Clinical and Experimental Rheumatology 2015; 33: 549-550.

Successful treatment of IgG-4 related sclerosing disease with rituximab: a novel case report

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Received on September 23, 2014; accepted in revised form on January 19, 2015.

Key words: IgG4-related sclerosing disease, rituximab

Competing interests: none declared.

ABSTRACT

IgG4-related sclerosing disease (IgG4-RSD) is a rare inflammatory disease that can affect multi organs. We describe a paediatric patient with ocular, nerve, and renal involvement successfully treated twice with corticosteroids and rituximab.

Introduction

IgG4-related sclerosing disease (IgG4-RSD) is a recently described disease entity often associated with mass forming lesions, elevated serum IgG4 levels and characteristic histopathologic features, including but not limited to diffuse lymphoplasmacytic infiltration (1, 2). It is most often seen in middle-aged males with pancreatitis being a common presentation but multi organ involvement is common once diagnosis is established (1-3). Epidemiology has been poorly described and is likely grossly underestimated due to poor disease recognition in adults (3) and the incidence and prevalence in the paediatric population is unknown.

Literature describing the clinical and diagnostic findings of IgG4 RSD in paediatrics is sparse. In addition, treatment regimens are not standardised and are only described in case reports or small case series. To our knowledge, a case describing a paediatric patient with primary nerve involvement does not exist. Case reports have described the efficacy of rituximab in the adult population (4), but none have described rituximab for IgG4-RSD in children.

Case report

A 7-year-old girl, originally from Liberia, presented with persistent proteinuria and was diagnosed with nephrotic syndrome. At presentation she also had swelling of the right eye and the right arm. A head MRI showed exophthalmos, preseptal swelling, increased density of the retrobulbar fat, maxillary sinus disease, loss of bone density in the medial aspect of the orbital floor and thickening of the optic nerve, all on the right. This was thought to be an infectious process and was treated with antibiotics. A right arm MRI showed extensive soft tissue oedema in the medial aspect of the arm above and below the elbow. The inflammatory process extended from the subcutaneous fat into the deeper soft tissues. She was treated with a long steroid taper in addition to antibiotics and swelling resolved in the eye and arm.

She was well until the age of 12 when she presented with blurry vision and vision loss in the right eye. An emergent MRI showed extensive intra- and extracranial findings likely from infiltrative tumour such as extensive infection or granuloma. Laboratory studies showed: haemoglobin 8.0 g/dL, platelets 496,000 x 10^3/μL with normal WBC count and ESR 73 mm/hr. All other labs were unremarkable, including a normal IgG4 level. She was started on steroids for a presumed diagnosis of inflammatory pseudotumour of the orbit and was discharged home for outpatient follow-up. A biopsy of the lesion showed chronic lymphoplasmacytic inflammation with lymphoid aggregate formation and fibrosis without granulomas. The biopsy was stained for IgG4 and absolute IgG4 cell count varied from 40 to over 50/high-powered field, which would be consistent with a diagnosis of IgG4-RSD.

During steroid taper, she developed a left 3rd nerve palsy and had an emergent MRI as seen in Figure 1. MRI of the cervical, thoracic and lumbar spine were normal. CT scans of the chest, abdomen and pelvis were also normal. She had improvement with daily oral steroids and high doses of IV methylprednisolone, however had ongoing 3rd nerve palsy. Due to lack of significant improvement with steroids, she received two doses of IV rituximab, one gram per dose (750 mg/m^2) given two weeks apart. One week after the first rituximab infusion her ophthalmology examination showed no proptosis, pupillary defect or motility deficit with normal vision. MRI one month after rituximab showed almost complete resolution of inflammation of the left side of the orbit but persistence of previous chronic inflammation and bony destruction on the right side. There was poor follow-up after repeat MRI, but she had one ophthalmology examination which was normal. The following year, she presented with left shoulder pain and swelling for one month duration. She described numb-

ness in the left arm with shooting pains, fatigue, decreased appetite, and weight loss. Physical exam revealed inability to adduct or abduct the left arm fully due to pain. Laboratory studies showed haemoglobin 7.2 g/dL, platelet count 856 X109/L, ESR 34mm/hr. MRI of bilateral arms revealed an inflammatory process as demonstrated in Figure 2. She received one gram methylprednisolone IV and rituximab one gram (750 mg/m^2) per dose, two weeks apart. Her symptoms resolved completely, her physical examination normalised, and steroids were tapered off.

This is the first paediatric case to our knowledge of IgG4-RSD with primary nerve involvement and successful treatment with rituximab. Nerve cupping (2), orbital nerve involvement, and peripheral nervous system involvement have previously been described in adults (5), however, no studies have demonstrated the bilateral brachial plexus involvement seen in the case of our patient. This is an unusual presentation of an uncommon disease entity. Rituximab was successfully used in this patient twice after failure of glucocorticoid therapy. Previous studies have shown that it specifically reduces the IgG4 subclass of immunoglobulins (6). It is unknown as to whether IgG4 is pathologic in itself or simply a by-product of a pathologic process, but it seems that reduction of IgG4 correlates with a reduction in disease activity (6). IgG4-RSD is a newly described disease entity most commonly seen in middle-aged males but is being described more frequently in the paediatric population. This case is an example of primary nerve involvement with likely renal involvement that was refractory to steroid therapy but responsive to treatment with rituximab. It also demonstrates that relapse can be successfully treated with a subsequent course of rituximab.

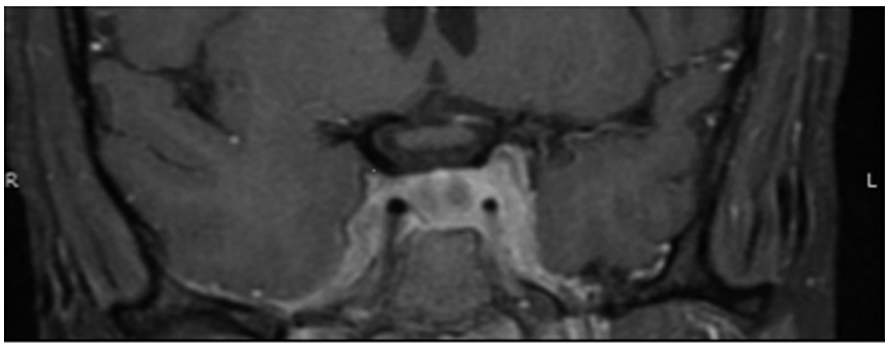

Fig. 1. Coronal T1 weighted fat-saturated post contrast image demonstrating bilateral cavernous sinus thrombosis and mild left internal carotid artery narrowing.

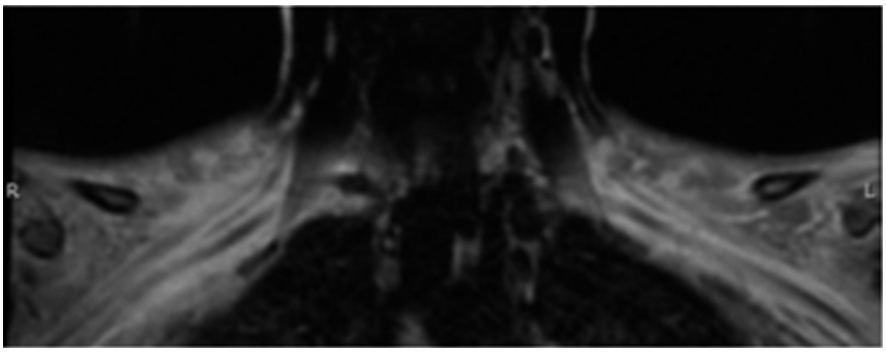

Fig. 2. Coronal T1 weighted fat-saturated post contrast image demonstrating enhancing perineural inflammation encasing the brachial plexus bilaterally.

References

1. KAMISAWA T, NAKAJIMA H, EGAWA N, FUNATA N, TRUSUTU K, OKAMOTO A: IgG4-related sclerosing disease incorporating sclerosing pancreatitis, cholangitis, sialadenitis and retroperitoneal fibrosis with lymphadenopathy. *Pancreatology* 2006; 6: 132-7.
2. DIVATIA M, KIM SA, RO JY: IgG4-related sclerosing disease, an emerging entity: a review of a multi-systemic disease. *Yonsei Med J* 2012; 53: 15-34.
3. SOLIOTIS F, MAVRAGANI CP, PLASTIRAS SC, RONTOGIANNI D, SKOPOULI FN, MOUTSOPOULOS HM: IgG-4 related disease: a rheumatologist's perspective. *Clin Exp Rheumatol* 2014; 32: 724-7.
4. KHOSROSHAHI A, BLOCH DB, DESHPANDE V, STONE JH: Rituximab therapy leads to rapid decline of serum IgG4 levels and prompt clinical improvement in IgG4-related systemic disease. *Arthritis Rheum* 2010; 62: 1755-62.
5. INOUE D, ZEN Y, SATO Y *et al*.: IgG4-related perineural disease. *Int J Rheumatol* 2012; 401890.
6. KHOSROSHAHI A, CARRUTHERS MN, DESHPANDE V: Rituximab for the treatment of IgG4-related disease: lessons from 10 consecutive patients. *Medicine* (Baltimore) 2012; 91: 57-66.