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Two cases of igg4 related disease in paediatric and young patients with ocular and ear canal involvement

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Abstract

IgG4 related disease is a newly recognised entity, more cases being reported, as pathologists and medical practitioners across the world are becoming more aware of this disease. It is an immune-mediated disease, that can appear with multiple organ involvement, as tumor-like swelling, mimicking other neoplasms like lymphomas, which must be carefully excluded. If untreated, the disease can lead to fibrosis and irreversible organ damage. Hence, early recognition of IgG4 related disease is important to avoid permanent organ dysfunction. IgG4 mostly has been described in adults, hence it is generally less known among the paediatricians. We report two cases – one is of an 11 year old male child with superior orbital swelling, clinically suspected to be an inflammatory lesion or a lymphoma. The other case is a 20 year old male, presented as small polyps in the left external auditory canal, these did not bleed on touch and covered the tympanic membrane.

Keywords: IgG4 related disease, lacrimal gland, inflammatory pseudotumor of orbit, autoimmune disease, external ear canal, plasma cells

Introduction

IgG4-related disease is a systemic autoimmune fibro-inflammatory disease which has surfaced recently, more cases being reported since last two decades. When such cases were described earlier, they were characterised as a form of autoimmune pancreatitis, the distinctive histopathology of IgG4 has now been described in every organ system^[1]. IgG4 mostly has been described in adults, hence it is less known among paediatricians. The disease is typically marked by several features: tendency to form tumefactive lesions at multiple sites; a dense lymphoplasmacytic infiltrate rich in IgG4+ plasma cells; storiform fibrosis; Obliterative phlebitis and often but not always, elevated serum IgG4 concentrations^[2].

Case Report

We report two cases

Case one

An 11year old male child presented with superior orbital swelling, since 5 months. Non contrast computerised tomography (NCCT) orbit showed a mass in lacrimal fossa region pushing the globe inferiorly. Post contrast T1 w images of orbit showed diffuse homogenous enhancement of the right lacrimal gland mass. Coronal reconstruction of NCCT Orbit showed homogenous isodense right intra-orbital soft tissue lesion in extraconal compartment in the lacrimal fossa causing smooth bony indentation of the roof of orbit and pushing the globe inferiorly - consistent with lacrimal gland mass.

The mass was subsequently excised and sent for histopathological examination. Grossly, it was a homogenous greyish white mass lesion, which measured 3.5 x 2.0 x 1.8 cm. The hematoxylin and eosin (H&E) sections revealed a predominant population of lymphoplasma cells, areas of fibrosis and obliterative phlebitis (Fig 1, 2). Also seen were entrapped lacrimal gland acini, within the inflammatory infiltrate- dacryoadenitis. Van Giesons elastin stain was performed to demonstrate obliterative phlebitis. There were no atypical mitoses, nor any granulomas. In view of significant number of plasma cells, immunohistochemical (IHC) evaluation was performed. It correlated with increased IgG + plasma cells with many IgG4+ plasma cells (Fig3). The IgG4 to IgG proportion was calculated to be more than 60 %.

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The patient was kept on clinical follow-up and recurrence has not been reported after surgical excision.

Case two

The second case was a 20 year old male, presented with small polyps in the left external auditory canal. The patient had progressive hearing loss. On clinical examination, the polyps covered the tympanic membrane and did not bleed on touch.

Excisional biopsies of the polyps were submitted for histopathological evaluation. H&E stained sections revealed the presence of similar dense lymphoplasma cell infiltrate as in case one, along with fibrosis and obliterative phlebitis. Immunohistochemical evaluation showed a significant population of IgG4 positive plasma cells, with IgG4 to IgG ratio of more than 55 %. A diagnosis of IgG4 related disease was given. However, follow-up of this patient was lost.

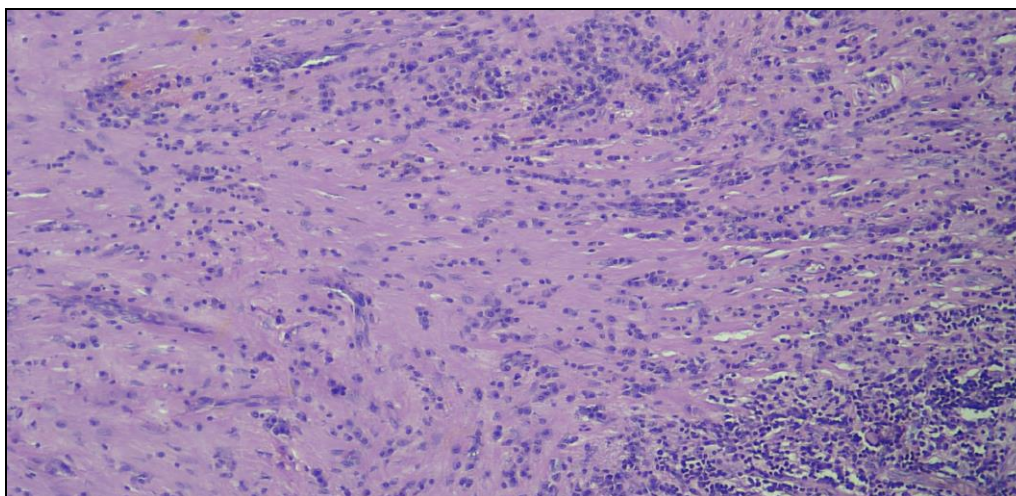


Fig 1: Low magnification 10 x - lymphoplasma cell aggregates, fibrosis (H&E*)

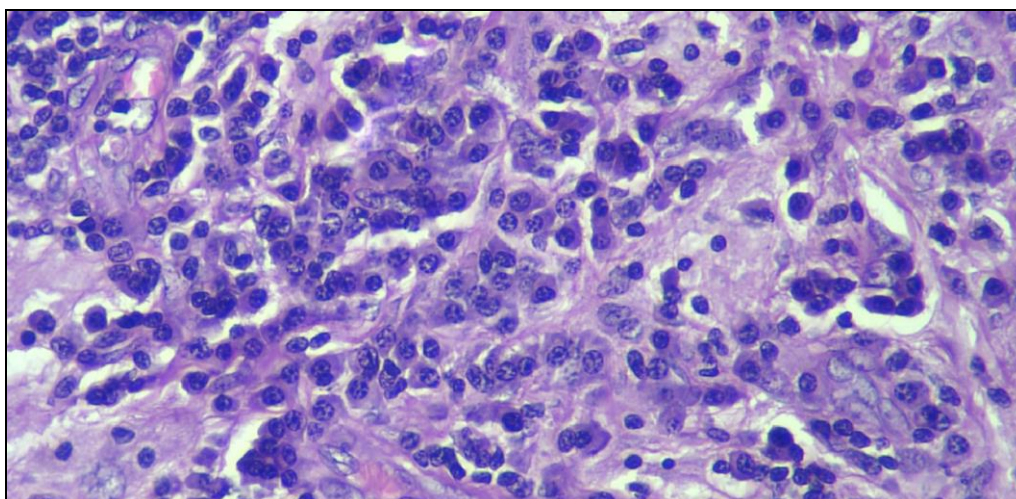


Fig 2: Higher magnification 40 x -lymphoplasma cell aggregates and obliterative phlebitis (H&E*) *Hematoxylin and eosin.

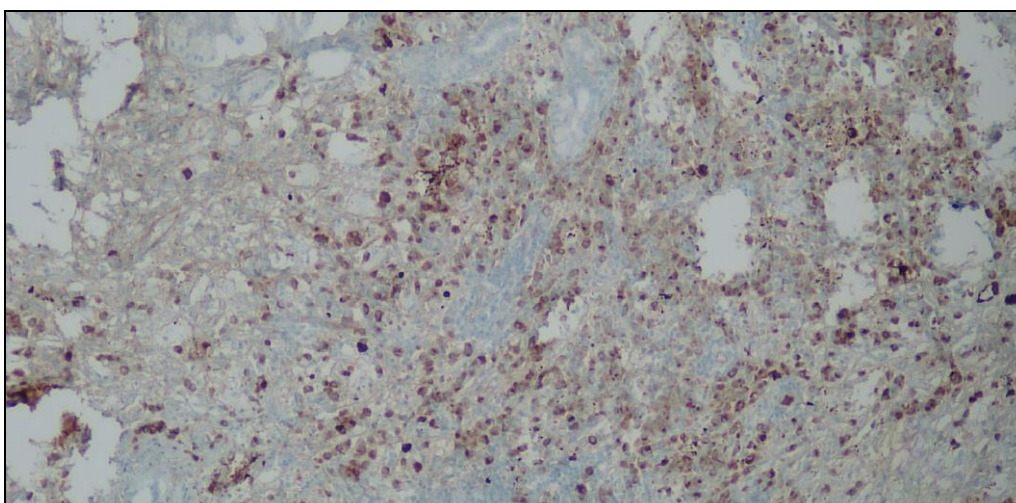


Fig 3: Many IgG4 + plasma cells seen > 50 % amidst the IgG+ plasma cells (IHC*). *Immunohistochemistry.

Discussion

IgG4RD generally occurs in middle aged adults, more often in men than in women [2].

In children, IgG4 RD is uncommon and its diagnosis might be delayed or be unrecognised.

Roubini *et al* have reported that ocular manifestations are more frequently observed in children than in adults. Also, the pattern of involvement is different, with extraocular muscles and soft tissues being more commonly affected than the lacrimal glands [3].

Karim *et al* found in their search, about 25 cases of IgG4RD reported in children. The median age of the children was 13 years, of which 64 % were girls.

The clinical spectrum is broad in this disease with different organ manifestations and different clinical outcomes. IgG4-related orbital disease (44 %) and autoimmune pancreatitis type 1/IgG4-related pancreatitis (12 %) predominantly occurred [4].

Our case presented herewith, also describes ocular involvement in a child.

Mahajan VS *et al* state that IgG4+/IgG+ plasma cell ratio in tissue, is a more powerful tool than IgG4+ plasma cell counts alone in establishing the diagnosis of IgG4-related disease. An IgG4+ / IgG+ plasma cell ratio of > 40 % is accepted as a cut off in any organ, in some studies [5].

In both of cases presented here, IgG4+/ IgG+ plasma cell ratio was calculated to be 60 % and 55 % which confirmed further the diagnosis, in addition to key histopathological features.

Carruthers MN *et al* evaluated the sensitivity, specificity and positive and negative predictive values of elevated serum IgG4 concentrations for the diagnosis of IgG4RD.

The diagnosis of IgG4RD cannot be predicted on serum levels alone, as many patients with biopsy proven IgG4RD may have normal serum IgG4 concentration.

Our case with ocular involvement had high serum IgG4 concentration of 140 mg/dl, whereas in other case with ear involvement, serum IgG4 was not increased.

Takagi *et al* described a prevalence of 12.8% (5/39) for otological IgG4-RD, of which four cases had associated sinus symptoms and middle ear exudation without granuloma and all cases presented with elevated serum IgG4.

Qinzhan Ren *et al.* reviewed the literature on otological IgG4RD and found 22 reported cases. According to these case studies, otological IgG4RD consists of progressive hearing loss, otalgia, tinnitus, and vertigo. Recurrent mastoiditis, secretory otitis media, otorrhea, and facial numbness are the main clinical symptoms [6].

The second case presented herewith shows ear involvement with symptoms of progressive hearing loss.

Serum IgG4 concentrations are often considered useful in rendering the diagnosis, in determining responsiveness to therapy, and in predicting the need for future treatment.

It is important for the histopathologist to be aware of this entity, and familiarity with its histopathologic features is essential to prevent the irreversible comorbidities associated with this treatable disease.

These case reports outline the clinical manifestations and histopathology of IgGRD, with the aim of increasing pathologist's awareness and ability to diagnose this disorder.

Conflict of Interest

Not available

Financial Support

Not available

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