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Oseltamivir-Induced Steven Johnson Syndrome, Case Report

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ABSTRACT

First described in 1922, Steven Johnson Syndrome (SJS) is an acute mucocutaneous disease with conjunctivitis, stomatitis, purple macules and skin necrosis in which an acute inflammatory process followed by the action of immune complexes has been identified. In the middle hypersensitivity, it should involve less than 10% of the total body surface. Its annual incidence in the world is unknown, it is estimated 1-2 cases per million in a year of which 20% will be pediatric patients; this can be triggered by drugs, infectious agents and biological agents. It manifests as lesions in the skin and mucous membranes of which it can involve ocular conjunctiva, oral, nasal, vaginal, urethral and perianal mucosa

KEYWORDS: Steven-Johnson, SSJ, Oseltamivir, hypersensitivity, drugs.

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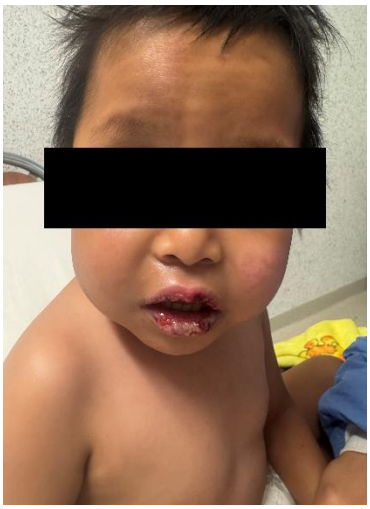
1.- INTRODUCTION

First described in 1922, Steven Johnson Syndrome (SJS) is an acute mucocutaneous disease with conjunctivitis, stomatitis, purple macules and skin necrosis in which an acute inflammatory process followed by the action of immune complexes has been identified. In the middle hypersensitivity, it should involve less than 10% of the total body surface. Its annual incidence in the world is unknown, it is estimated 1-2 cases per million in a year of which 20% will be pediatric patients; this can be triggered by drugs, infectious agents and biological agents. It manifests as lesions in the skin and mucous membranes of which it can involve ocular conjunctiva, oral, nasal, vaginal, urethral and perianal mucosa [1].

Drugs are the most common cause of SJS, some of which are anticonvulsants, sulfonamides, NSAIDs, allopurinol, among others. After the appearance of the AH1N1 influenza epidemic in 2009, an antiviral drug was developed that inhibits neuraminidase that although it has been very well tolerated, there are reports of skin reactions and hypersensitivity.

A rare case of Stevens Johnson syndrome induced by Oseltamivir is presented.

2.- PRESENTATION OF THE CASE



This is a 3-year-old preschooler, originally from and resident in Querétaro, with no significant personal pathological history, complete vaccination schedule for his age, and no reported previous allergies. His illness began a week earlier with respiratory symptoms characterized by fever up to 39.3°C, rhinorrhea, general malaise, irritability, and dry cough; he went to a private doctor who performed PCR for influenza A and B with a positive result for type A. He began treatment with Oseltamivir, sodium metamizole, and Loratadine. On the second day of treatment, his mother noticed that after the administration of the antiviral, he began to have a rash, which resolved with the subsequent administration of antihistamines. On the fifth day of treatment, the patient presented the appearance of erythematous macules and papules with a violet center on the lips and perioral region. They went to a

private doctor again, who prescribed conservative management, including bromhexine and ibuprofen. However, there was no improvement and the patient developed bleeding ulcers and spread to the genitals, perianal region, and hands. The parents decided to go to the hospital emergency room.

The patient was admitted to the hospital with a probable diagnosis of Stevens Johnson syndrome. His laboratory tests on admission showed leukocytes (13,550 cells/µL) with neutrophil predominance, elevated C-reactive protein (7.64 mg/dL). He was evaluated by pediatric dermatology with a positive diagnosis for Stevens Johnson with a 2% affected body surface area, SCORTEN 0 points, 3.2% mortality. Management was started with gammaglobulin and prednisone. He was evaluated by ophthalmology to rule out injury, ruling out and leaving prophylactic management with lubricant and ophthalmic steroid. After 10 days of treatment, the patient showed improvement in his condition with complete resolution of the lesions and discharge home.

3.- DISCUSSION

Oseltamivir is an antiviral drug indicated for the treatment of influenza A and B that inhibits the neuraminidase responsible for the replication of the virus. In general, there are few adverse effects reported with its administration, but some cutaneous side effects have been documented, including SJS and TEN.

Most of the severe reactions are documented in Asian patients, particularly Japanese, and related to polymorphisms of the human sialidase enzyme that is homologous to neuraminidase, which would cause Oseltamivir to bind to it and generate adverse reactions. In the same way, in Asia, a relationship has been found that is not yet clearly established between HLA-A*0206 and SJS, which may be related to a reaction to Oseltamivir.

In this case, of the drugs mentioned, Oseltamivir was the only one that the patient had never taken in his life, nor does he have a family or personal history of allergies, which helps us to identify more easily who could have caused the hypersensitivity reaction. As far as management is concerned, although the use of steroids remains controversial, its use in conjunction with gammaglobulin in various studies has shown that it manages to block keratinocyte apoptosis and in this particular case it was successful. It is important to mention that an adequate diagnosis allows a limitation of the damage and, in this case, of the mortality rate, since the progression to a toxic epidermic necrolysis reaches up to 30%. [2]

4.- CONCLUSIONS

SJS is associated with the use of drugs, most patients present symptoms 7 to 21 days after starting the drug, the management depends on the degree of affectation which includes support measures, skin care and pharmacotherapy. Although there is still no consensus on management, gammaglobulin prevents the spread of damage by blocking keratinocyte apoptosis and has been accepted in various studies in pediatrics for the management of SJS, the use of corticosteroids remains controversial. It is important to make a timely diagnosis to avoid a fatal outcome; this syndrome should be suspected when administering any drug not previously exposed and that presents rapidly progressive lesions to improve survival.

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