Stevens Johnson Syndrome-Toxic Epidermal Necrolysis Overlap induced by sulfasalazine treatment: A case report

Un nouveau cas de syndrome de chevauchement entre SSJ/NET à la sulfasalazine.

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RÉSUMÉ

Prérequis : Le Syndrome de Stevens-Johnson (SJS) et la nécrolyse épidermique toxique (NET) sont des réactions cutanées indésirables graves des médicaments, potentiellement mortelles, caractérisés par un décollement épidermique se traduisant par des bulles et la mise à nue cutanée. SJS, le syndrome de chevauchement et la NET ne diffèrent que par l'étendue de la surface cutanée décollée.

Observation : Nous rapportons ici le cas d'une jeune femme (de 33 ans), admise au service de dermatologie pour un décollement épidermique (18% de la surface corporelle), des bulles et des lésions maculo-papuleuses érythémateuses apparues 15 jours après la prise de sulfasalazine. Par ailleurs, la patiente a présenté un état fébrile, un œdème facial douloureux avec dysphagie La biopsie cutanée était compatible avec un SSJ et NET. Vu que la surface du décollement épidermique se situait entre 10% et 30%, elle a été diagnostiquée comme un syndrome de chevauchement. L'évolution à l'arrêt de sulfasalazine était favorable, avec régression progressive des signes cliniques et normalisation des paramètres biologiques au bout de 17 jours d'hospitalisation.

Conclusion: Les praticiens et les patients doivent être conscients des signes cliniques des effets indésirables cutanés graves des médicaments tels que la fièvre, symptômes pseudo-grippaux, dysphagie, de brûlure oculaires ou décollement épidermiques. L'arrêt précoce du médicament reste le meilleur moyen permettant d'améliorer le pronostic des patients atteints du syndrome de Stevens-Johnson et nécrolyse épidermique toxique.

Mots-clés

Réactions cutanées sévères ; Syndrome de Stevens-Johnson (SJS) ; Nécrolyse épidermique toxique ; Syndrome de chevauchement SSS-NET ; sulfasalazine

SUMMARY

Introduction: Stevens Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are life-threatening and severe adverse cutaneous drug reactions characterized by epidermal detachment presenting as blisters and areas of denuded skin. SJS, SJS-TEN overlap and TEN differ only by their extent of skin detachment.

Case presentation: We report here the case of a young woman (33-year old) admitted to the dermatological unit for epidermal detachment (at 18% of the body surface area), blisters, red macular and papular lesions, developed 15 days after administration of sulfasalazine. Prior to this, she complained of fever and discomfort upon swallowing. Skin biopsy had shown epidermal necrosis compatible with Stevens Johnson Syndrome and Toxic Epidermal Necrolysis. As the epidermal detachment was between 10% and 30%, she was diagnosed as a Stevens Johnson Syndrome/Toxic Epidermal Necrolysis overlap. The course was favorable 17 days after stopping the drug and starting a symptomatic treatment.

Conclusion: Practitioners and patients need to be aware of the initial clinical signs of severe cutaneous adverse drug reactions such as fever, influenza-like symptoms, dysphagia or burning eyes. Early discontinuation of medication remains the best way to improve prognosis of patients with Stevens Johnson's Syndrome and Toxic Epidermal Necrolysis.

Key-words

Severe cutaneous adverse reactions ; Stevens-Johnson Syndrome ; Toxic epidermal necrolysis ; SJS-TEN overlap ; Sulfasalazine

Sulfasalazine, a combination of salicylate and a sulfa-antibiotic, is a bowel anti-inflammatory widely used for the treatment of ulcerative colitis. Sulfasalazine may cause severe adverse cutaneous drug reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). TEN and SJS occur rarely with an incidence ranging respectively from 0.4 to 1.5 cases and from 1 to 7 cases per million person-years [1]. To date, few cases of SJS and TEN associated with the use of sulfasalazine are published in the English and French-language literature [2-8]. We report here the case of a SJS-TEN overlap due to the administration of sulfasalazine.

CASE PRESENTATION

A 33-year old woman, without any medical history, was admitted on June 25, 2013 to the dermatology unit for a severe mucocutaneous adverse reaction.Sulfasalazine (2g/day) had been prescribed by a general practitioner for rectal bleeding that had been recurrent for about six months. Fifteen days after the introduction of sulfasalazine, the patient had a fever (40°C), developed a painful facial edema and complained of discomfort upon swallowing. She stopped taking sulfasalazine and started paracetamol (1.5g/day) and aspirin (3g/day) for 2 days. The patient restarted sulfasalazine and stopped it immediately with the appearance of pruritic widespread macular and papular lesions, large confluating blisters and oral erosions leading to her hospitalization.

On admission, she had fever (temperature between 38°C and 39°C). The cutaneous exam showed polymorphic lesions: dusky red macular and papular lesions, atypical targets and blisters. The lesions were isolated with confluence on face and trunk (Fig 1 and 2).

Figure 1 : Epidermal detachment and a large blister on the neck.

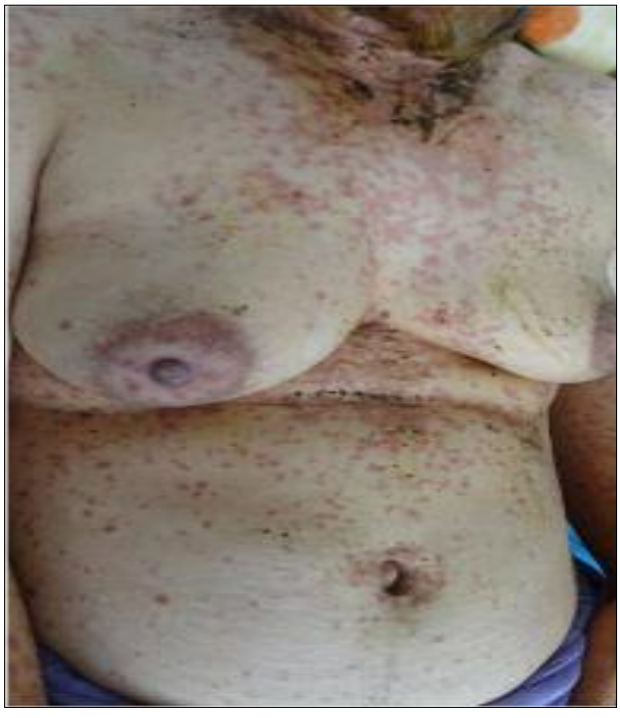
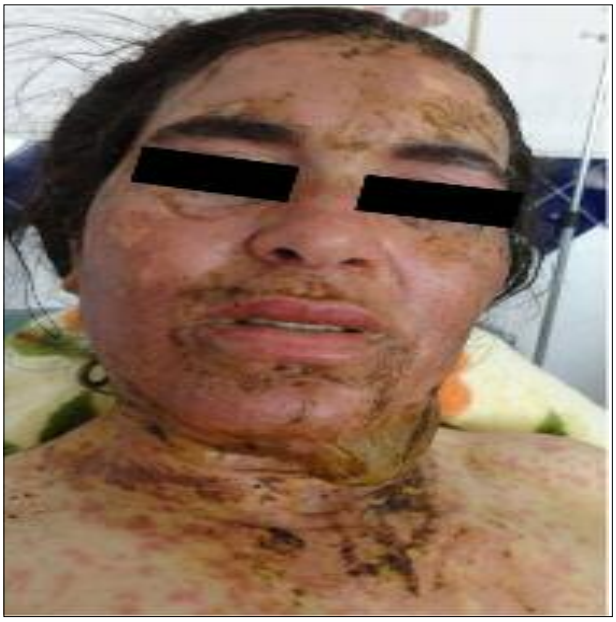


Figure 2 : Dusky red maculo-papular lesions on the trunk.



Nikolsky sign was positive. Epidermal detachment occurred on 18% of the body surface. The mucosal exam revealed cheilitis with oral erosions and conjunctival hyperemia. Laboratory tests revealed a CRP level ×16N (90mg/L), low level of lymphocytes (500/mm3) and hyperglycemia (1.56g/L), ALT (×2.5N), γ-GT (×2N) and normal values of blood urea and creatinine. Bacterial and viral infections were ruled out. The chest-X ray, electrocardiogramm and abdominopelvic ultrasound were normal. Histopathological examination of a skin biopsy showed an epidermal necrosis. The outcome was favorable after discontinuation of sulfasalazine and initiation of symptomatic treatment allowing the patient to be discharged from hospital 17 days after.

DISCUSSION

SJS, TEN and their overlap are severe and life-threatening exfoliative skin diseases with mortality rates of 10% for SJS, 50% for TEN and 30% for SJS/TEN overlap [9].In adults, women are more frequently affected by a ratio of 3:2 to 2:1 with a female preponderance of approximately 65% in the SJS/TEN overlap. In 74% to 94% of cases, SJS and TEN are drug-induced. Infections, particularly of the upper respiractory tract, may also be involved [1,9]. As described in the literature, fever and dysphagia were the first symptoms observed in our patient and preceded the cutaneous and mucosal lesions [10].The characteristic mucosal involvement of SJS was present with a positive Nicolsky sign. The skin detachment at about 18% of the body surface was compatible with a SJS/TEN overlap.

The delay of 2 weeks to present the symptoms is suggestive of the role of sulfasalazine. An interval of 4 to 28 days between the administration of the suspected drug and onset of the adverse reaction is reported [11]. According to the largest studies conducted up to now [12,13],

sulfasalazine is one of the drugs with a high risk to induce SJS and TEN, besides cotrimoxazole (RR 102) and other infective sulfonamides (RR 53), allopurinol (RR 11), carbamazepine (RR33), lamotrigine (RR>14), nevirapine (RR>22), NSAIDs (oxicam type) (RR 72), phenobarbital (RR 45) and phenytoin (RR 53). The SCORTEN, which is a severity-of-illness score for TEN [10] used to predict mortality, in our patient is 1.Thus, the predictive mortality rate is estimated at about 3.2%.

CONCLUSION

Practitioners and patients need to be aware of the initial clinical signs of SJS and TEN such as fever, influenza-like symptoms, dysphagia or burning eyes, that are more often prior to the onset of the mucocutaneous lesions. Early withdrawal of the drug contributes to improved prognosis, as was the case of our patient.

Some Asian studies have identified genetic markers for severe cutaneous adverse reactions that could help to identify predisposing HLA subtypes and thus predict rare hypersensitivity reactions [14, 15]. However, can we extrapolate the results of Asian or European studies to the African population? Pharmacogenetic and epidemiological studies in African countries are needed to answer the question. Until then, early discontinuation of the suspected drug remains the best way to improve prognosis of patients developing SJS, TEN or SJS/TEN overlap.

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