vitamin A and eye drops for a period of five days were given.

The evolution was slow but favorable with the attenuation of the cutaneous-mucosal lesions. After 18 days, the patient was discharged from Hospital with discrete periorificial scars and without exanthema on the trunk and limbs.

Discussion

Multifocal erythema, SJS and toxic epidermal necrosis (TEN) are three entities that are considered to be related due to the link with the medication and common clinical and histological characteristics. However, SJS/TEN does not represent the final stage of an erythema multiforme [7].

SJS is a cutaneous mucosal disorder characterized by extended necrosis and detachment of the epidermis affecting <10% of the body surface, whereas TEN affects >30% [1].

The most frequent drugs involved in triggering SJS are: lamotrigine, paracetamol, carbamazepine, phenytoin, phenobarbital, sodium valproate and antibiotics [2–6]. Levi et al. [5] considers that four drugs are more frequent: sulfonamides, phenobarbital (PH), carbamazepine (CBZ) and lamotrigine.

Ferrándiz-Pulido & García-Patos [8] consider that PH, CBZ and lamotrigine are the most involved anticonvulsants in SJS. Famularo et al. [4] show that the association of lamotrigine with valproic acid favors SJS, and Yapici et al. [9] suggest that the two enhance their serum level. Usually, the cutaneous lesions appear after seven days [9] or between 30–60 days [10].

In a study performed on 3783 patients, SJS was reported in 0.03% of the patients taking lamotrigine [3].

The therapy is controversial.

Corticotherapy is indicated early in cases where multiple mucosal surfaces involved. The clinical response needs to be carefully monitored. The corticotherapy must be promptly suspended if the condition worsens [11].

Intravenous administration of immunoglobulins represents the optimal therapy in case of rapidly progressing SJS. It is used with care in case of hypercoagulability, renal failure or IgA deficit. A study done by Aires et al. [12] shows that intravenous Ig treatment is more efficient than corticotherapy in severe cases. Another study by Ferrándiz-Pulido et al. [13] on 14 children with SJS/TEN shows that 86% of the patients received corticosteroids and 25% intravenous immunoglobulins. SJS mortality is lower in children than adults. The combination of corticotherapy and intravenous immunoglobulins are useful in some cases [14].

Our case has correlated a viral co-infection (norovirus + rotavirus) with digestive impact that coincided with the onset of a SJS after the association of lamotrigine with valproic acid. We do not believe that this co-infection played a role in triggering the cutaneous lesions (the
norovirus–rotavirus–SJS relation has not been reported in the literature).

The apparition of cutaneous lesions seven to 60 days after the administration of an antiepileptic or of a new antiepileptic must raise the suspicion of a SJS.

The therapy remains controversial and sometimes a conservative treatment is sufficient.

Conflicts of interests

All authors have nothing to declare.

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References


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