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Stevens Johnson´s syndrome induced by leflunomide and methotrexate in a young patient with rheumatoid arthritis

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Abstract

We report a case of Stevens-Johson´s syndrome secondary to the use os leflunomide and methotrexate in a patient dignosed with rheumatoid arthritis. Treatment with corticosteroids and cyclosporine were successful and mucose and skin lesions relieved in less than a month. A review of the Stevens-Johnson´s syndrome in terms of management is also presented.

Clinical Presentation

We present the case of a 33 year old male diagnosed with rheumatoid arthritis five years ago, who was treated with methotrexate 15mg weekly until 1 month ago. Due to insufficient control of symptoms was added to treatment leflunomide 20mg daily. Meanwhile the patient increased the dose of methotrexate to 20 mg daily, on its own initiative.

Four days after modification of the treatment, patient experienced the onset of erythematous, papular and even blisters lesions symmetrically distributed in the chest, abdomen, arms and legs. Also presented target lesions on the palm of the hands and soles of the feet as well as oral ulcers and dysphagia. (Picture 1).

Lab tests showed a mild anemia and leukopenia. The ESR was 93mm / h and CRP

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56mg / L. Hepatic and renal function were normal.

The patient was diagnosed with Stevens-Johnson´s syndrome and was treated with cyclosporine 200 mg every 12 hours, prednisone 40mg/day, 100ml albumin 20% / day, hydration and parenteral feeding. were stopped methotrexate and leflunomide.

During evolution the patient developed worsening anemia, leucopenia and thrombocytopenia, which were attributed to overdose of methotrexate, with good response to neutrophils colony stimulators. Repeatedly controls of hepatic and renal function were normal throughout evolution.

On the third day of treatment the trunk and abdominal lesions had significantly improved and on the seventh day leg injuries began to subside. The patient began oral tolerance on the tenth day smoothly.

To our knowledge, this is the first case of Stevens-Johnson´s syndrome secondary to concomitant use of methotrexate and leflunomide in a patient with rheumatoid arthritis.

Discussion

Stevens Johnson´s syndrome is the most serious manifestation of diffuse multiform erythema can occur in response to almost all drugs and some viral or fungal infections. Its prevalence is estimated at 1-6 cases per million people.(1,2) It is defined a skin reaction mechanism mediated dysregulation of toxins purification capacity by keratinocytes and consequent massive apoptosis. This assumption, however, does not explain the presence of mucosal signs.(1,3,4) The most severe forms are associated with exposure to medications, being the most common aromatic anticonvulsants, antibiotics and anti-inflammatories.(3,5,6) Reports of Stevens Johnson´s syndrome associated with methotrexate are anecdotal and there are none reported associated with the use of leflunomide.

Cutaneous manifestations are the most florid: confluent erythematous papules, target lesions and bullae distributed symmetrically on the chest, abdomen, arms, palms, soles and legs.(4,7) Along with the cutaneous, mucosal involvement is very important as the commitment of the eye condition, mouth and oropharyngeal tract.(1,5,8)

Treatment of Stevens Johnson´s syndrome should be done from two approaches: measures based support and treatment of the disease. The patient should receive supportive measures depending on the type and degree of impairment. The presence of blisters or peeling of the corneum (known as Nikolsky´s phenomenon) can prevent using albumin and ensuring adequate hydration of the patient.(1,3,4) In specific cases antibiotic therapy should be considered in order to prevent skin infections. Depending on the degree of oropharyngeal commitment parenteral feeding should be consider.(5,8) Finally, special attention to ophthalmological surveillance to prevent ocular synechiae, should be paid.(6,9) Skin lesions benefit from the administration of topical

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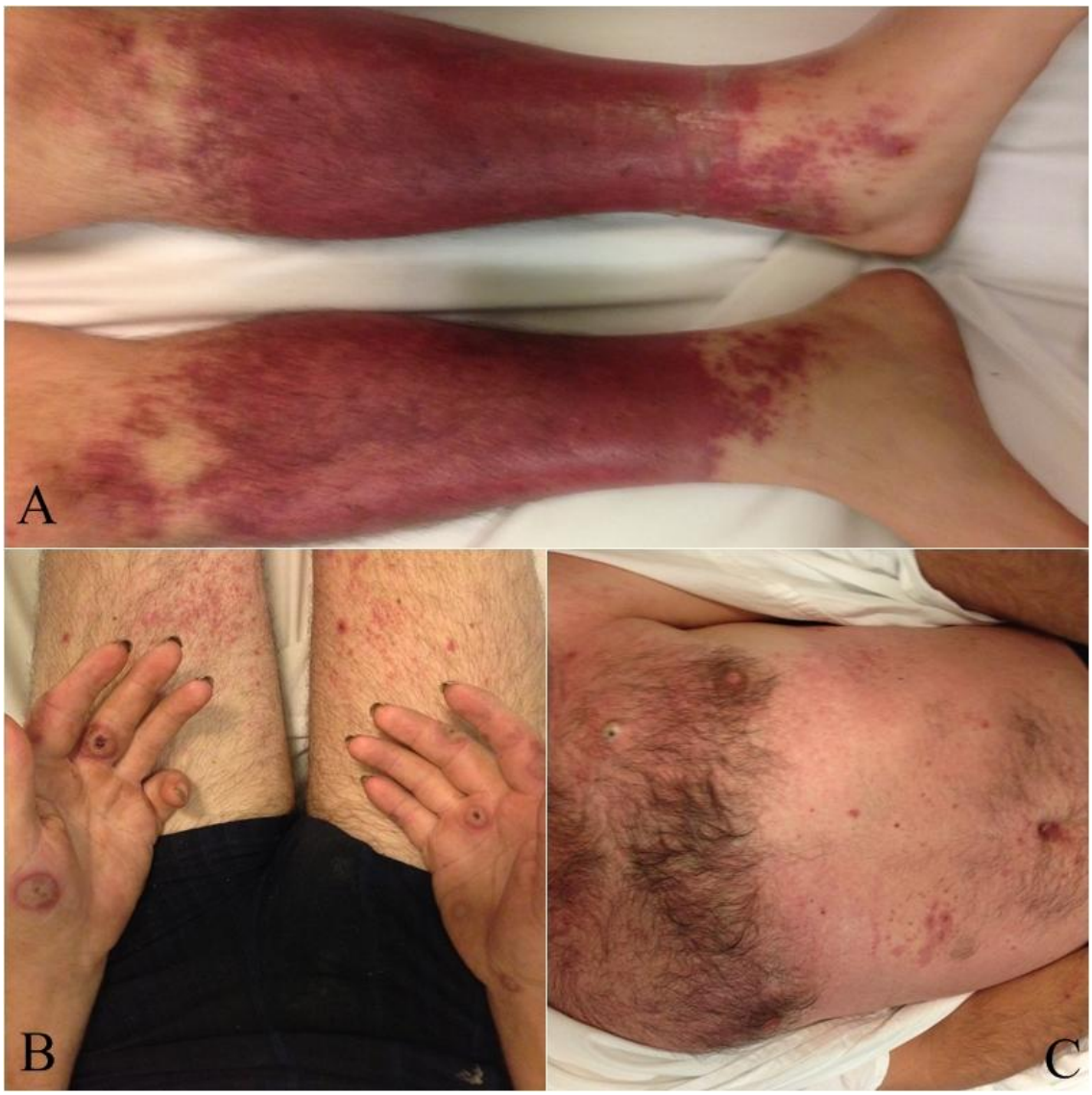
corticosteroids. There is not a universally accepted treatment for the disease. There is consensus that the drugs suspected of having induced the box should be removed completely. As treatment, using oral cyclosporine and corticosteroids has been tested successfully. In situations of greater systemic involvement immunoglobulin administration has been employed with positive results.(1,4,7)

The peculiarity of this case is that the patient developed jointly a typical feature of diffuse major multiform erythema attributable to a reaction to leflunomide and methotrexate new dose as well as the manifestations of methotrexate overdose. Although mucositis is a process attributable to own johsons stevens syndrome, overdose with methotrexate may have played a role in this component of the disease.



Picture 1. A: Confluent erythematosus lesion in legs; B: Target lesions on the palms; C: Papullae and bullae over the chest and abdomen.

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