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Immunoglobulin G4-related orbital disease: a report of two paediatric cases

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ABSTRACT

IgG4-related disease is a systemic fibro-inflammatory disorder mainly affecting the middle-aged and elderly population. IgG4-related orbital disease is very rare in childhood. We present here two children with IgG4-related orbital disease, one of whom responded well to prednisolone treatment while the other one was refractory to most immunosuppressive agents. It is important to treat patients at the early active stage of disease before fibrotic changes predominate. Thus, although rare, increased awareness of IgG4-related orbital disease in childhood may avoid delays in diagnosis and treatment.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibro-inflammatory disorder mainly affecting the adult population (1). IgG4-related orbital disease (IgG4-ROD) is very rare in children (2-4). We report here two children with IgG4-ROD. There was neither consanguinity nor family history of IgG4-RD in our patients.

Patient 1

Patient 1 was a 14-year-old girl presenting with progressive painful protrusion of her right eye. Acute phase reactants (APRs) were normal, anti-neutrophil cytoplasmic antibodies (ANCA) were negative. Orbital magnetic resonance imaging (MRI) revealed a focal, diffuse thickening in right lateral rectus muscle with inflammatory changes. The rectus muscle biopsy showed a fibro-inflammatory infiltrate. With the diagnosis of orbital pseudotumour, she was started on oral prednisolone which was discontinued 1.5 months later with successful control of symptoms. One week later, her complaints recurred. The control MRI revealed similar findings except that the thickening was more in the first MRI consistent with clinic. Retrospective review of biopsy showed 14 IgG4-positive cells/high power field (hpf) and IgG4-positive plasma cells/IgG-positive plasma cells ratio of 30%. Serum IgG4 was 7.5 g/L (0–12.5 g/L). Oral prednisolone was started with a diagnosis of IgG4-ROD. Prednisolone was gradually tapered with good control of symptoms, and methotrexate was added as a steroid sparing agent at second month. Physical examination was normal at the last follow-up of four months.

Patient 2

Patient 2 was a 9-year-old female presenting with progressive painful protrusion of the right eye. Orbital MRI showed diffuse thickening of lateral rectus muscle with inflammatory changes. Upper lid biopsy revealed inflammatory infiltrate. APRs were elevated, ANCA was negative. She had been initially diagnosed as having localised granulomatosis with polyangiitis (GPA) (Wegener's granulomatosis). There was no response to prednisolone, methotrexate, or mycophenolate mofetil. At 12 months she complained of severe headache with an increase in the protrusion. MRI showed progressive findings, thus pulse methylprednisolone and cyclophosphamide were started. Her headache subsided and she was feeling better, however, the protrusion remained the same. During the two-year follow-up, she had four MRIs at 6-monthly intervals. The lesion was stable in the last two with no inflammatory changes, which was consistent with the clinicals. Re-evalution of biopsy demonstrated an average of 15 IgG4-positive plasma cells/hpf with IgG4-positive plasma cells/IgG-positive plasma cells ratio of 60% (Fig. 1). A recent serum IgG4 was 3.7 g/L. Thus, the patient was diagnosed as IgG4-ROD.

IgG4-RD is characterised by varying degrees of fibrosis and diffuse IgG4-positive lymphoplasmacytic infiltration (>10/hpf IgG4-positive plasmacytes and/or the ratio of IgG4/IgG positive cells >40%) with biopsy being the golden standard of diagnosis (5). Serum IgG4 may be normal in 10–30% of patients, especially after immunosuppressive treatment; these patients are more likely to be younger, have <3 organs involved, and have normal APRs than the ones with elevated serum IgG4 (6). Both of our patients had normal serum IgG4 levels which may be due to young age, involvement of only one organ, or the use of immunosuppressive agents before serum IgG4 testing.

Besides IgG4-ROD, orbital inflammatory disease (or orbital pseudotumour) represents a group of heterogeneous disorders including infections, local inflammatory conditions (*e.g.* myositis, dacryoadenitis, cellulitis, etc.), vasculitis (*e.g.* GPA), neoplasms, and idiopathic hypertrophic pachymeningitis (7, 8). Imaging and histopathological evaluation help with the differential diagnosis.

There are no controlled trials analysing the optimum treatment in IgG4-RD. Corticosteroids are usually the first choice; however, relapses are common following discontinuation (9). Other immunosuppressants including mycophenolate mofetil, methotrexate, cyclophosphamide, rituximab, and radiotherapy have also been used in treatment (9). It is important to treat patients at the early active stage of IgG4-RD before progression with fibrosis (10).

Although rare, increased awareness of IgG4-related orbital disease in childhood may avoid delays in diagnosis and treatment.

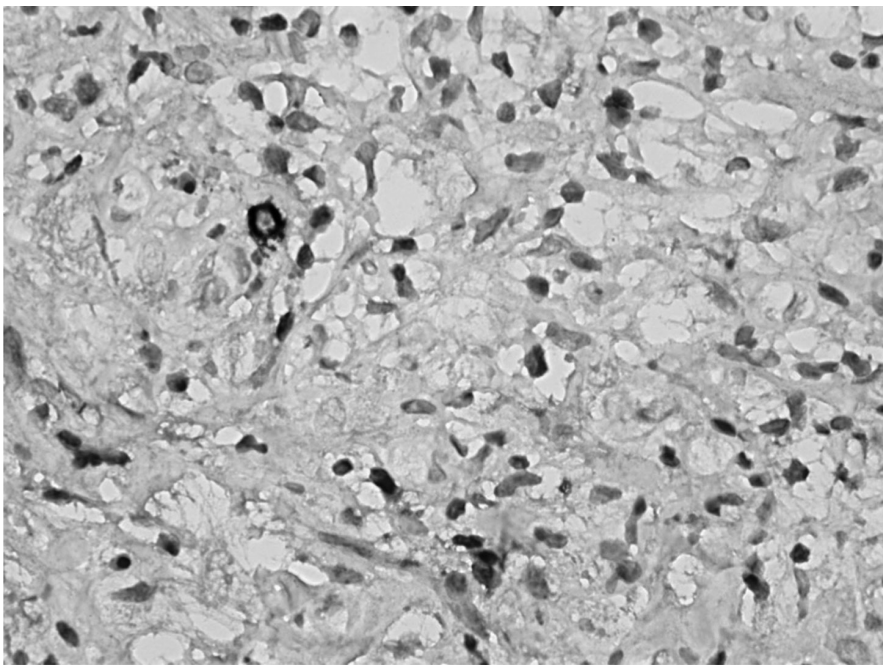

Fig. 1. IgG4 positive plasma cells (immunoperoxidase, original magnification, x400).

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