Efalizumab-induced aseptic meningitis

To the Editor:

Efalizumab is a humanised monoclonal antibody, authorised for the treatment of adult patients with chronic plaque psoriasis (moderate to severe) in cases of failure to respond, contraindication or intolerance to other systemic treatments, including ciclosporin, methotrexate and PUVA. The drug works by specifically binding to a superficial leukocyte protein, interfering with the adherence of the T lymphocytes to other types of cell, including the endothelial and keratinocyte cells found in psoriasis plaques. The most frequent adverse effects (> 5% of patients) of treatment with efalizumab are infection, pruritus and arthritis. Mild to moderate acute flu-like symptoms usually appear after administration of the initial dose, symptoms that usually decrease or disappear from the third dose onwards. Anti-efalizumab antibodies have been detected in approximately 5% of patients. It is contraindicated in the case of patients with a history of malignant tumours, active tuberculosis or other serious infections, and specific forms of psoriasis such as: psoriasis in gout, psoriatic erythrodermia and pustular psoriasis, when these are the only type of psoriasis or the predominant type, as well as patients with immunodeficiency.

Set out below is the case of a patient with chronic plaque psoriasis treated with efalizumab, presenting with aseptic meningitis.

Description of the case

Male, aged 40, diagnosed with plaque psoriasis (affecting the torso, head, upper and lower limbs) for the past 15 years and thalassemia minor. Positive Mantoux in study prior to biological therapy. No known allergies to medications, smoker (20 cigarettes/day), herniated lumbar discs, previously underwent surgery for cataracts, vasectomy and surgery to the flexor tendon of the second finger of the left hand. Treated with ciclosporin for psoriasis between November 1998 to August 2001; the treatment was withdrawn due to lack of efficacy. Treatment with methotrexate was started in January 2002, and was discontinued due to possible neurological adverse effects. From the time of diagnosis to date, intermittent topical treatment with medium to high strength corticoids has been used according to the area of application. Psoralen plus UVA treatments have also been used. On 20 April 2006, treatment with efalizumab was started (0.7 mg/kg subcutaneous). Forty-eight hours after receiving the first dose, the patient suffered severe headache, fever and vomiting. The patient went to the emergency department where he was given symptomatic treatment for the headache, including: Paracetamol, tramadol and metoclopramide, zolmitriptan and diazepam. Leucocytosis (15,900 cel/mm³) was observed in the haemogram. An indirect funduscope was performed with negative results and a computerised axial tomography was normal. The headache did not remit and after 12-16 hours the first systems of rigidity of the nape of the neck appeared and the patient was taken in for observation and a lumbar puncture, which gave values of: Leucocytes 400 cel/mm³, polynuclears 70%, mononuclears 30%, glucose 61.96 mg/dl, xantochromia (negative) and cerebrospinal fluid (CSF) proteins 45.50 mg/dl. With this information it was decided to admit him to the neurology ward, with meningitis due to predominant polymorphonuclears. Treatment was started with vancomycin 1 g/12 h and ampicillin 2 g/4 h (for two days), and ceftriaxone 2 g/12 h (for ten days). The microbiological and serological studies in blood and CSF carried out while on the ward were normal or negative. The patient was released from hospital on the 3rd May 2006 with the final diagnosis of efalizumab-induced aseptic meningitis. When applying the modified Karch and Lasagna algorithm the adverse reaction to the drug was qualified as probable. Subsequently, this was notified to the Centro Andaluz de Farmacovigilancia (Drug Monitoring Centre in Andalusia).

Discussion

Aseptic meningitis is a disease characterised by headache, fever and inflammation of the meninges. It can be caused by viruses (coxsackie, echovirus), fungi, tuberculosis, medications (antibiotics, antiinflammarories), and infections of the central nervous system (CNS).

The most frequent symptoms are headache, fever, rigidity of the neck, general discomfort, nausea, vomiting, sleepiness, abdominal and muscular pain, and photophobia. Elevated or low white blood cell count, high white blood cell count in CSF and absence of growth in bacterial cultures are among the related signs. CSF culture and other special tests detect viral and other types of infection.

There is no specific treatment for aseptic meningitis. Antibiotic treatment is necessary for the mycotic and mycobacterial causes of this disease. Particular attention must be paid to possible serious complications such as encephalitis. Supporting treatment consists of analgesic medications.

Aseptic meningitis is a benign disease and patients generally recover completely within five to 14 days after the symptoms appear. Fatigue and dizziness can persist for longer. Encephalitis is a rare complication and the infection can continue for much longer in immunodeficient patients.

An in-depth bibliographical search failed to find any other published cases similar to ours. The Sistema Español de Farmacovigilancia (Spanish Drug Monitoring System) was consulted, and gave a total of ten suspected adverse effects for efalizumab. None of them make any mention to meningitis as an adverse effect. With regard to the central nervous system and the peripheral nervous system, there is only one adverse reac-
tion-paralysis. The medication and healthcare products regulatory agency in the United Kingdom, which makes its information available to healthcare professionals on the internet, has received no reports of cases of efalizumab-induced aseptic meningitis since its launch.

This is the first case of efalizumab-induced aseptic meningitis reported in Spain.

There is a need to carry out close follow-ups of adverse reactions to drugs that have been recently introduced on the market, since the launch of a new medication does not imply its benefit/risk ratio has been finally established, and means only that its efficacy is well documented and that the adverse effects detected before its launch were acceptable.

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References