LETTER TO THE EDITOR

Meningococcal meningoencephalitis after certolizumab pegol treatment in a patient with Crohn’s disease

Dear Sir,

We report the case of a 51-year-old female who presented with fever, altered sensorium and agitated behavior. She was diagnosed with Crohn’s disease two years back and had been in clinical remission on certolizumab pegol (CZP) for the last six months. At admission she had a temperature of 103 °F, heart rate of 110 per minute and her blood pressure was 125/76 mm Hg. Physical exam revealed nuchal rigidity without any pupillary abnormalities, skin rash, or focal neurological deficits. Cerebrospinal fluid (CSF) analysis revealed a white cell count of 6900 cells/mm³ with 90% granulocytes and was positive for Neisseria meningitidis group C/W135 antigen. She was treated with ceftriaxone and had an uneventful recovery.

There is substantial evidence to support an increased risk of serious infections in patients treated with anti-TNF agents. In a comprehensive systematic review the pooled odds ratio for serious infection was 2.0 (95% CI, 1.3–3.1) and the number needed to harm was 59 (95% CI, 39–125) during a treatment period of 3 to 12 months.¹ A significant proportion of these cases are granulomatous infections with a reported rate of approximately 0.24% in patients treated with infliximab.² Although traditionally tuberculosis has been the most common infection identified in this cohort, isolated cases of histoplasmosis, listeriosis, nocardiosis, bartonellosis and candidiasis have been reported.²

Certolizumab pegol (CZP) is the Fab fragment of a humanized monoclonal anti-TNF antibody linked to polyethylene glycol. The major difference between CZP and other anti-TNF agents is the absence of an Fc portion. As a result CZP does not activate the complement cascade or cause cellular apoptosis. It received FDA approval in 2008 for treatment of Crohn’s disease in adult patients with poor response to conventional therapy and is the third anti-TNF molecule approved for the management of Crohn’s disease, the others being infliximab and adalimumab. Long-term efficacy and safety data for CZP is currently unavailable except for a few case reports describing non-infectious adverse effects ranging in severity from fatal fibrosing alveolitis to oral lichen planus and psoriatic skin lesions.³,⁴ The PRECISE-2 trial which evaluated efficacy of certolizumab pegol maintenance therapy in adults with moderate-to-severe Crohn’s disease reported serious infectious adverse event in 3% of the study population.⁵ However, to our knowledge, this is the first reported patient with meningococcal meningitis during treatment with CZP.

Data from multi-center post-marketing clinical trials is needed to establish the adverse effect profile of CZP. Until then the possibility of life-threatening CNS infection should be borne in mind by gastroenterologists using this drug in the treatment of Crohn’s disease. Based on our experience, patients on CZP presenting with CNS symptoms would benefit from a prompt CSF analysis to rule out bacterial meningoencephalitis.

References


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10 June 2012