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Infliximab and listeria monocytogenes meningitis

Introduction

Infliximab (Remicade®) has been approved for marketing on 13-8-1999 in the EU for treatment of rheumatoid arthritis and Crohn's disease. The therapeutic indication is[1]:
Rheumatoid arthritis. The reduction of signs and symptoms as well as the improvement in physical function in patients with active disease when the response to disease-modifying drugs, including methotrexate, has been inadequate. In this patient population, a reduction in the rate of progression of joint damage, as measured by X-ray, has been demonstrated. Efficacy and safety have been demonstrated only in combination with methotrexate.
Treatment of severe, active Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and an immunosuppressant; or who are intolerant to or have medical contraindications for such therapies. Treatment of fistulising Crohn's disease, in patients who have not responded despite a full and adequate course of therapy with conventional treatment (including antibiotics, drainage and immunosuppressive therapy).
Infliximab is a chimeric IgG1 monoclonal antibody against tumour necrosis factor a (TNFa). TNFa, which level is increased in joints of rheumatoid patients and colonic tissue of Crohn's disease patients, is a cytokine with multiple biologic actions including mediation of inflammatory responses and modulation of the immune system. The most commonly encountered adverse drug reactions during treatment were upper respiratory infections, headache, nausea, sinusitis, rash, cough and acute infusion reactions. Contra-indications include infections and moderate to severe heart failure. Moreover, due to post marketing data, comprehensive precautions were included in the SPC to prevent tuberculosis infections during therapy[1].

Reports

A female aged 43 received infliximab for the indication of therapy resistant Crohn's disease. She used azathioprine (125 mg/day) and prednisolone (15 mg/d) as co medication. A fortnight after the first administration of infliximab, a listeria monocytogenes meningitis was diagnosed. She was treated with parenteral antibiotics and recovered.

Other sources of information

Literature

Very recently, FDA affiliated authors published an overview about the association between eternacept, infliximab and listeria infections [2]. This publication reviews literature on this topic [3-6]. The authors discuss 15 patients and mention another 10 cases in association with infliximab in an addendum. All patients for whom information was reported were receiving immunosuppressant drugs. From these 25 patients, eight died, two patients had not recovered at the moment of notification, six patients had recovered including one with persisting neurological damage. From the other patients, the outcome remained unknown. An annual reporting rate of 43 : 1,000,000 for all patients treated with infliximab could be calculated; 29 : 1,000,000 for users with Crohn's disease and 61 : 1,000,000 for users with rheumatoid arthritis.
The background incidence of listeria infections is 3 : 1,000,000/year for all ages with a mortality of 21%. In the elderly (= 60 y), the incidence is higher; 13 : 1,000,000/year [7]. Background incidences in populations with rheumatoid arthritis or Crohn's disease are unknown.

Databases

The reported case is the first in the Lareb database. The WHO database does not allow a specific search for listeria infections.

Mechanism

Tumour necrosis factor alpha is substantially involved in defence mechanisms. A pharmacological blockade of TNFa will decrease the defensive mechanism, which is especially relevant for intracellular micro organisms like listeria monocytogenes and tuberculosis.

Conclusion

The report associates the infection with listeria monocytogenes with the use of infliximab. This association is supported by literature, including an article on the FDA database.
The mortality of a listeria infection is above 20% in the general population, and may be even higher in patients with rheumatoid arthritis or Crohn's disease.
As with tuberculosis, preventive strategies might be able to reduce listeria infections. Avoidance of non-pasteurised milk or cheese consumption, as recommended during pregnancy, are examples [8].

References
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