Case Report

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Pathology Section

Primary Orbital Marginal Zone B-cell Lymphoma: A Rare Case Report

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ABSTRACT

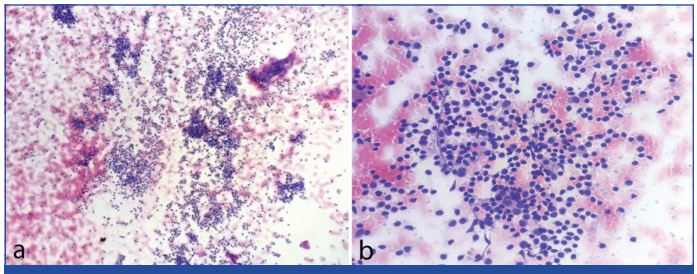
Orbital Lymphomas (OL) account for 1 to 2% of Non Hodgkin Lymphomas (NHLs) and 2 to 11% of all orbital tumours. The most common primary OL is low-grade marginal zone B-cell lymphoma. This is a case of primary orbital NHL mimicking an orbital pseudotumour. A 67-year-old male presented with a swollen right eye associated with lacrimation for two months. On examination, there was right eye proptosis. Thyroid, liver and renal function tests were within normal limits. Contrast Enhanced Computed Tomography (CECT) revealed a homogenously enhancing intraconal mass measuring 4.1×3.2×2.8 cm, with features favouring a benign aetiology. Cytosmears revealed features suggestive of inflammatory pseudotumour of the orbit. Histopathological findings suggested low-grade NHL. Immunohistochemistry (IHC) showed positivity for CD20, CD79a, PAX5, and Bcl2, and negativity for CD3, CD5, CD10, CD23, Bcl6, and Cyclin-D1. Hence, a final diagnosis of marginal zone B-cell lymphoma was rendered. Detailed clinical and radiological evaluations did not reveal lymphadenopathy anywhere else or any other focus of tumour, indicating the primary origin of this tumour in the orbit. Primary NHL of the orbit is rare. It can occur in the orbit without any systemic features. It must be diagnosed early and can be treated with surgery and chemotherapy.

Keywords: Immunohistochemistry, Non hodgkin lymphomas, Pseudotumour

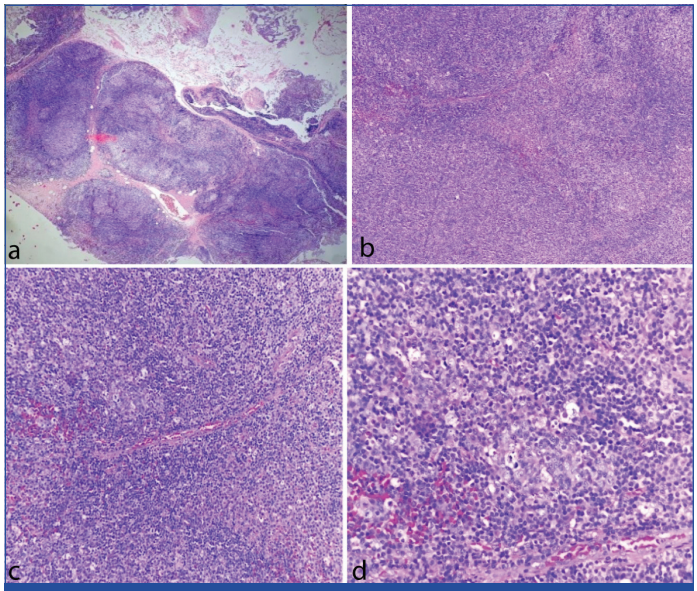
CASE REPORT

A 67-year-old male presented to the neurosurgery Outpatient Department (OPD) with complaints of painless swelling in the right eye for two months, associated with lacrimation. On examination, the Glasgow Coma Scale score was normal, i.e., 11. Right periorbital swelling with a 4 mm deviation of the right eye and right anterior conjunctival oedema was noted. Bilateral pupil diameters were equal and reactive to light. Fundoscopy revealed a mildly pale disc with anterior attenuation and a tessellated fundus. Perimetry showed a left eye Visual Field Index (VFI) of 48% (normal) and a right eye VFI of 89% with borderline or general reduction. The Total Leukocyte Count (TLC) was 13,300/cu.mm, with a Differential Leukocyte Count (DLC) of 67% neutrophils, 24% lymphocytes, 8% monocytes, and 1% eosinophils. No atypical cells were noted. The HbA1c was 6.5%. Liver, thyroid and renal function tests were within the normal reference range. Serum IgG4 was 137 mg/dL (normal), and serum acetylcholinesterase levels were 12 U/mL (normal), excluding IgG4-related disease and sarcoidosis. A contrast CT of the right orbit showed a moderately homogenously enhancing intraconal mass measuring 41×32×28 mm, with extension up to the right superior eyelid and focal thinning of the orbital roof causing proptosis. The lesion encased the anterior part of the optic nerve and involved the superior rectus muscle. There was no intraocular extension of the intraconal mass, with features suggesting a benign aetiology.

Ultrasonography (USG)- guided Fine Needle Aspiration Cytology (FNAC) from the right orbital mass revealed reactive lymphoid cells in varying stages of maturation, tingible body macrophages, occasional lymphohistiocytic tangles, along with a few plasma cells and eosinophils in a haemorrhagic background [Table/Fig-1a,b]. These features suggested the possibility of an inflammatory pseudotumour of the orbit. Due to the persistence of clinical symptoms, the intraconal mass was excised and subjected to histopathological examination. Gross examination showed multiple bits of greyish-white to greyish-brown tissue, altogether measuring 0.5 cm to 0.8 cm. Microscopically, some areas revealed numerous reactive lymphoid follicles with germinal centers [Table/Fig-2a]. Focal areas showed a diffuse arrangement of monotonous small lymphoid cells [Table/Fig-2b]. The cells were small with scant cytoplasm, irregular nuclear membranes, and dense chromatin. Occasional mitotic figures were present. In view of the monotonous



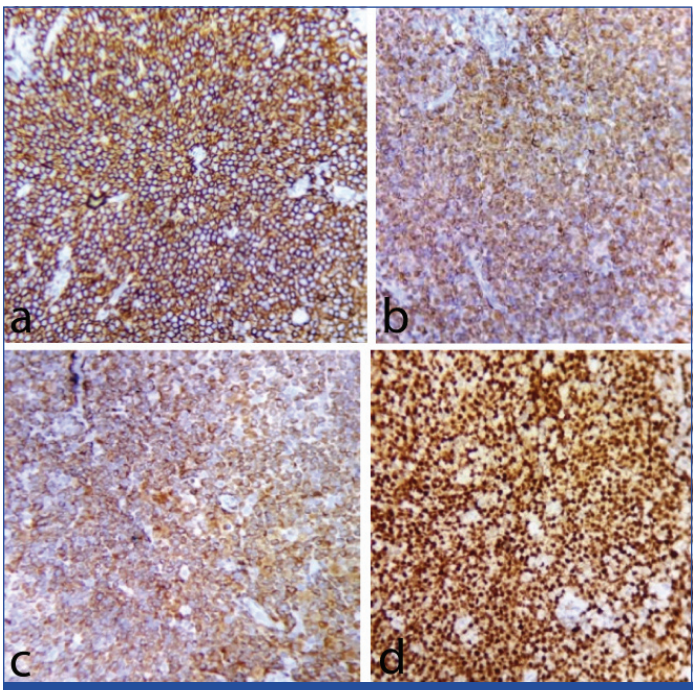
[Table/Fig-1]: a) Sheets of small blue cells (H&E, 100x). b) Lymphoid cells of variable size (H&E, 400x).



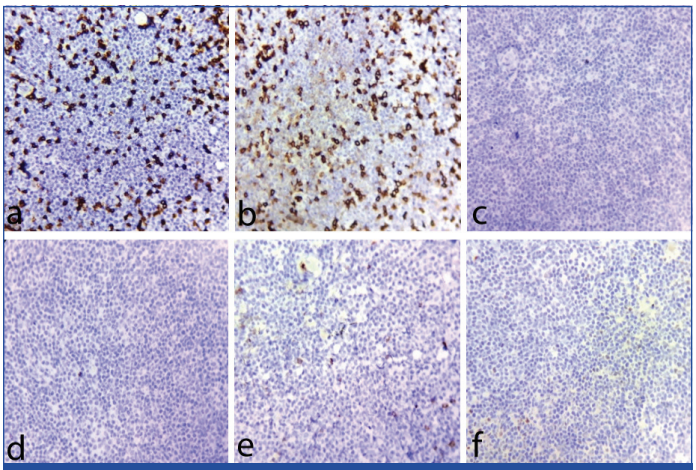
[Table/Fig-2]: a) Reactive lymphoid follicles (H&E, 40x); b) Diffuse arrangement of lymphoid cells (H&E, 100x); c) Sheets of atypical lymphoid cells (H&E,100x); d) Small to medium size atypical lymhoid cells (H&E, 400x).

population of these atypical small-sized lymphoid cells, a morphological possibility of 'NHL-small cell type' was made based on the biopsy.

On IHC, positivity for CD20, CD79a, PAX5, and Bcl2 [Table/Fig-3a-d] and negativity for CD3, CD5, CD10, CD23, Bcl6, and cyclin D1 was noted [Table/Fig-4a-f] in the tumour cells. Therefore, a final diagnosis of small cell NHL- marginal zone lymphoma was made.



[Table/Fig-3]: a) CD20; b) CD79a; c) PAX5; d) Bcl2, all images (IHC, 100x).



[Table/Fig-4]: a) CD 3; b) CD 5; c) CD 23; d) Cyclin D1; e) CD 10; f) Bcl6, all images (IHC, 100x).

A detailed clinical and radiological evaluation did not reveal lymphadenopathy or tumour foci anywhere else in the body, confirming the primary origin of the orbital lesion.

DISCUSSION

Primary ocular adnexal lymphoma is defined as a condition without evidence of concurrent systemic lymphoma and with no prior history of lymphoma [1]. Since orbital and adnexal lymphoma is associated with systemic lymphoma in 30-35% of cases, all patients with ocular lymphoma should undergo a complete work-up to rule out systemic lymphoma [1,2]. Lymphomas of the ocular adnexa are a heterogeneous group of malignancies, comprising approximately 1 to 2% of NHLs, 8% of all extranodal lymphomas, and 2 to 11% of orbital tumours [1,2]. The most common subtype, accounting for up to 80% of cases of primary ocular adnexal lymphoma, is B-cell lymphoma, specifically marginal zone lymphoma of Mucosa-Associated Lymphoid Tissue (MALT) type [2]. Other histopathological subtypes include follicular lymphoma, diffuse large B-cell lymphoma, mantle cell lymphoma, small lymphocytic lymphoma and lymphoplasmacytic lymphoma [2]. MALT lymphoma is most commonly seen in individuals in their 5th to 7th decade of life, with a median age of 65 years and a typical female predominance. The most frequent sites of origin are the orbit, followed by the conjunctiva, lacrimal gland and eyelid [2]. MALT lymphomas typically arise in tissues or organs that are normally devoid of organised lymphoid tissue, such as the orbital region, but acquire reactive lymphoid tissue in response to persistent antigenic stimulation, which occurs as a result of chronic inflammatory or autoimmune disorders [2].

Primary ocular lymphoma appears to correlate with the risk of systemic involvement. In general, conjunctival primaries are associated with the lowest (~20%) risk, orbital with an intermediate (~35%) risk, and eyelid with the highest (~65%) risk of disseminated disease [2]. Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) with contrast is valuable in determining the extent of local disease in the orbit, eyelid and paranasal sinuses [3]. Positron Emission Tomography (PET) is superior for the initial staging of ocular adnexal lymphoma [4]. However, there is no single radiological feature that can reliably discriminate between lymphoma and lymphoid hyperplasia [5]. Before the advent of immunophenotyping and molecular diagnostic techniques, MALT lymphomas were frequently misdiagnosed as reactive lymphoid hyperplasia or "pseudotumours" due to their cellular heterogeneity and the presence of reactive germinal centers [2]. Many treatment modalities are available, including surgical resection, radiotherapy, chemotherapy and immunotherapy. Surgery alone is not sufficient, as it can lead to relapse. The selection of the treatment modality is made after considering multiple factors such as the patient's age, size and site of the lymphoma, extent of visual impairment, and both patient-related and disease-related prognostic factors. Radiotherapy is often used as the primary treatment for indolent lymphomas [6].

Ocular adnexal lymphoma spreads to many sites, of which the most common are lymph nodes. Other sites include the skin, bone marrow and spleen [7]. Despite the indolent course of extranodal marginal zone B-cell lymphoma, it is known to recur in extranodal sites, including the lungs, salivary glands and other ocular adnexal sites. Chemotherapy includes Cyclophosphamide, Vincristine, Doxorubicin, Prednisolone and Rituximab monotherapy, followed by radiotherapy [8]. Long-term follow-up with a six-month examination is recommended [7,8].

CONCLUSION(S)

OLs can be confused with reactive lesions in radiology and cytology. Primary orbital lymphomas are very rare and a complete and meticulous systemic examination is essential to exclude systemic lymphomas. Clinical examination, radiology and histopathology with IHC are crucial for a final and accurate diagnosis. Since most primary OLs develop systemic disease, regular follow-up is essential.

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