Original Article

Idiopathic inflammatory diseases of orbit and ocular adnexa: Histopathological and immunochemical analysis

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Purpose: To present histopathological and immunohistochemical analysis of idiopathic inflammatory diseases of orbit and ocular adnexa. **Methods:** Design- A retrospective laboratory-based study. The study was carried out in an ocular pathology laboratory in a tertiary institute of northeast India where analysis of 93 cases was done in 5 years, during the period from 2011 to 2016. Hematoxylin--eosin and special stains were done for the diagnoses. Immunohistochemistry (IHC) panel was also carried out. For infectious pathology, Grocott's methenamine silver (GMS) stain for fungus, tissue Gram's stain for bacteria's, and acid-fast stains for tubercular bacilli were done. IHC panels were done for CD 20 (B-cells), CD-3 (T-cells), CD-45 (Leukocyte common antigen, LCA), BCL-2, CD-138 (Plasma cells), Kappa, Lambda, IgG-4 in tissue, IgG-4 in serum, etc. IHCs were done using kit methods (standardized) and adequate controls were taken for each sample. **Results:** 93 cases of nonspecific orbital inflammation were reported out of 1,467 specimens. Orbital pseudotumors (idiopathic orbital inflammatory disease, IOID) were seen in 27 cases (sclerosing variety-6); benign lymphoid hyperplasia in two cases; reactive lymphoid hyperplasia in 10 cases; atypical plasma lymphoproliferative reactive (polyclonal immunophenotypically, IgG4 negative) lesions in four cases; IgG-4 related disease in one case; nonspecific inflammatory reactions (conjunctiva, sclera, and lid) in 49 cases. In all the diagnoses, infections and lymphomas were excluded. **Conclusion:** Biopsy supported study on nonspecific orbital inflammation was important to know the pattern.

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Non-specific orbital inflammation affects orbital tissue including fat, lacrimal glands, extraocular muscles, etc., focally or diffusely.[1-4] Affection of Tenon's capsule is the least frequent location.[2-4] Incidence and prevalence findings of nonspecific inflammatory disease of orbit based on scientific literature was difficult as it depended on inclusion or not of specific and nonspecific inflammatory pathologies.[3-8]

Orbital inflammatory disease can clinically present as acute, subacute, and chronic stage based on onset and extent of the lesion.[2-5] Patients usually present with periocular pain, orbital edema, conjunctival congestion, ptosis, and proptosis. Histopathology is the cornerstone of the diagnosis depending on various stages of inflammation.[2-4,6,7] We present 5 years study of histopathological and immunohistochemistry (IHC) profile of the adnexal and orbital inflammatory disease.

Methods

This retrospective laboratory-based was carried out in an ocular pathology laboratory in a tertiary institute of northeast India where analysis of 93 cases was done in 5 years duration during the period from 2011 to 2016. Routine hematoxylin--eosin and other special stains were done for the diagnoses. IHC panel was also carried out. For infectious pathology, Grocott's methenamine silver (GMS) stain for fungus, tissue Gram's stain for bacteria's, and acid-fast stains for Tubercular bacilli were done. IHC panels were done for CD 20 (B-cells), CD-3 (T-cells), CD-45 (Leukocyte common antigen, LCA), BCL-2, CD-138 (Plasma cells), Kappa, Lambda, IgG4 in tissue, IgG-4 in serum, etc. IHCs were done using kit methods (standardized) and adequate controls were taken for each sample.

Results

93 cases (6.64%) of nonspecific orbital inflammation were found out of 1,467 specimens [Fig. 1]. Orbital pseudotumors (IOID) were seen in 27 cases (sclerosing variety-6); benign lymphoid hyperplasia in two cases; reactive lymphoid hyperplasia in 10 cases; atypical plasma lymphoproliferative reactive (polyclonal immunophenotypically, IgG4 negative) lesions in four cases; IgG4-related disease in one case; nonspecific inflammatory reactions (conjunctiva, sclera, and lid) in

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49 cases [Fig. 2]. In all the diagnoses, infections and lymphomas were excluded. Controls were taken for special stains and IHCs. All positive controls showed appropriate positive immunostaining. Negative control slide did not show immunostaining.

Discussion

Pathology of typical nonspecific orbital inflammation was characterized by inflammation cellular infiltrate, vascular congested tissues, altered lacrimal gland tissue, and disturbances in other orbital structures.[1-4] Grossly, the lesions displayed greyish white colored tissues and microscopically, it revealed inflammation in the orbital structures and cellular infiltrates that were focal, multifocal, or diffuse.[3,4] Cellular infiltrations were of differentiated mature lymphocytes, intermixed with plasma cells, eosinophils, polymorphs, and rarely with histiocytes and macrophages.[1-5] The infiltrates were polyclonal and lymphoid follicles could be seen with germinal centers occasionally. The lesions were highly vascular due to capillary proliferations and were accompanied with perivascular and lymphoplasmacytic infiltrations and eosinophils were sometimes seen tracing near capillary adventitia.[1,2] Endothelial cells showed hyperplasia and sometimes there were reactive increase in the number of cells. In some long-standing cases, sclerosing patterns were noticed and periductal fibrosis in lacrimal tissue with atrophied acini was seen.[1-5]

We had seen 93 cases (6.64%) of nonspecific inflammation out of 1,467 specimens. IOID were seen in 27 cases (sclerosing variety-6 cases), benign lymphoid hyperplasia in two cases, reactive lymphoid hyperplasia in 10 cases, polyclonal atypical plasma lymphoproliferative reactive which were negative for IgG4 were seen in in four cases, IgG4-related disease in one case, nonspecific inflammatory reactions (conjunctiva, sclera, and lid) in 49 cases. In all the diagnoses, infections, rheumatoid arthritis, granulomatous polyangiitis, thyroid orbitopathy, and lymphoma were excluded from the cohort. A representative case of a young lady presented with ocular pain, conjunctival injection, and mild proptosis [Fig. 3a] and imaging consisting with nonspecific orbital inflammation which was biopsy proven. Follow-up magnetic resonance imaging (MRI) with contrast showed improvement of her findings following steroid treatment [Fig. 3b and c].

In IHC, both T cells and B cells marker were positive. Orbital inflammatory tissue showed strong expression of CD20 in around 35% of lymphocytes and CD3 were expressed around 25--30% in our series. CD45 (LCA) was expressed 20--25% in our cases. However, we did not see dendritic cell expression in our cases. BCL2 and Ki-67 were moderately expressed in the lymphoproliferative variety of lesions. In one isolated case, we had seen IgG-4-related disease in the orbital tissue where the storiform pattern was particularly noticed with obliterative vasculitis. IHC for IgG-4 in the tissue was positive in more than 50% and the serum IgG4 elevation confirming the condition [Fig. 4].

Moreiras and Prada *et al*. studied 189 cases of noninfectious inflammatory disorders (specific and nonspecific) and found an incidence of 12.8% among orbital lesions excluding thyroid orbitopathy.[1,7] Pseudotumors or nonspecific inflammations were frequently diffuse variety in 30 cases, anterior in 20 cases,

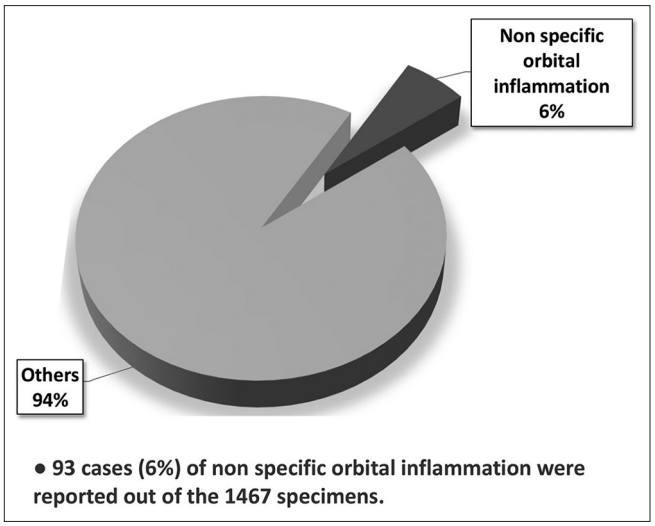

Figure 1: Graph showing nonspecific orbital inflammatory cases in respect to total cases received in the ocular pathology laboratory during 2011-2016

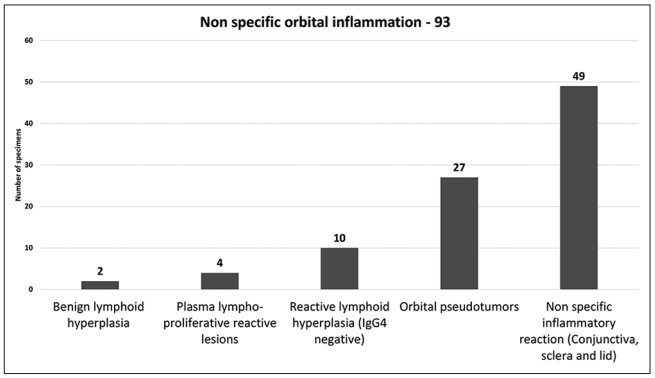

Figure 2: Graph showing distribution of inflammatory disorders of orbit and adnexa

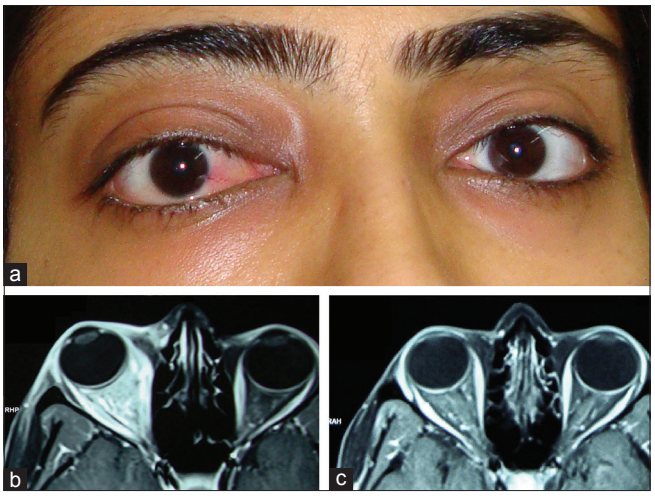

Figure 3: (a) Clinical photograph showing proptosis with conjunctival injection in the right eye. (b) Axial Gadolinium-enhanced T1-weighted MRI showing moderate to a marked diffuse enhancement in the right orbit. (c) Axial Gadolinium-enhanced T1-weighted MRI at 3 months showing reduced enhancement in the right orbit after a course of oral steroids

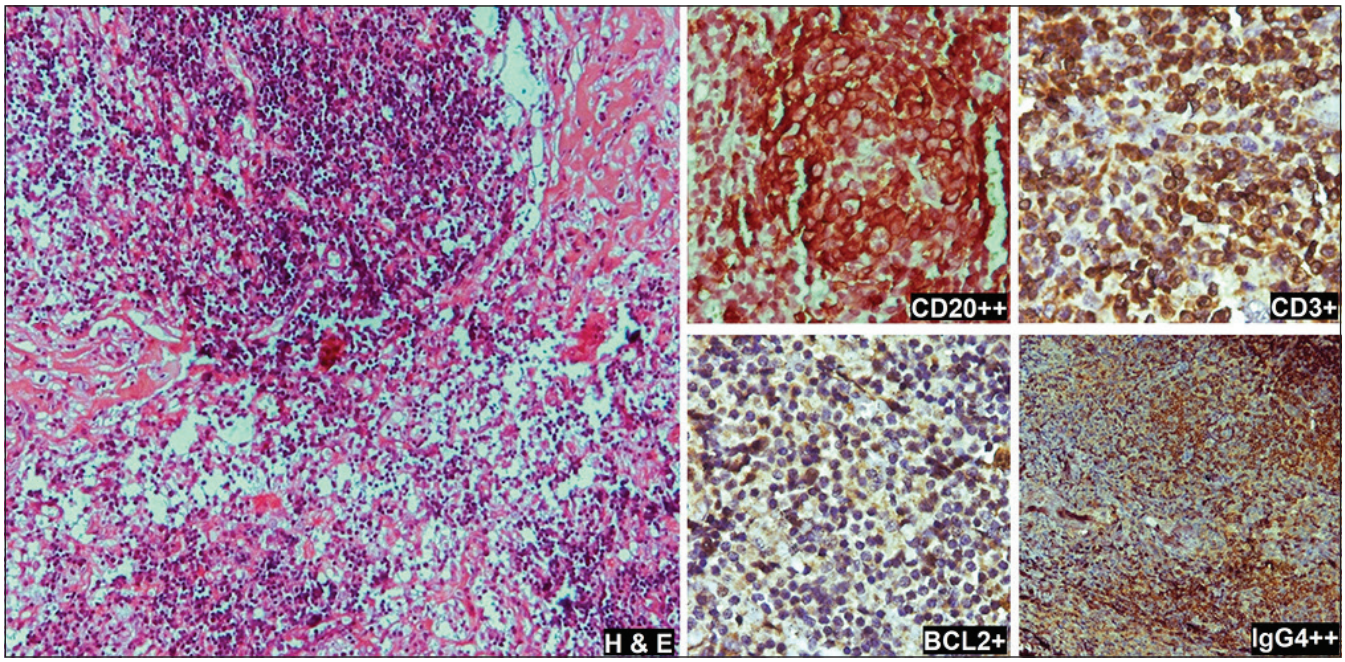

Figure 4: An index case of IgG-related orbital inflammation (Histopathology and IHCs)

dacryo-adenitis in 26 cases, and myositis in 24 cases.[1,4,6,7,9] Our study showed 6.64% cases which were almost half the above-mentioned study.[7]

The clinical course of inflammatory diseases of orbit and adnexa may be determined by how often the patients encounter the primary antigen in B cell and T cell lineage.[8,9] There could be single and intermittent exposure to activate the immunological cells. If self-antigen is involved in the course of the disease then chronic autoimmune process sets in.[7-9]

Conclusion

Biopsy study of nonspecific orbital inflammation was important to know the pattern. Further, larger multicenter studies will give better insight into the clinicopathological aspect with additional gene profiling evidence that could give a guideline to classify them better.

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Conflicts of interest

There are no conflicts of interest.

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