Successful Corticosteroid-Sparing Effect of Rituximab in the Treatment of Refractory Idiopathic Orbital Inflammatory Disease

Emily H. Shao^a Andreas Karydis^a Maria Gemenetzi^a
Simon R.J. Taylor^{a, b}

^aRoyal Surrey County Hospital NHS Foundation Trust, Guildford, and ^bFaculty of Medicine, Imperial College London, London, UK

Key Words

Rituximab · Idiopathic orbital inflammatory disease

Abstract

Idiopathic orbital inflammatory disease (IOID) is an idiopathic inflammatory process within the orbit that can result in permanent visual impairment. Although high-dose oral corticosteroids are currently the mainstay of therapy, their long-term usage can cause significant toxicity. We present a case of IOID that was successfully treated with the anti-CD20 monoclonal antibody rituximab following failed steroid sparing with conventional second-line immunosuppressive agents.

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Introduction

Idiopathic orbital inflammatory disease (IOID) is an idiopathic inflammatory process within the orbit that can result in permanent visual impairment. Although high-dose oral corticosteroids are currently the mainstay of therapy, their long-term usage can cause significant toxicity [1]. We present a case of IOID that was successfully treated with the anti-CD20 monoclonal antibody rituximab following failed steroid sparing with conventional second-line immunosuppressive agents.

Simon R.J. Taylor, MA, PhD, FRCOphth
Faculty of Medicine, Imperial College London
Room 5N8B, 5th Floor Commonwealth Building, Hammersmith Hospital
London W12 0NN (UK)
E-Mail s.r.taylor@imperial.ac.uk

Case Report

A 61-year-old woman presented with symptoms of left-sided headache, peri-orbital pain and left-sided ocular protrusion. Examination revealed a decrease in her visual acuity from 6/6 to 6/24, which was associated with a left-sided relative afferent pupillary defect. Her left eye was proptotic by 3 mm on exophthalmometry, with associated ocular pain and conjunctival injection (fig. 1a). Extraocular movements were normal and intraocular examination proved unremarkable.

Blood investigations including thyroid function tests, fasting blood glucose, liver and renal function tests, erythrocyte sedimentation rate and serum ACE were all normal, as was an immune screen including rheumatoid factor, antinuclear antibody and antineutrophil cytoplasm antibody.

A provisional diagnosis of left IOID was made based on the clinical findings and negative blood investigations, and oral prednisolone was started at a dose of 60 mg/day. Her symptoms resolved rapidly and her vision and proptosis improved within days, supporting the diagnosis. However, she suffered a disease relapse when her prednisolone was tapered to 20 mg/day. Subsequent attempts at steroid sparing with mycophenolate mofetil 1 g b.i.d. and methotrexate 20 mg p.o. weekly proved ineffective over a period of 8 months. The patient started again at 60 mg/day prednisolone together with each second-line agent, but she was unable to get below 20 mg prednisolone without renewed disease activity. Measurement of IgG subclasses at this point demonstrated normal IgG4 levels, although this result may have been confounded by her concurrent treatment with corticosteroids and other immunosuppressive medication.

She then received 2 infusions of rituximab 1 g i.v. separated by an interval of 2 weeks. This effected disease remission within 4 weeks and enabled her prednisolone to be tapered to 7.5 mg o.d. without relapse over a period of 2 months. Nine months on, she remains in remission on 7.5 mg prednisolone only and maintains a visual acuity of 6/6 with no relative afferent pupillary defect, and no abnormalities on repeat MR scanning (fig. 1b).

Discussion

Although the pathophysiology of IOID is poorly understood, raised IgG4 levels in serum samples and tissue biopsy of sufferers have implicated IgG4 in its aetiology, although the levels in this case were normal [2, 3]. Rituximab (a chimaeric monoclonal antibody against B-cell CD20) has been reported in the successful treatment of refractory orbital disease in granulomatosis with polyangiitis [3, 4] as well as in some cases of IOID [5–7]. Our case differs from previously reported cases in that our patient was sensitive to oral corticosteroids, but it proved impossible to effect steroid sparing with conventional second-line immunosuppressive agents, in contrast to rituximab.

As IOID is rare and presents with heterogeneous clinical manifestations, prospective and randomised evidence investigating the role of rituximab in its treatment is unlikely to occur. Nevertheless, case reports including ours increasingly suggest that rituximab should be considered in refractory IOID unresponsive to conventional immunosuppression or in place of conventional immunosuppression in selected cases.

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Fig. 1. Transverse MR images of the brain and orbit (T1-weighted images), before (a) and after (b) the treatment with 2 doses of rituximab 1 g i.v.