IgG4-related intraocular inflammation masquerading as ciliary body melanoma in a young girl

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Immunoglobulin G4 (IgG4-related diseases) affects various tissues and organs of the human body. Orbital, adnexal, and scleral inflammations were already reported in the medical literature. To the best of our knowledge, we report the first case of intraocular IgG4-associated inflammatory mass in the ciliary body mimicking as a melanoma in a 23-year-old female from Northeast India. Characteristic histopathology, immunohistochemistry in the tissue, protein chemistry, and raised serum IgG4 were supportive for the diagnosis. As this newly diagnosed disease has multi-organ affection and little is known about its pathogenesis particularly in eye and adnexa, the present case will open many challenges in clinico-pathological diagnosis and research in the future.

Key words: Ciliary body, immunoglobulin G4-related disease, immunohistochemistry, inflammation

Immunoglobulin G4-related disease (IgG4-RD) is a relatively new and uncommon clinical entity seen in various organs and tissues of the body and associated with elevated serum levels of IgG4.[1,2] The disease has a relapsing-remitting course, and it is associated with local tissue damage in various sites with characteristic histopathological appearance.[1,2]

We report a case of IgG4-RD in uveal tissue masquerading as a ciliary body melanoma.

Case Report

A 23-year-old Indian female presented to a tertiary institute of Northeast India with the chief complaints of dimness of vision, pain and redness in the right eye (OD) for 3 months. The patient was previously treated elsewhere with two posterior sub-Tenon injections of triamcinolone acetonide given 6 weeks apart. She was also on topical steroids and cycloplegic. She did not report any benefit from the previous treatment. There was no history of trauma to the eye or elsewhere. Other medical, surgical, and family histories were unremarkable.

On examination, ocular alignment was normal with a visual acuity of counting finger at 3 m in the OD. There was minimal sclerouveitis noted in the inferior-temporal quadrant of OD. On slit-lamp examination, OD showed 360° posterior synechiae with anterior chamber flare and cells (+++) with 1 mm hypopyon [Fig. 1a]. There was a suspected mass in the inferior-temporal quadrant behind the iris, pushing it anteriorly. The left eye examination was unremarkable.

B-scan ultrasound (B-scan USG) of OD was suggestive of ciliary body mass with adjoining exudative retinal detachment (ERD). USG bio-microscopy findings were consistent with the findings of B-scan USG. The patient was advised with complete blood count with peripheral blood smear which was within normal limit. Syphilis screening (venereal disease research laboratory) was nonreactive with normal thyroid function test and negative Mantoux test (5TU) reading. Based on the clinical examination and baseline investigations, we came to the differential diagnosis of ciliary body melanoma or similar tumors. Magnetic resonance imaging suggested the possibility of ciliary body melanoma in OD [Fig. 1b and c]. After obtaining informed consent, enucleation was carried out in OD, and eyeball specimen was sent to ocular pathology laboratory for histopathological analysis. In grossing, there was

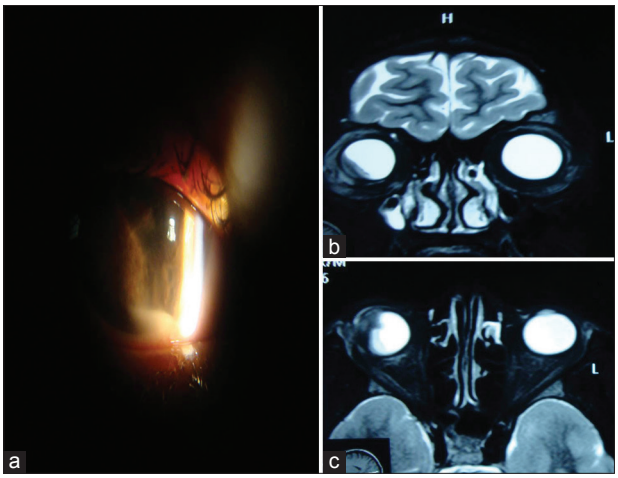

Figure 1: (a) Slit-lamp photograph of anterior chamber of right eye showing hypopyon with anterior chamber reaction (flare +++, cells +++); (b and c) the lesion in the ciliary body region of right eye in T2-weighted image of magnetic resonance imaging in coronal and axial planes, respectively. Imaging gave the probable diagnosis of ciliary body melanoma

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Quick Response Code:

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DOI: 10.4103/0301-4738.191510

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Manuscript received: 06.03.16; Revision accepted: 11.07.16

Cite this article as: Das D, Deka P, Verma G, Kuri GC, Bhattacharjee H, Bharali G, *et al*. IgG4-related intraocular inflammation masquerading as ciliary body melanoma in a young girl. Indian J Ophthalmol 2016;64:601-3.

a grayish-white-colored tumor seen in the inferior-temporal part of the ciliary body measuring (10.99 × 7.98) mm. Adjoining the grayish-white ciliary body mass, there was an ERD noted [Fig. 2].

Microscopic description of enucleated eyeball showed peripheral corneal vascularization. Few inflammatory cells were seen in the anterior chamber [Fig. 3b]. Part of the iris tissue showed inflammation. An eosinophilic mass was seen in the ciliary body with diffuse plasmacytoid cells, with reactive lymphoid follicle and other inflammatory cells [Fig. 3a]. Episcleral and scleral tissue were inflamed and infiltrated by various inflammatory cells [Fig. 3c and d]. Occasional vascularization of the sclera was noted [Fig. 3c]. Cut end of the optic nerve did not show any tumor involvement. Immunohistochemistry (IHC) was advised to explore the possibility of various inflammatory lesions. The steps for IHC were carried by kit methods available commercially.

IHC for both Kappa and Lambda was positive. Cluster differentiation (CD20, CD3, and CD45) was focal-positive. CD138 was positive in the specimen and HMB45 was negative. IHC for IgG4 was positive in occasional cells which also expressed CD138 (plasma cells). All positive controls showed appropriate

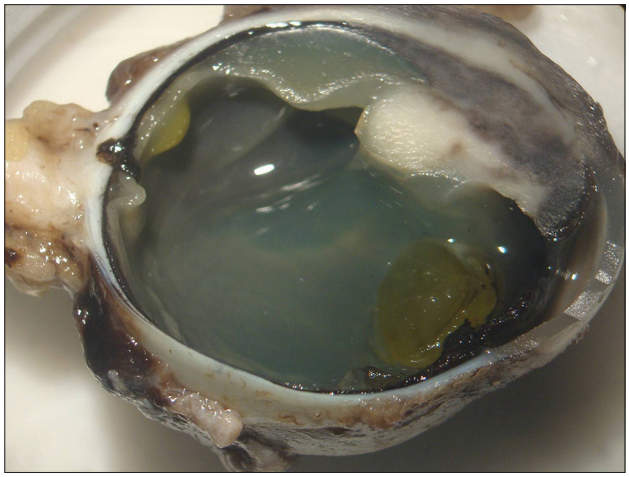

Figure 2: Gross photograph of eyeball showing grayish-white mass in the ciliary body region with gross thickening of ciliary body and adjoining exudative retinal detachment

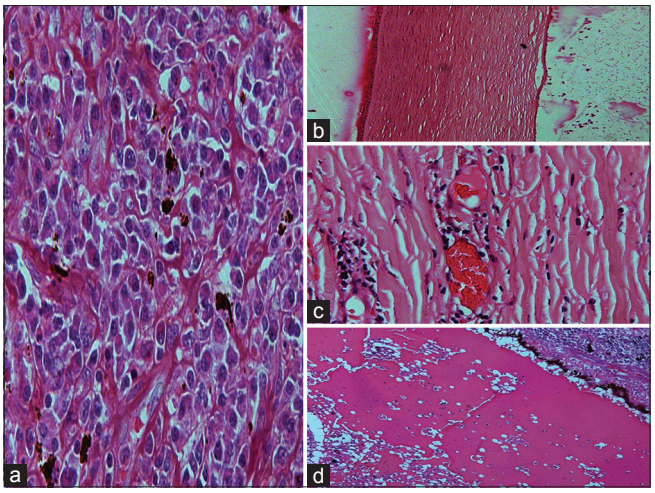

Figure 3: (a) Plasmacytoid cells (H and E, ×200); (b) exudation in anterior chamber (×200); (c) the scleral vascularization with inflammatory cells (×400); and (d) the eosinophilic exudation of the adjoining exudative retinal detachment (×200)

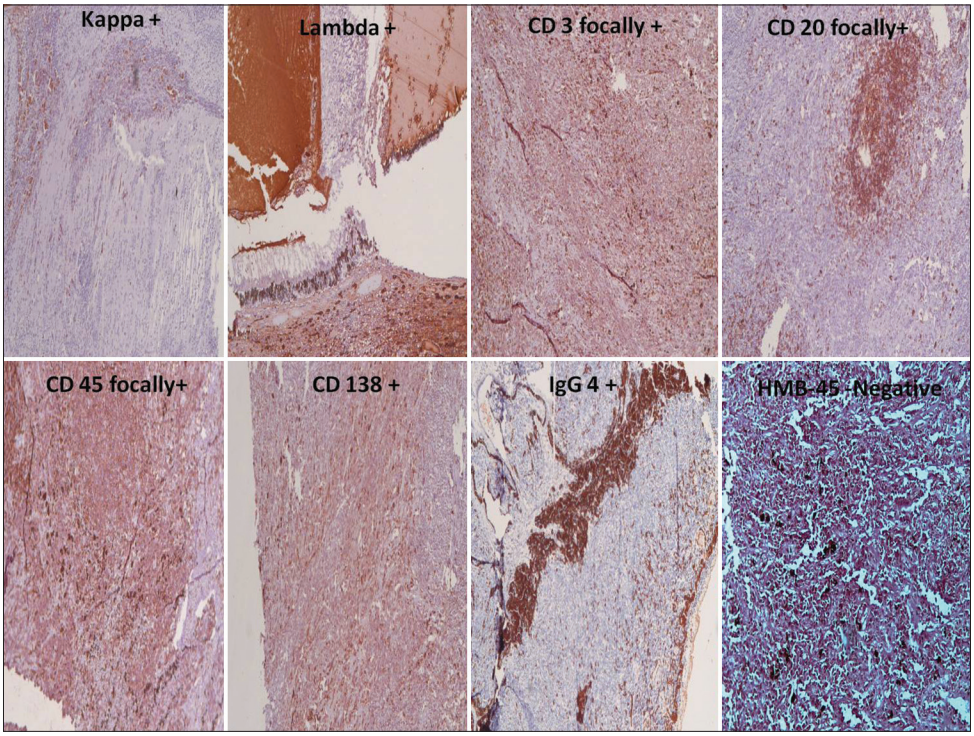

Figure 4: Immunohistochemistry done in the case. Please note that the immunoglobulin G4 positivity was around 30% of total CD-138 plasma cells positivity. All positive controls showed appropriate positive immunostaining. Negative control slide did not show immunostaining

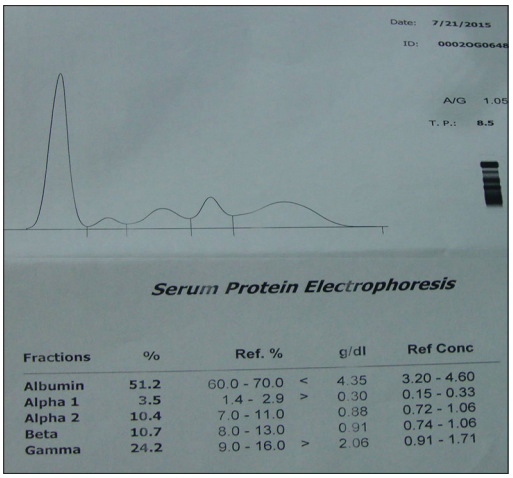

Figure 5: Protein chemistry revealed hypergammaglobulinemia with higher total protein (8.5 g/dl; normal 6.4–8.2 g/dl) and gamma fraction (2.06 g/dl; normal 0.91–1.71 g/dl). Albumin, fraction alpha 1, alpha 2, and beta were normal. No myeloma band was detected

positive immunostaining. Negative control slide did not show immunostaining. IgG4-positive plasma cells were seen in high-power field in the documented slides. Nearly, 30% of all the CD138 positive plasma cells were found to be IgG4-positive [Fig. 4].

Protein chemistry revealed hypergammaglobulinemia with higher levels of total protein and gamma fraction. No myeloma band or Bence Jones protein was detected [Fig. 5]. Serum IgG4 levels were also elevated. A hematologist was consulted, and bone marrow examination revealed mild anemia, for which she was given supportive treatment. In the postoperative period, the patient was given a course of oral steroids. On follow-up at 6 weeks, she was given prosthesis in OD, and the patient was doing well till her last review.

Discussion

IgG4-RD is a systemic condition characterized by tissue IgG4-positive lymphoplasmacytic infiltrative lesions in the body with high serum level of IgG4.[1,2] It was initially found that Mikulicz's disease was related with IgG4-RD[3] and later established that this condition can occur in any of the ocular adnexal tissue.[4] The median age of patients with IgG4-RD was 59 years (varies from 30 to 86 years), and almost equal preponderance was found in both sexes.[5-7]

IgG has four subclasses: IgG1, IgG2, IgG3, and IgG4. Serum IgG4 is the rarest group contributing <6% of IgG in normal serum.[2-5] IgG4-RD is a recently proposed clinical entity with varied clinical features, but its pathogenesis remains to be understood clearly.[5-7]

Our case was a 23-year-old female presented with sclerouveitis in OD. Ancillary imaging of OD showed ciliary body melanoma. After enucleation, on histopathology, plasma-lymphocytic inflammations were noted in iris and ciliary body region. No intraocular tumor was seen in the ciliary body region. On IHC, plasmacytoma was ruled out due to polyclonality in Kappa and Lambda light chain positivity. Bone marrow examination did not show any other abnormality, consistent with the pathology discussed here. Review of literature showed that IgG4-RD occurs in orbit and adnexal tissue in older age group.[5-7] The patient in our case was younger and presented with intraocular inflammation.

Our present understanding of ophthalmic IgG4-RD having several unique characteristic is limited to orbital and adnexal tissues.[7-10] To the best of our knowledge, this is the first described IgG4-RD in intraocular structures mimicking as a ciliary body melanoma.

Financial support and sponsorship

This study was funded by Sri Kanchi Sankara Health and Educational Foundation, Guwahati, India.

Conflicts of interest

There are no conflicts of interest.

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