Indian J Pediatr (October 2014) 81(10):1108–1110
DOI 10.1007/s12098-014-1471-y

CLINICAL BRIEF

IgG4-Related Orbital Inflammation Presenting as Unilateral Pseudotumor

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Received: 14 October 2013 / Accepted: 23 April 2014 / Published online: 23 May 2014

Abstract IgG4 related systemic disease (IgG4-RSD) has been recognised in the last few years. Orbital pseudotumor as a presentation of IgG4-RSD is one of the rare complaints encountered in pediatric population. It is an inflammatory condition of unknown etiology characterized by tumorous swelling of the organs, characteristic histopathologic changes and elevated IgG4: IgG plasma cells ratio. The disease is also characterized by involvement of varied organ systems. The authors describe a seven-year-old boy with orbital pseudotumor after two years of initial onset with waxing and waning course, steroid responsive lesion and biopsy suggestive of IgG4-RSD involving the extraocular soft tissue. Treatment with oral corticosteroids and Azathioprine produced a significant decline in the pseudotumor size. It is important for pediatricians to be aware of this condition as appropriate recognition and management is important to prevent long-term damage of the tissue involved. This is the first case of IgG4 related orbital pseudotumor reported from India.

Keywords IgG4 related disease · Orbital swelling · Pseudotumor

Introduction

Immunoglobulin G4–related systemic disease (IgG4-RSD) is a relatively new subset of inflammatory disorder. Multiple organ systems are involved, characterized by variable clinical features, raised IgG4 levels and characteristic histopathology. The authors describe the clinical and histopathological findings of a child with chronic orbital inflammation as a manifestation of IgG4-RSD.

Case Report

A seven-year-old boy was referred to the pediatric rheumatology services for a persistent left orbital swelling. The orbital swelling was noted two years back and was insidious and gradually progressive (Fig. 1a). He was diagnosed to have a pseudotumor of the orbit with an otherwise unremarkable ophthalmic evaluation and systemic features. Contrast MRI imaging was suggestive of soft tissue lesion with homogenous contrast enhancement and enlargement of left inferior rectus muscle likely due to a lymphoproliferative disease or myocysticercosis. A probable diagnosis of inferior rectus muscle cysticercosis was given and he was started on Albendazole followed by Praziqantel and Prednisolone with minimal improvement.

A biopsy was done and was suggestive of inflammatory reaction with lymphocytes and plasma cells with interspersed eosinophils. There was associated dense fibrocollagenous tissue and hyalinization (Fig. 2a). No evidence of storiform fibrosis or obliterative phlebitis was seen. He received six doses of pulse methylprednisolone with significant though short-lived improvement. The child had a recurrence of the lesion a month after the last dose of methylprednisolone. At this stage he was referred to authors' center. History suggested that the lesion was exquisitely steroid sensitive. He also had a past history of atopy. There was no history of any other organ system involvement.

Laboratory findings revealed thrombocytosis and eosinophilia with absolute eosinophil count (AEC)=708 (40–440).

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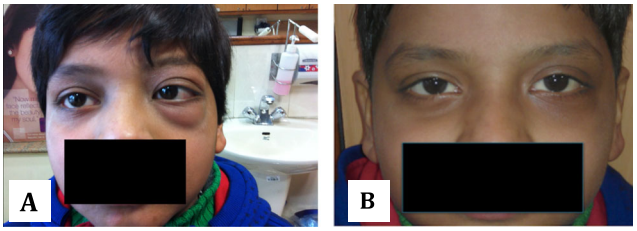

Fig. 1 **a** and **b** Photograph of the child showing left orbital swelling pre and post treatment with steroids

The inflammatory markers were within normal limits. His Immunoglobulin levels were; IgG=943 (673-1,734 IU/ml), IgM=85 (47–311 IU/ml), IgA=175 (41–368 IU/ml) and IgE=688 (0–248 IU/ml). Serum levels of C3, C4 was within normal limits. In view of steroid sensitive nature of the lesion, IgG4 related orbital inflammatory lesion was suspected and Serum IgG4 level was sent which was 109.3 (0.4-98 mg/dl). Immunohistochemistry was done on the biopsy specimen which was suggestive of IgG4 related orbital disease with IgG4/IgG positive plasma cells>40 % (Fig. 2b). Child was started on prednisolone (1 mg/kg/d) and Azathioprine (2 mg/kg/d) as a steroid-sparing agent with significant improvement (Fig. 1b).

To the best of authors' knowledge this is the first reported case of IgG4-RSD in pediatrics from India.

Discussion

IgG4-RSD was first described in 2003 as a syndrome of unknown etiology comprising of a collection of disorders that share specific pathologic, serologic, and clinical features. It is characterized by a lymphoplasmacytic infiltrate that stains positively for IgG4-bearing plasma cells in affected organs [1]. Multiple organ systems like the salivary glands, pancreas, biliary tree, retroperitoneum, lacrimal gland and thyroid may be involved [2].

IgG4-RSD can involve one or multiple organs in 60-90 % cases [3]. Presentation is often sub-acute with development of a mass in the affected organ (*e.g.*, an orbital pseudotumor) or diffuse enlargement of an organ (*e.g.*, the pancreas) [2]. Approximately 40 % of patients have history of asthma, allergy or atopy [4].

In terms of ocular involvement, IgG4-RSD usually presents with ocular adnexal masses which can involve the orbit, extraocular muscles, lacrimal system, optic nerve, or sclera [3]. Unilateral or bilateral eyelid or periorbital swelling is the most common disease manifestation [4, 5]. Bilateral ocular adnexal involvement is reported in 50-80 % of patients. Proptosis without swelling is seen in about 1/3rd of patients [5]. Bilateral chronic sclerosing dacryoadenitis is seen in upto 50 % of patients with IgG4 related orbital disease.

The diagnosis is based upon characteristic histopathologic findings and immuno-histochemical staining. The three major histopathological features associated with IgG4-RSD are, dense lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis.

Various diagnostic criteria have been used for the diagnosis based on histopathology. Plaza et al. suggested>10 IgG4+ cells/hpf to consider IgG4-RSD [5]. Elevated IgG4-to-IgG ratio of>40 % is commonly accepted [5, 6]. Deshpande et al. havesuggested that a ratio need not be estimated in every case: cases with classic histopathological features and robust elevations in IgG4-positive plasma cells may be diagnosed as IgG4-RSD [7].

Serum IgG4 levels of>135 mg/dl have been suggested to be specific for IgG4-RSD [6, 8]. IgG4 levels often correlate with disease activity, the number of involved organs and glucocorticoid use [6]. Thirty percent of patients whose biopsy is suggestive of classical histopathologic and immunohistochemistry findings have been reported to have normal IgG4 levels [9]. Serum IgG4 concentrations are therefore neither sufficiently sensitive nor specific for this disease.

Glucocorticoids are the first line of therapy. Response is characterized by symptomatic improvement, reduction in the size of mass or organ enlargement, improvement in organ function, and often a decrease in serum levels of IgG4. Azathioprine, methotrexate or mycophenolate mofetil have been used with limited success in patients who are resistant toor dependent on glucocorticoids [10]. Patients resistant to glucocorticoids may benefit with the use of rituximab.

Children with IgG4 related diseases are not yet well described in literature. This case report is a "primer". It is important for pediatricians to be aware about this condition

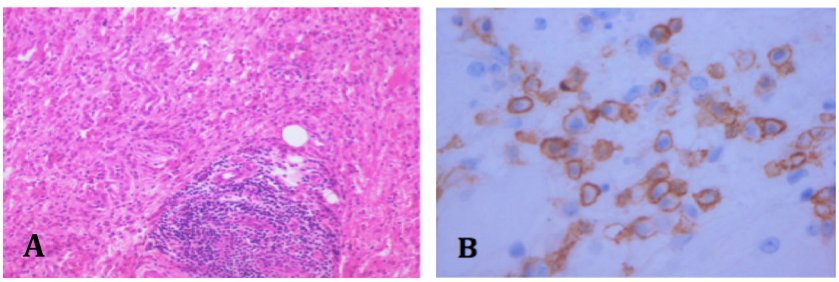

Fig. 2 Histopathology of pseudotumor mass showing lymphoplasmacytic infiltrate with surrounding fibrosis (**a**) and displaying IgG4 stained plasma cells (**b**)

as appropriate recognition and management is important to prevent long-term damage of the tissue involved.

Conflict of Interest None.

Source of Funding None.

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