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Case report

An unusual cause of Steven-Johnson Syndrome

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Summary. SJS is a rare mucocutaneous syndrome characterized by skin and mucous detachment. The main etiological factors are drugs and infections; sometimes the cause remains unknown. In the prodromal phase we observed non-specific symptoms, followed by mucocutaneous manifestation. Due to risk of complications and mortality a multidisciplinary approach is needed. We present a case of a girl with an atypical presentation of SJS related to Enterovirus. (www.actabiomedica.it)

Key words: Steven-Johnson Syndrome, allergy, enterovirus, corticosteroids, cyclosporine A

Introduction

The Steven-Johnson Syndrome (SJS) is a potentially lethal acute mucocutaneous syndrome characterized by erythematous maculae with development of central necrosis, bullous lesions, followed by painful dermo-epidermal detachment with a frequency up to two cases per million every year, 10-20% of which in pediatric ages (1-3).

The cutaneous and mucosal manifestations are preceded by non-specific symptoms such as fever, rhinitis, headache, conjunctivitis, sore throat lasting approximately one week. Complication are infections, eye involvement (potentially leading to blindness) (2), scars that involve mouth, pharynx, esophagus, rectus, middle airways, genitourinary tract (phimosis, vaginal stenosis, dysuria) (4). Patients may develop renal and/or hepatic failure, dehydration, and sepsis.

The most common triggers are drugs, followed by infections and idiopathic.

The pathogenesis is not completely clear. However, SJS should be caused by a lymphocytotoxic response resulting in apoptosis of keratinocytes. The diagnosis is based on clinical findings, possibly supported by histology showing full thickness necrosis of keratinocytes in the absence of antibody deposits.

We describe a girl who had an unusual presentation and uncommon etiology of SJS.

Case report

A 14 years old girl went to the A&E because she was suffering for the last 3 days from rhinoconjunctivitis, edema of the lips and sore throat that developed after a day spent at the stable. She had a history of rhinoconjunctivitis and asthma due to grass allergy. She didn't take any drugs during 8 weeks before the onset of symptoms (5).

An allergic reaction was suspected and methyl prednisone 40 mg I.M. and chlorphenamine maleate 10 mg I.M. were given.

Symptoms persisted and the following day she went to A&E of the local Hospital. The patient had normal vital parameters, edema of the lips, rhinoconjunctivitis and generalized reduction of vesicular murmurs.

She was treated with oral cetirizine and prednisone and inhaled salbutamol. The ophthalmologist prescribed antihistamine eye drops.

On the following day, the patient developed fever (38.2°C), seropurulent ocular secretion and crusted lips lesions with de-epithelialization of the oral mucosa. At the A&E, complete blood count showed neutrophilic leukocytosis with normal CRP. Aphthous stomatitis was diagnosed. Oral acyclovir and tobramycin eye drops were prescribed, and previous treatments were stopped.

After two days, the patient had been visited by GP who diagnosed bronchitis and prescribed second-generation cephalosporin. The day after the girl returned to A&E due to persistent fever, catarrhal cough, bilateral palpebral edema, conjunctival hyperemia, edema and painful de-epithelization of the lips with crusted lesions, hyperemia and painful de-epithelization of gums and palate, erythematous maculae on the chin and on the left hand. At auscultation she had vesicular breath sound with rare scattered rales. She had normal vital parameters. The girl was admitted at hospital with a diagnosis of SJS. She had normal complete blood count with increased CRP (51.3 mg/L). Chest X ray was normal. Intravenous fluids were administrated. Furthermore, a *Mycoplasma pneumoniae* infection was suspected and Azithromycin was given.

Serological test results for antibodies to *Mycoplasma pneumoniae* (Virion/Serion, Würzburg, Germany), EBV (Vidas®, bioMérieux, Marcy-l'Etoile, France), HSV 1-2 (DiaSorin S.p.A., Saluggia (VC), Italy), Coxsackievirus (Virion/Serion), Adenovirus (NovaTec Immunodiagnostica GmbH, Dietzenbach, Germany) were negative. The nucleic acid amplification assay (AllplexTM respiratory assays, Seegene, Seoul, Korea), performed on the pharingeal swab, revealed the presence of Enterovirus RNA. The amplicon of a nested PCR targeting the Enterovirus VP1 gene was submitted to sequencing (TIB Molbiol s.r.l., Genoa, Italy) in order to type the virus: the obtained sequences (forward and reverse) were not univocal and did not allow the typing. The viral cultivation of the pharyngeal swab, performed according to standard procedures (6), did not lead to the strain isolation. Renal and hepatic functions were normal. During hospitalization, the girl presented worsening of ocular symptoms with appearance of pain, visual loss and diplopia in the median fields. Ocular pseudo membranes were removed. Lubricant eye drops, corticosteroid eye ointment and chloramphenicol eye ointment were given. At the same time, she developed skin erosions at both ankles, onset of hyperemia, edema and painful ulcerous lesions at genitals, palate and tongue.

The girl was treated with daily oral rinses with chlorhexidine, viscous lidocaine at oral cavity, daily washing with neutral detergents at external genitals.

Because of severe oral pain with inability to be fed and the discomfort at the genital level, a pain-relieving therapy with morphine hydrochloride was given for 5 days.

SCORTEN score (7) was about 0, so the girl did not need to be managed in an intensive care unit.

The patient resumed eating from the sixth day of hospitalization; also, genital, cutaneous and oral lesions progressively improved.

On the eleventh day of hospitalization the patient was dismissed and mild de-epithelialization at the dorsal surface of the tongue was still present.

After 1 month from discharge, an ophthalmological visit was performed, and recovery of the eye was observed.

Discussion

We have presented a girl with SJS associated with Enterovirus infection.

The most common triggers of SJS are drugs, in 53-95% of cases (carbamazepine, phenobarbital, phenytoin, erythromycin, cefotaxime, trimethoprim-sulfamethoxazole, cloxacillin, amoxicillin, allopurinol, NSAID), followed by infections in 5-31% of cases (*Mycoplasma pneumoniae*, *Group A β-haemolytic Streptococcus, Rickettsia*, *Mycobacterium*, Cytomegalovirus, Herpevirus, Coxsackievirus, Parvovirus, Influenzavirus) and idiopathic in 5-18% of cases (1-3, 8-10). Many tests are warranted to identify the cause of SJS. When all of them are performed, it may be possible that they would clarify the etiology of many SJS that would be classified as idiopathic. In our patient, we did not find any relation between drug intake and onset of SJS. Investigations reveled an Enterovirus infection. To our knowledge this is the first case of SJS probably due to Enterovirus infection. The diagnosis of SJS is based

on clinical features and it is difficult to be suspected in the prodromal phase due to the non-specificity of the symptoms (1-3).

During the phase of epidermal detachment, we have also excluded by clinical and laboratory findings DRESS, Kawasaki syndrome, Staphylococcical scalded skin syndrome, atopic erythrodermia, pseudolymphoma (1-3, 11, 12).

The therapeutic approach to be used for SJS is controversial. In our case, the girl was treated topically until complete resolution of ocular, genital and cutaneous lesions. Moreover, she received systemic antibiotic because of the risk of sepsis, intravenous fluid replacement because of losses and food refusal, and analgesic.

High dose of systemic corticosteroids may be useful at the beginning of the disease but increased the risk of sepsis and GI bleeding (13). No difference on mortality rates between corticosteroids and supportive care has been described (13-14). In our patient a 3-day course of systemic corticosteroid during initial phase of the disease was not beneficial. There are promising results regarding effectiveness of cyclosporine A in re-epithelialization and prevention of skin lesions. However, further studies are necessary to evaluate its efficacy and safety in pediatric age (15).

In conclusion, our report shows that there is a need of a reliable biomarker for identifying patients with SJS. Such marker should be determined in samples collected by a non-invasive, safe and fast to perform method such as the use of exhaled breath condensate (16). The rarity of SJS hampers trials on therapy. However, further studies are warranted to clarify whether there is an individual response to different drugs and what the optimal treatment plan of SJS beyond supportive care is.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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