Stevens-Johnson syndrome on treatment with sulfasalazine for Crohn's disease: Need for a multidisciplinary approach

Anna Viola[1], Anna Maria Caltagirone[2], Giuseppina Campisi[3], Girolamo Guarneri[4], Maria Cappello[1]

[1]*Gastroenterology Section, DBiMis, University of Palermo, Palermo, Italy*
[2]*Dermatology Section, DiBiMis, University of Palermo, Palermo, Italy*
[3]*Stomatology Section, DiChirOns, University of Palermo, Palermo, Italy*
[4]*Gynecology Section, Mother & Child Department, University of Palermo, Palermo, Italy*

Cite this article as: *Viola A, Caltagirone AM, Campisi G, Guarneri G, Cappello M. Stevens-Johnson syndrome on treatment with sulfasalazine for Crohn's disease: Need for a multidisciplinary approach. Turk J Gastroenterol 2018; DOI: 10.5152/tjg.2018.17728.*

Dear Editor,

Sulfasalazine has long been used for the treatment of inflammatory bowel disease (IBD), in particular, for its effectiveness in patients with persistent peripheral arthritis, the most common extraintestinal manifestation in IBD (1). Its role has recently been confirmed by the ECCO guidelines for the management of extraintestinal manifestations (2). The use of sulfasalazine is limited by adverse events including severe skin reactions, such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), life-threatening disorders with high mortality and significant long-term morbidity. The incidence of SJS and TEN ranges from 0.4 to 1.2 and from 1.2 to 6 per million person-years, respectively (3). There are only few cases published in the literature of SJS related to sulfasalazine for the treatment of IBD (4).

We report the case of a 32-year-old woman. Ileocolonic Crohn's disease was diagnosed on the basis of clinical (diarrhea without blood and mucus), endoscopic, and histological criteria in March 2015. She was treated with prednisone and mesalamine with a partial response. Because of joint pain, mesalamine was replaced with sulfasalazine (SALAZOPYRIN®; Pfizer). In April 2015, she was hospitalized for persistence of arthralgia and fever (37.5°C). She experienced a worsening skin rash with maculo-papular lesions rapidly evolving to bullous manifestations involving the face (Figure 1), the mouth (Figure 2), the trunk, the arms and the legs, and the vulva 3 days after admission. She could not eat or walk without pain because of the bullae in her mouth and her feet. Ocular lesions also appeared. She was also complaining of odynophagia and a feeling of lingual and laryngopharyngeal swelling. ENT consultation excluded edema of the glottis. All medications were discontinued. Bacterial and viral infections were ruled out. Laboratory tests revealed a C-reactive protein level 6 times above the normal limits; blood cell count was normal, and no electrolyte abnormalities were observed. The consultant dermatologist diagnosed SJS related to sulfasalazine. Intravenous steroid therapy (methylprednisolone, 1 g/day, tapered), antihistamines (chlorphenamine, 10 mg/day), topical antibiotics (chlortetracycline), and topical steroids were administered with progressive clinical improvement. Gynecology and stomatology specialists provided additional topical therapies. She was discharged in May 2015. Skin lesions were significantly improved; she had no fever and was able to eat liquid meals. On follow-up, skin lesions progressively disappeared without sequelae. Steroids were slowly tapered and stopped in August 2015. Bowel symptoms did not recur, and colonoscopy in October 2015 showed mucosal healing.

For this report, the patient provided informed consent to publish her clinical details.

The diagnosis of SJS is based on clinical data and histological findings showing full-thickness necrosis of the epidermis and keratinocyte apoptosis (5). Symptoms typically begin 1-3 weeks after the initiation of the causative medication (6). Other possible etiologies, including infections or other drugs, should be excluded. Clinical presentation at onset varies among patients, but generally. fever, malaise, cough, rhinorrhea, and anorexia precede inflammation and ulcerations of the ocular, oral, and genital mucosa. After few days, a painful generalized erythematous vesiculobullous rash develops (7). The immediate cessation of any potential causative agents is mandatory, and the goal of treatment is to provide symp-

Corresponding Author: ***Anna Viola; annaviola88@gmail.com***
Received: ***April 1, 2018*** *Accepted:* ***July 3, 2018*** *Available online date:* ***December 3, 2018***

DOI: ***10.5152/tjg.2018.17728***

tomatic benefit, avoid severe complications, and reduce mortality. We did not perform skin biopsy, but symptoms, signs, and clinical course are in accordance with published literature. Our report has the aim of increasing physicians' awareness of this potential, lethal, or disabling, though rare, hypersensitivity reaction related to sulfasalazine, a drug still used for the treatment of IBD. We would like also to stress that a multidisciplinary approach with the involvement of a team of specialists guarantees prompt recognition, correct choice of tailored therapies, management optimization, and improved outcome without sequelae. The limit of our study is the lack of histological diagnosis because the patient had not been biopsied, but the presentations were in line with previous descriptions.

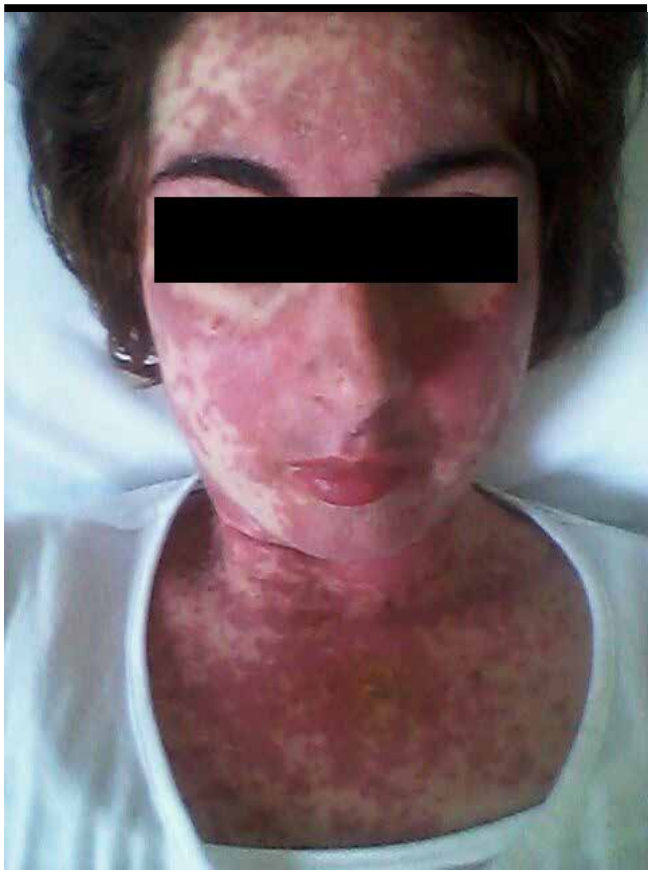

Figure 1. Severe skin rash due to Steven-Johnson Syndrome

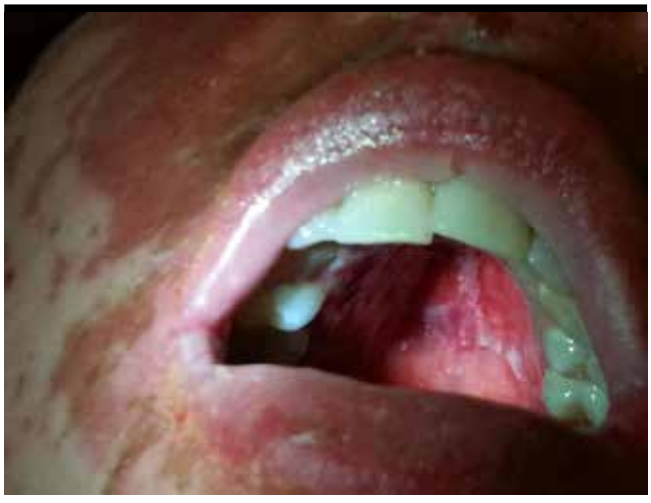

Figure 2. Lesions of the oral mucosa due to Steven-Johnson Syndrome

Informed Consent: Informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - A.V., M.C.; Design - A.V., M.C.; Supervision - A.M.C., G.G., G.C.; Data Collection and/or Processing - A.V., M.C.; Analysis and/or Interpretation - A.V., M.C., A.M.C., G.G., G.C.; Literature Search - A.V., M.C.; Writing Manuscript - B.C.S.; Critical Review - A.M.C., G.G., G.C.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Peluso R, Iervolino S, Vitiello M, et al. Articular and other immune-mediated extra-intestinal manifestations in inflammatory bowel diseases. Eur J Inflamm 2014; 12: 251-9. [CrossRef]
2. Harbord M, Annese V, Vavricka SR, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. J Crohns Colitis 2016; 10: 239-54. [CrossRef]
3. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. N Engl J Med 1994; 331: 1272-85. [CrossRef]
4. Tremblay L, de Chambrun GP, Vroey BD, et al. Stevens-Johnson syndrome with sulfasalazine treatment: report of two cases. J Crohn's Colitis 2011; 5: 457-60. [CrossRef]
5. Endorf FW, Cancio LC, Gibran NS. Toxic epidermal necrolysis clinical guidelines. J Burn Care Res 2008; 29: 706-12. [CrossRef]
6. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. N Engl J Med 1994; 331: 1272-85. [CrossRef]
7. Goodman H. Nikolsky sign; page from notable contributors to the knowledge of dermatology. AMA Arch Derm Syphilol 1953; 68: 334-5. [CrossRef]