



Use of Tocilizumab in Castleman's Disease

Evidence Based Medicine

Official recommendations

Expert opinion

Castleman's disease, also known as angiofollicular hyperplasia, is a rare lymphoproliferative disease first described in 1956. It is characterised by benign lymphovascular hyperplasia with polyclonal lymphoplasmacytic proliferation either in a single lymph node (unicentric form, the most common) or in multiple lymph nodes. The main sites of involvement are the mediastinum and retroperitoneal space. Progression is slow and may lead to lymphoma. The HHV8 has been implicated as an initiating factor, and cases of Castleman's disease have been reported in patients with HTLV1 infection.

Rationale for targeting IL-6 in Castleman's disease

Tocilizumab was licensed in Japan in April 2005⁽¹¹⁴⁾ for the treatment of Castleman's disease (angiofollicular hyperplasia) based on its ability to specifically block IL-6.

The clinical manifestations are related to IL-6 overproduction by the affected lymph nodes. This "syndrome of inappropriate IL-6 secretion" explains the full range of manifestations, which include constitutional symptoms (fever, weight loss, lymphadenopathy, splenomegaly...) and laboratory test abnormalities (anaemia, systemic inflammation, hypergammaglobulinaemia, autoantibodies, cold agglutinins...). Patients may experience complications such as haemolytic anaemia, amyloidosis, cardiac involvement, or interstitial lung disease⁽¹⁰²⁾.

IL-6 antagonist therapy in Castleman's disease: data from the literature

The conventional treatment rests on surgical removal of focal lesions and on glucocorticoid and antimitotic therapy in patients with diffuse lesions.

In the seminal study of tocilizumab⁽¹¹⁴⁾, 28 patients with Castleman's disease refractory to all other treatments (including surgery and long-term glucocorticoid therapy) received tocilizumab 8mg/kg every 15 days for 4 months. The main clinical and biological abnormalities improved⁽¹¹⁴⁾. The lymphadenopathy resolved, as well as the clinical and laboratory evidence of inflammation. Furthermore, gradual improvements occurred in the anaemia, hypoalbuminaemia, total cholesterol, and body mass index. All patients reported significant alleviation of fatigue^(115, 116).

In 28% of patients, a decrease in the tocilizumab dosage was possible (down to 4 mg/kg/month), as well as an increase in the interval between infusions (up to 1 month). In 73% of patients, the glucocorticoid treatment was decreased or stopped⁽¹¹⁴⁾.

In the open-label extension phase, whose mean duration was 1191 days, the safety and efficacy of tocilizumab therapy were maintained^(114, 116, 117). The main adverse events were nasopharyngitis (88.6%), rashes (31.4%), pruritus (28.6%), and neutropenia (25.7%). Overall safety was good. The optimal treatment duration remains to be determined^(115, 117).