Paediatr Croat. 2013;57:268-70
PRIKAZ BOLESNIKA / *CASE REPORT*
www.paedcro.com

Stevens-Johnson syndrome: case report

Manisa Muci, Numila Kuneshka*

Stevens-Johnson syndrome is a rare and life-threatening acute allergic reaction affecting the skin and mucous membranes. We discuss the clinical presentation, evaluation, and treatment of a 9-year-old girl with Stevens-Johnson syndrome, which occurred due to the antiepileptic drug carbamazepine (Tegretol™).

Keywords: Stevens-Johnson syndrome; carbamazepine; child

INTRODUCTION

Stevens-Johnson syndrome (SJS) is an immune complex-mediated hypersensitivity disorder that typically involves the skin and mucous membranes. SJS is characterized by mucous membrane erosions and blisters on less than 10% of total body surface area (BSA), whereas another form of the disease is called toxic epidermal necrolysis (TEN), involving more than 30% of total BSA (1). Historically, SJS was first described in 1922 by two American physicians *Stevens and Johnson*. They described an acute mucocutaneous syndrome in two young boys, characterized by severe purulent conjunctivitis, severe stomatitis with extensive mucosal necrosis, and "erythema multiforme-like" cutaneous lesions (2, 3). SJS is a serious systemic disorder with the potential for severe morbidity and even death. Drugs, particularly allopurinol, sulfonamides, nonsteroid anti-inflammatory drugs (NSAIDs), antibiotics, and anticonvulsants, are the most common precipitants of SJS and TEN (4). *Mycoplasma pneumoniae* is the most convincingly demonstrated infective cause of SJS.

The disorder occurs in all age groups but is more common in people over age 40, probably because this age group tends to use more prescribed drugs (5, 6).

CASE REPORT

A 9-year-old girl was admitted to the pediatric ward in Mother Theresa University Hospital Center in Tirana, with skin rashes and eruption almost all over the body, along with high-grade continuous fever and cough. The fever appeared 3 weeks after the girl had started taking carbamazepine (Tegretol™) prescribed by a pediatric neurologist for severe episodic headaches. She had no previous history of adverse drug reactions. Other personal and family history was unremarkable. She was agitated and complained of increasing dysphagia, dysuria, and photofobia.

On examination, she appeared ill, febrile (39.5˚C), with marked conjunctivitis, and with small vesicles on nasal and oral mucosa. Vesicles were also present on her genitalia. An erythematous cutaneous eruption coalesced especially on her trunk, with many small vesicles and a few necrotic lesions (Figures 1 and 2).

Laboratory tests produced the following results: total white blood cell count $11x10^9$/L; serum transaminases were mildly elevated, creatinine and blood urea nitrogen were normal, C-reactive protein 31 mg/L, routine and microscopic examination of urine showed no abnormality; blood culture and mycoplasma detection were negative.

Chest X-ray and ultrasonography of the whole abdomen revealed normal findings.

At first, the suspected drug (carbamazepine) was withdrawn immediately. Then she was administered supportive and symptomatic treatment with intravenous fluids (isotonic solution, 5% dextrose solution, cefazoline, analgesics (paracetamol), dexamethasone in 4 divided doses, cetirizine b. i.d., glycerin swabs on the lips, eye drops and ointment. After about 48 hours, the child became stable; however, her treatment and other supportive care were continued for 10 days. Finding her clinically stable, the child was discharged after 15 days of hospital stay, with the advice for regular fol-

* University Hospital Center of Tirana "Mother Teresa", Tirana, Albania

Correspondence to:
Manisa Muci, MD, University Hospital Center of Tirana "Mother Teresa", Tirana, Albania, e-mail: manisa_hasa@yahoo.com

Primljeno/Received: 14. 2. 2012., Prihvaćeno/Accepted: 14. 1. 2013.

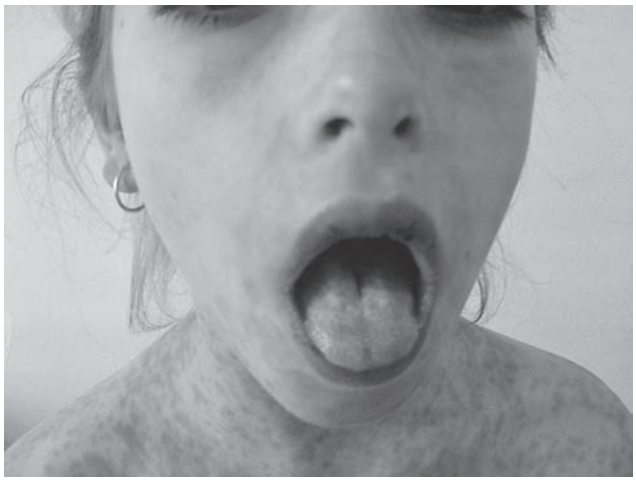

FIGURE 1. Lesions on oral mucosa

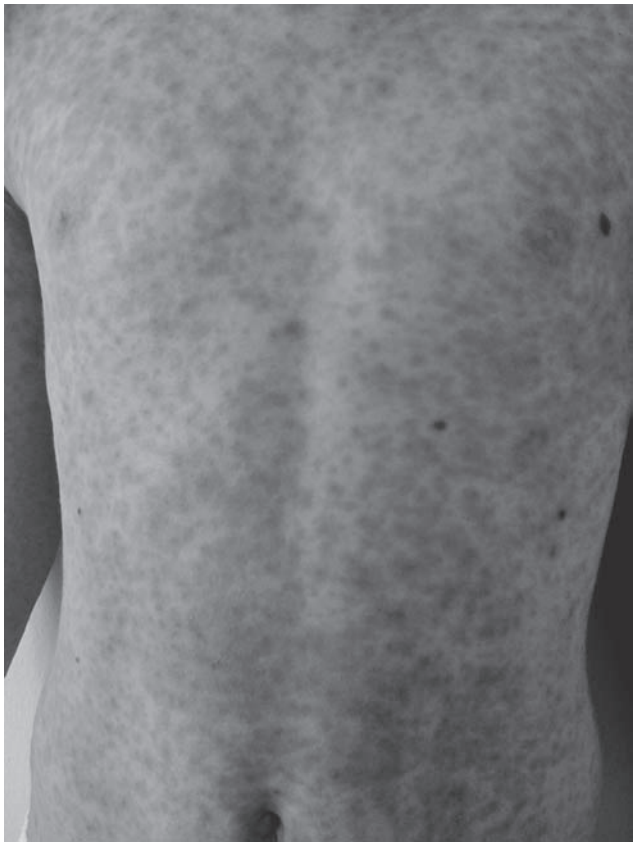

FIGURE 2. Erythematous eruption on the skin with many small vesicles and a few necrotic lesions

low-up and avoidance of carbamazepine and other related medications in the future.

DISCUSSION

Stevens-Johnson syndrome is a life-threatening adverse drug reaction characterized by an acute eruption of vesicles and bullae involving the skin and mucous membrane. Its incidence ranges from 1.2 to 6 cases *per* million *per* year. The pathogenesis of SJS/TEN is largely unknown, although several theories have been developed. The widespread epidermolysis and blistering results from keratinocyte apoptosis – an organized series of biochemical reactions leading to cell changes and cell death. Keratinocyte apoptosis mediated by cytotoxic T-lymphocytes (CD8+) in SJS and TEN is modulated by plasma TNF-alpha and interferon-gamma, which are increased in patients with SJS and TEN (2, 7). Several drugs are at "high" risk of SJS/TEN, including allopurinol, sulfonamide, antibiotics and NSAIDs of the oxicam type. Antiepileptics such as phenytoin, phenobarbital, and carbamazepine play an important role in the development of drug-induced serious skin reactions such as SJS and TEN. These reactions generally appear in the first 8 weeks of treatment (4). Diagnosis relies mainly on clinical signs together with histologic analysis of skin biopsy showing typical full-thickness epidermal necrolysis due to extensive keratinocyte apoptosis (3).

Differential diagnosis includes linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosis, disseminated fixed bullous drug eruption, and staphylococcal scalded skin syndrome.

Management includes hospitalization, discontinuation of the suspected drug, and supportive treatment. Drug treatment for SJS and TEN is controversial. High-dose systemic corticosteroids (e.g., methylprednisolone 80 to 200 mg *i.v.* or prednisone 80 mg *p.o.* once daily for 7 to 10 days or until progression stops), or cyclophosphamide (300 mg *i.v.* 24 h for 7 days or until significant improvement) can be administered to inhibit T-cell-mediated cytolysis. Cyclosporine (3 to 5 mg/kg *p.o.* once daily) inhibits CD8 cells and has been shown to decrease the duration of active disease by 2 to 3 days in some instances. However, corticosteroids are controversial and are thought by some to increase mortality. Plasmapheresis can remove reactive drug metabolites or antibodies. Early high-dose *i.v.* immune globulin (IVIG) 0.5 to 1.0 g/kg should be administered for 3 days to a total dose of 1.5 g/kg to 3.0 g/kg (2, 8). Despite some remarkable results using high-dose IVIG for TEN, clinical trials involving small cohorts have reported conflicting results.

CONCLUSION

Stevens-Johnson syndrome is a potentially fatal skin and multiorgan disease with a strong etiologic link to some medications. Physicians must therefore consider SJS as a potential complication of treatment, especially when the use of "high risk" medication is questionable. Affected pa-

tients and their first-degree relatives should be instructed to avoid any identified drug that may be responsible (9).

NOVČANA POTPORA/*FUNDING*
Nema/*None*

ETIČKO ODOBRENJE/*ETHICAL APPROVAL*
Nije potrebno/*None*

DOPRINOSI AUTORA/*DECLARATION OF AUTHORSHIP*
Muci M. – pretraživanje literature, prikupljanje podataka, pisanje rada/*literature search, data collection, writing paper*
Kuneshka N. – slike/*figures*

SUKOB INTERESA/*CONFLICT OF INTEREST*
Autori su popunili *the Unified Competing Interest form na www.icmje.org/coi_disclosure.pdf (dostupno na zahtjev)* obrazac i izjavljuju: nemaju potporu niti jedne organizacije za objavljeni rad; nemaju financijsku potporu niti jedne organizacije koja bi mogla imati interes za objavu ovog rada u posljednje 3 godine; nemaju drugih veza ili aktivnosti koje bi mogle utjecati na objavljeni rad./*All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.*

REFERENCES

1. Castana O, Rempelos G, Anagiotos G, Apostolopoulou C, Dimitrouli A, Alexakis D. Stevens-johnson syndrome: a case report. Ann Burns Fire Disasters. 2009;22:147-51.
2. French LE. Toxic epidermal necrolysis and Stevens Johnson syndrome: uur current understanding. Allergol Int. 2006;55:9-166.
3. Harr T, French LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. Orphanet J Rare Dis. 2010;5:39.
4. Rzany B, Correia O, Kelly JP, Naldi L, Auquier A, Stern R. Risk of Stevens-Johnson syndrome and toxic epidermal necrolysis during first weeks of antiepileptic therapy: A case-control study. Study Group of the International Case Control on Severe Cutaneous Adverse Reactions. Lancet. 1999;953:2190-4.
5. Morelli JG. Stevens Johnson Syndrome. In: Kliegman RM, Behrman RE, Jenson HB, Stanton B, eds. Nelson Textbook of Pediatrics. 18th ed. Philadelphia, PA: Saunders Elsevier; 2007:2687.
6. Atkinson TP, Boppana S, Theos A, et al. Stevens-Johnson syndrome in a boy with macrolide-resistant Mycoplasma pneumoniae. Pediatrics. 2011;127: e1605–e9.
7. Abe R, Shimizu T, Shibaki A, Nakamura H, Watanabe H, Shimizu H. Toxic epidermal necrolysis and Stevens-Johnson syndrome are induced by soluble fas ligand. Am J Pathol. 2003;162:1515-20.
8. Shear NH. Use of IVIG in children with SJS and TEN. J Watch Dermatol. 2004;112:1430-6.
9. Smelik M. Stevens Johnson syndrome: a case study. Perm J. 2002;6:31-4.

SAŽETAK

Stevens-Johnsonov sindrom: prikaz bolesnika

Manisa Muci, Numila Kuneshka

Stevens-Johnson-ov sindrom je rijetkak i po život opasna akutna alergijska reakcija koja utječe na kožu i sluznicu. Prikazali smo kliničku sliku, vrjednovanje i liječenje 9-godišnje djevojčice sa Stevens-Johnson-ovim sindromom, koji se pojavio nakon uzimanja antiepileptičkog lijeka karbamazepina (Tegretol ™).

Ključne riječi: Stevens-Johnson-ov sindrom; karbamazepin; dijete