should be performed cautiously in patients with severe reactions.

Challenge tests with diclofenac confirmed the diagnosis in five patients. All patients tolerated therapeutic doses of indomethacin and piroxicam or metamizole. In our opinion, patients with suspected selective hypersensitivity to diclofenac should be orally challenged with other NSAIDs with high potency of COX inhibition, such as indomethacin, in order to rule out an intolerance mechanism. The correct diagnosis is very important in order to recommend therapeutic alternatives.

Two of our patients diagnosed with hypersensitivity to diclofenac had reported adverse reactions after aceclofenac ingestion. This fact suggests that cross-reactions among phenylacetic-derived NSAIDs could exist. Our patients were advised to avoid administration of diclofenac and other drugs derived from phenylacetic acid such as aceclofenac and fenoclofenac. Other groups of NSAIDs were not forbidden. Patients with intolerance to NSAIDs should be advised to avoid most NSAIDs.

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Diclofenac-induced fever

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Key words: diclofenac; fever; nonallergic hypersensitivity; NSAID.

• Non-steroidal anti-inflammatory drugs (NSAIDs) are frequently involved in allergic and nonallergic drug reactions. Most of these adverse responses are related to inhibition of the cyclooxygenase enzyme. Diclofenac sodium is a widely used NSAID derivative of phenylacetic acid and continues to be the most commonly prescribed (1).

The patient was able to tolerate other NSAIDs.

Diclofenac-induced fever has been reported in patients with streptococcal myositis/fasciitis and toxic shock syndrome after intramuscular diclofenac injection (2). We report the case of a patient with diclofenac-induced fever who was able to tolerate other NSAIDs.

A 66-year-old white man with a personal history of polyarthralgias for 26 years, chronic hepatitis (virus C), and no personal or family history of allergy, developed an acute burning pain in the perineal region after ingestion of one tablet of Voltaren® (50 mg diclofenac). Five years later, after a new ingestion of Voltaren, he developed tiredness, headache, myalgias, sweating, chills, and fever. The patient recovered after discontinuation of treatment, and was treated with other NSAIDs (acetylsalicylic acid, niflumic acid, paracetamol, and nimesulide) without any adverse reaction. He was challenged with 50 mg of diclofenac in a single-blind, placebo-controlled study. Five hours after diclofenac administration, generalized pain and fever appeared. The patient was treated orally with 4 mg dexchlorpheniramine (Polaramine®), and the symptoms resolved in 2 h. No abnormalities were detected in laboratory blood tests, with the exception of an increase in γ-glutamyl-transpeptidase, 63 IU/l (normal values <6–28 IU/l), and eosinophil cationic protein, 57.8 μg/l (normal value <20 μg/l). Blood count was normal with 136 eosinophils/mm^3. No change was observed in tryptase serum levels (7.7 and 8.9 μg/l). Skin prick test and patch test with diclofenac were negative.

Drug-induced fever consists of the appearance of fever after administration of a drug and disappearance of the fever for no justifiable reason when the drug is withdrawn, while physical examination and laboratory parameters remain within normal ranges (3). The pathogenicity of this entity is unknown; however, an immunologic pathogenesis is considered for several reasons: previous exposure is required, and the fever is not dose-dependent, relapses with challenges, and is accompanied occasionally by eosinophilia. Fever, however, could be the only manifestation of this entity (4). A desensitization treatment has been proposed in some cases with successful results (5). We proposed a desensitization protocol, but it was refused by the patient. To our knowledge, this is the first reported case of fever induced by diclofenac.

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Allergy to gelatin

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Key words: allergy; gelatin; paresis.

• On 27 March 1998, a 28-year-old man was admitted to the neurosurgery clinic of the University of Messina (Italy) for bilateral back pain with a left prevalence, which had begun about 2 months before. Therefore, before admission, he underwent conventional anti-inflammatory and analgesic treatment without result, and acupuncture and physiokinesis therapy with moderate results. A month before admission, in view of the accentuation of symptoms, the patient underwent magnetic resonance imaging and computerized axial tomography. These methods detected a median posterior hernia at the L3–L4 level. The consultant neurosurgeon advised surgery.

Lower limb paresis due to contact allergy.

An operation by the L3–L4 left interlaminar approach was carried out on 7 April 1998. At 24 h after surgery, the patient first complained of tingling of the lower limbs and, subsequently, paresis and complete bilateral deficit of foot dorsiflexion. Therefore, he underwent repeated magnetic resonance imaging of the lumbosacral spine, and this showed dural sac L3–L4 compression because of the edematous reaction of the soft tissues.

A subsequent allergy consultation led to the suspicion of an allergic reaction to a hemostatic gelatin sponge (Spongostan, Ferrosan, Denmark) placed at the end of surgery at the site of the wound. Therefore, the patient underwent disruption of the wound, cleansing of the phlogistic focus, removal of the Spongostan, and biopsy.

The biopsy examination, carried out on a specimen obtained from the dural sac compression zone, showed the presence of phlogistic infiltration, mainly by eosinophils, neutrophils, and histiocytes, together with chips of the gelatin sponge.

After removal of the Spongostan, there was a gradual and rapid improvement of the neurologic objectiveness, supported by courses of daily rehabilitative physiokinesiotherapy. The patient was discharged on 2 May 1998.

After 2 months, the patient returned for a checkup, during which patch tests were carried out with the International Contact Dermatitis Research Group (ICDRG) series (True Test, Pharmacia, Milan, Italy) and an extemporaneous preparation consisting of a dilution in vaseline of the gelatin sponge.

The patch tests were scored at 48 and 72 h by the 1+ to 3+ system recommended by the ICDRG. They proved to be highly positive for gelatin (+++) at 48 h, and negative for the other substances.

Absorbable gelatin sponges have been used for many years either as a wound-dressing material (1) or for transcatheter arterial embolization in the treatment of various disorders (2). In recent years, cases of immediate-type allergic reaction caused by gelatin present in the vaccines (3) or in the recombinant human erythropoietin (4) have been reported in which specific IgE to gelatin was found in the sera of the patients.

It has also been shown that there is a possibility of delayed-type hypersensitivity to gelatin, consisting of granulomatous arteritis with massive eosinophil leukocyte infiltration subsequent to transarterial embolization therapy with a gelatin sponge (5).

We describe here an adverse reaction subsequent to the application of a gelatin sponge, at the end of surgery for a disk hernia, at the site of the wound. The clinical course, the biopsy findings, and the high positivity to the specific patch test suggest either a causative role of the gelatin or a pathogenic mechanism of delayed-type hypersensitivity. Our case represents the first report of lower limb paresis by dural sac compression related to an allergic reaction to gelatin.

Lastly, since the number of operations for disk hernia is very high and gelatin sponges are used frequently as hemostat, such an allergic reaction should always be taken into consideration.

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