Transient and Slight Thrombocytopenia Induced by Etanercept During Treatment of Psoriatic Arthritis

Giuseppe Stinco, Fabio Piccirillo and Pasquale Patrone
Department of Clinical and Experimental Pathology and Medicine, Institute of Dermatology, University of Udine, Piazza Rodolone 1, IT-33013 Gemona del Friuli, Italy. E-mail: giuseppe.stinco@uniud.it
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Sir,

Tumour necrosis factor-alpha (TNF-α) is a cytokine that has been implicated in the pathogenesis of several inflammatory diseases. Blocking TNF-α, via anti-TNF antibodies or soluble TNF-α receptor molecules, is a strategy currently employed in the treatment of patients with psoriasis or psoriatic arthritis. Etanercept is a fully soluble TNF receptor fusion protein that binds primarily to soluble TNF-α as well as TNF-β (lymphotoxin), thereby effectively blocking its physiological function (1). The possible development of side-effects during its use, including infections, demyelinating disease, lupus-like syndromes, congestive heart failure, malignancies and cytopaenias, have been described (2).

CASE REPORT

A 61-year-old man suffering from psoriatic arthritis for over 12 years was treated for about 10 years with methotrexate, which was stopped due to development of a toxic hepatopathy. He was also affected by a psychosis, which was treated with risperidone 1 mg/day with good control of his psychiatric symptoms. The patient took no other drugs. Baseline Psoriasis Area and Severity Index (pASI) and Ritchie index were 31.6 and 7, respectively. We started therapy with etanercept 25 mg subcutaneously twice a week and, before starting treatment, investigations including chest X-ray, complete blood count, urea, creatinine, transaminases, cholesterol, triglycerides, antinuclear antibody (ANA), anti ds-DNA, extractable nuclear antigens), antiphospholipid antibody (lupus anti-coagulant and anti-cardiolipin), tumour markers, haemoculture and urine culture had been performed; no significant aberrations were found. The Mantoux test was negative. Anti-citrulline antibody and rheumatoid factor was normal, while C-reactive protein (CRP) was 5.8 mg/l (normal value 0–5 mg/l). Complete blood count, hepatic and renal tests were repeated monthly during treatment with the biological drug. From the second month of therapy, with good control of skin and joint symptoms (pASI 14.3 and Ritchie index 4), we observed a decrease in platelet count (99×10^3/μl; baseline value 134×10^3/μl; reference value 130–450×10^3/μl), which occurred after 3 doses of etanercept; the platelet count improved 9 days after stopping the biological drug. Kuruvilla et al. (4) described a case of pancytopenia with a severe thrombocytopenia (33×10^3/μl) after 4 months of treatment with etanercept for rheumatoid arthritis; the platelet count improved 3 weeks after stopping the treatment. Furthermore, several cases of thrombocytopenia induced by other anti TNF-α agents, such as infliximab and adalimumab, have been described (5–7).

Leucopaenia and thrombocytopenia, although not common, are recognized side-effects of TNF-α blockers. In the literature some reports describe a decrease in pancytopenia during treatment with etanercept. Pathare et al. (3) described a case of severe thrombocytopenia (38×10^3/μl), which occurred after 3 doses of etanercept; the platelet count improved 9 days after stopping the biological drug. Kuruvilla et al. (4) described a case of pancytopenia with a severe thrombocytopenia (33×10^3/μl) after 4 months of treatment with etanercept for rheumatoid arthritis; the platelet count improved 3 weeks after stopping the treatment. Furthermore, several cases of thrombocytopenia induced by other anti TNF-α agents, such as infliximab and adalimumab, have been described (5–7).

The exact mechanism of thrombocytopenia during treatment with TNF-α blockers is unclear. To our knowledge this is the first report of a transient, slight and asymptomatic thrombocytopenia during treatment with etanercept. A gradual decrease in platelet count started between the second and third months of therapy and the number of platelets recovered to the initial value at the fourth month of treatment. A lupus-like syndrome, an anti-phospholipidic syndrome, or an autoimmune thrombocytopenia, possible mechanisms of thrombocytopenia during the treatment with biological drugs, were excluded due to absence of clinical and laboratory signs. In addition, a potential haematological toxicity induced by risperidone could have been considered, but our patient had had a stable blood count for over 15 years of therapy with this drug, and thrombocytopenia appeared only after the administration of etaner-
cept. We do not know the exact mechanism that led to thrombocytopenia and why it occurred between the second and third months of treatment. We hypothesize that it is the expression of an idiosyncratic reaction in patients with a genetic predisposition. In fact TNF-α is not only a molecule that plays a pivotal role in inflammatory processes, but it also takes part in a complex and still not well understood cytokine network that controls haematopoiesis. Its role in the bone marrow is still debated. In fact TNF-α can elicit a stimulatory or inhibitory effect on the in vitro growth of haematopoietic progenitors depending on its concentration and on the type of cytokines interacting with it (stimulatory effect: G-CSF, CSF-1, Epo, SCF, Fl; inhibitory effect: GM-CSF and IL-3) (8).

REFERENCES