Case report

Response to rituximab in a patient with Wegener's granulomatosis refractory to conventional therapies

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ARTICLE INFO

Article history:
Received December 22, 2008
Accepted April 3, 2009
Available online October 17, 2009

Keywords:
Wegener's granulomatosis
Rituximab
Biological therapies

ABSTRACT

Male patient with a diagnosis of Wegener’s granulomatosis associated to anti-proteinase 3 antibodies that improved initially to treatment with high dose glucocorticoids and cyclophosphamide but who relapsed, with a poor response to glucocorticoid treatment, cyclophosphamide, methotrexate and azathioprine. The patient received treatment with rituximab in 4 doses with clinical and radiographic improvement.

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RESPUESTA A RITUXIMAB EN UN PACIENTE CON GRANULOMATOSIS DE WEGENER REFRACTARIO A TERAPIA CONVENCIONAL

RESUMEN

Se presenta el caso de un paciente con granulomatosis de Wegener asociada a anticuerpos antiproteinasa 3 que tuvo mejoría inicial con dosis altas de glucocorticoides y ciclofosfamida, pero que posteriormente a una recaída no respondió a los mismos medicamentos, ni a metotrexate ni a zatioprina. Por tal motivo, recibió tratamiento con rituximab en 4 dosis, además de glucocorticoides, obteniendo mejoría del cuadro tanto clínica como radiográficamente.

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manifestations. In 2001 he suffered a relapse of the nasal and sinus symptoms as well as left orbital pseudotumor, with a Birmingham Vasculitis Activity Score of 28 out of 63, and was treated with oral steroids at a dose of 1 mg/kg/day in a descending pattern (reaching an accumulated dose of 5 g of prednisone) and intramuscular methotrexate at a dose of 20 mg a week. We opted not to use cyclophosphamide in this occasion to avoid complications due to treatment. Methotrexate had to be suspended after a year due to elevated liver enzymes and, in order to maintain remission, he was started on azathioprine (150 mg/day), maintained for 18 months. In January 2008, while the patient was receiving no steroids or immunosuppressants and after not having visited his physician for at least 2 years due to work-related problems and having moved to another city, the patient was seen again with nasal and sinus symptoms that had lasted for at least 6 months. A computerized tomography (CT) scan of the nasal sinuses and facial bones was performed, finding occupation of practically all of the etmoidal cells, the sphenoid sinus as well as the frontal and maxillary sinuses and the nasal cavity, with lack of visualization of the median concha and destruction of the totality of the nasal septum and the median walls of the maxillary sinus and the bony trabecula of the etmoidal cells.

Discussion

WG is a necrotizing vasculitis that affects the upper and lower respiratory tract and, in most cases, the kidneys. Nasal disease is seen in up to 80% of cases and includes inflammation of the mucosa with nasal obstruction, ulcers and perforations of the septum, nasal bleeding and “saddle nose” deformity. Treatment is based on high dose steroids and associated immunosuppressants. The use of cyclophosphamide has revolutionized the treatment of WG type vasculitis and is considered the drug of choice for the control of the disease; however, its use is limited in the long term. The appearance of other drugs (such as mycophenolate mofetil, methotrexate, azathioprine, cyclosporine or immunoglobulins), local radiotherapy and biological treatments have become a beacon of hope for patients who do not respond to conventional therapy or who have developed treatment derived complications. B cell eradication with rituximab (4 weekly doses of 375 mg/m² or, occasionally, 2 doses of 1 g every 2 weeks) has induced complete but temporal remission in patients with ANCA associated vasculitis that have been proven resistant to conventional treatment in small studies56 improving disease in patients with subglotic stenosis, retrobulbar granulomas and sinus affection unresponsive to conventional therapy.57 However, cases in which granulomatous manifestations predominate do not seem to respond to rituximab.58 It repeated administration has been suggested and proven to be effective, although complications and adverse events might arise, making more studies on the subject necessary. Current trials are dealing with determining the effects and new indications for rituximab.59

References