Toxic Epidermal Necrolysis Related to Ketoprofen

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Toxic epidermal necrolysis (TEN) is a severe idiosyncratic, exfoliative disease of skin and mucous membranes [1, 2], most often drug related.

We present a case of TEN which was attributed to the use of the non-steroidal anti-inflammatory drug ketoprofen.

A 92-year-old woman was treated with ketoprofen for arthralgia. She used no other medications. Three weeks after starting the drug, she developed a symmetrical erythematous rash affecting the face, chest, back, forearms, thighs, palms and soles. Rectal temperature was elevated to 39.8 °C. Four days after the development of the first cutaneous signs, she developed dysphagia and dysuria.

On admission to hospital, 5 days after the development of the first cutaneous signs, flaccid bullae and extensive erythematous, necrotic and denuded areas had developed. Twenty percent of the body surface area was involved on friction and pressure areas of the shoulders, back and extremities. These areas were both tender and painful. Nikolsky’s sign was positive. In addition, there was conjunctivitis and severe stomatitis.

WBC count was $4.6 \times 10^7$ (48 segmented and 7 non-segmented neutrophils, 4 eosinophils, 2 basophils, 32 lymphocytes and 7 monocytes per 100 cells). Erythrocyte sedimentation rate was 25 mm in the first hour. A punch biopsy specimen of the skin showed necrosis of the epidermis and subepidermal release with a mononuclear cell infiltration of the dermis suggestive of TEN.

On admission ketoprofen was stopped. Treatment consisted of extensive fluid replacement, parenteral nutrition and intravenous penicillin. Local therapy consisted of daily bathing in 0.05% chlorhexidine and application of silver-sulphadiazine cream. She was nursed in an isolated room with an environmental temperature of 32 °C. The wounds re-epithelialized spontaneously within 2-3 weeks. Aside from the urinary tract infection, there were no complications. After 4 weeks of hospitalization, she was discharged in good condition.

The time course of the reaction in relation to ketoprofen use, the clinical presentation including high fever, cutaneous pain, extensive erythematous necrotic areas of skin with a positive Nikolsky sign, mucous membrane involvement and the biopsy findings are all very suggestive of the diagnosis of TEN related to ketoprofen.

Drugs are considered to be the most important cause of TEN. Drugs repeatedly incriminated include sulphonamides, barbiturates, allopurinol and pyrazolone derivates. Also other non-
steroidal anti-inflammatory drugs such as benoxaprofen and an oxicam derivate, isoxicam, have been implicated in many cases of TEN [3-7].

In addition, food additives [8, 9], fumigants [10] and contact with chemicals have also been implicated in some cases.

This is the first documented case in which TEN was attributed to the use of ketoprofen (Medline).

References
Roujeau JC: Clinical aspects of skin reactions to NSAIDs. Scand J Rheumatol 1987;65 (suppl):131-134.

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