Reactive Lymphoid Hyperplasia

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Introduction

The benign form of ocular adnexal lymphoproliferative disorder (OAL) is reactive lymphoid hyperplasia (RLH). About 16% of all OAL is reactive and benign, based on immunohistopathological staining and molecular studies. All cases of RHL have to be investigated for coexistence of lymphoma elsewhere in the body and should be followed up closely for relapses and transformation to lymphoma.

Clinical Scenario

A 66-year-old Indonesian female with no past medical history presented with painless right upper lid swelling of 1–2 years' duration. She had not noticed any other lumps in the neck or axilla. Examination revealed normal visual acuities in both eyes. She was noted to have a 2 mm proptosis with a ptosis in her right eye along with fullness in the upper temporal quadrant (Fig. 34.1). A firm mass was felt in the right lacrimal fossa. She had limitation of the right eye in upgaze. The rest of the ophthalmic examination was normal.

CLOSE summary is given in Table 34.1.

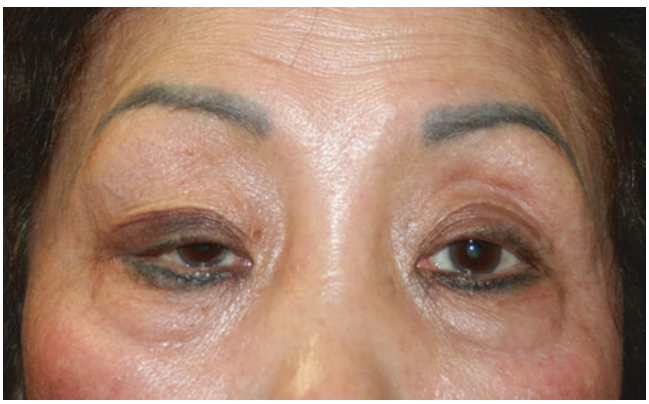

Fig. 34.1 Clinical picture showing the fullness in the temporal quadrant of the right upper lid with ptosis

Table 34.1 CLOSE summary

*C*linical process: infiltrative, mass lesion
*L*ocation: right lacrimal gland
*O*nset: chronic
*S*igns and symptoms: painless proptosis, upper lid swelling, and ptosis
*E*pidemiology: 66-year-old Indonesian female

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Differential Diagnosis

- Lymphoproliferative disorder
- Specific orbital inflammations such as sarcoid lesion, Wegener's (GPA), Sjogren's, TB, etc.
- Non-specific orbital inflammatory disease (NSOID)
- Lacrimal gland malignancies such as adenoid cystic carcinoma, adenocarcinoma, etc.
- Pleomorphic adenoma of the lacrimal gland

Patient underwent imaging.

Radiology

CT scan of the orbits showed an enhancing lesion in the right lacrimal gland (Fig. 34.2). It seemed to wrap around the globe without indentation. There was no bony remodeling or erosion. The rest of the orbit was normal.

Intervention

An anterior orbitotomy with biopsy of the right lacrimal gland was performed through the lid crease incision. The specimen was sent fresh for histopathology.

Histopathology

Histology showed seromucinous glandular structures accompanied by heavy lymphoid infiltrate composed of small-sized lymphocytes arranged in follicles (Fig. 34.3). CD3 mainly highlighted the T-cells in the inter-follicular region, while CD20 highlighted the B-cells in the follicles (Fig. 34.4). CD21 highlighted the regular and well-demarcated follicular dendritic meshwork, which are readily seen in germinal centers in reactive follicles. Bcl-2 highlighted the marginal, mantle, and inter-follicular areas only; the germinal centers did not stain for Bcl-2, thus excluding a

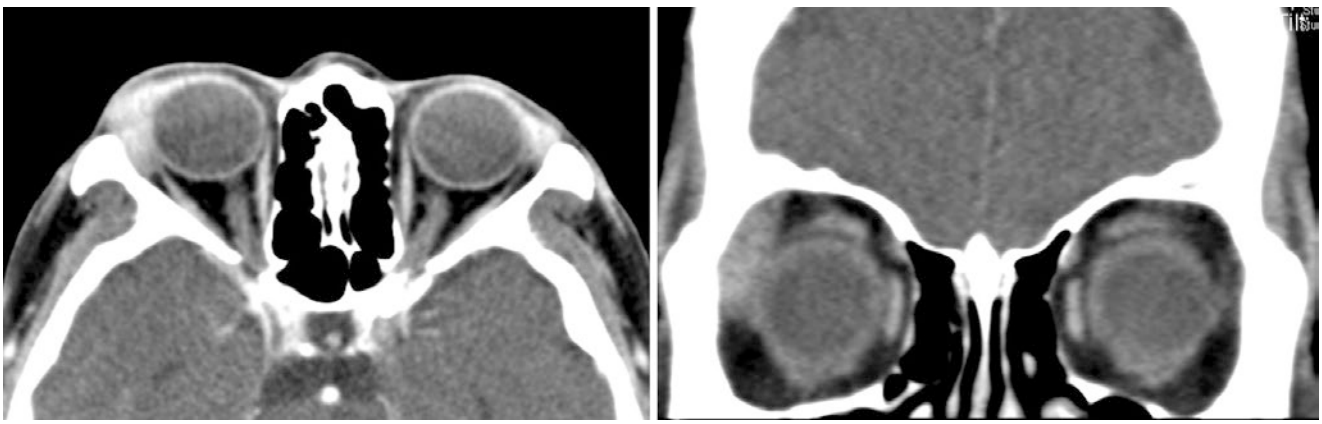

Fig. 34.2 Axial and coronal post-contrast CT images showing diffuse, homogeneous enlargement of the right lacrimal gland

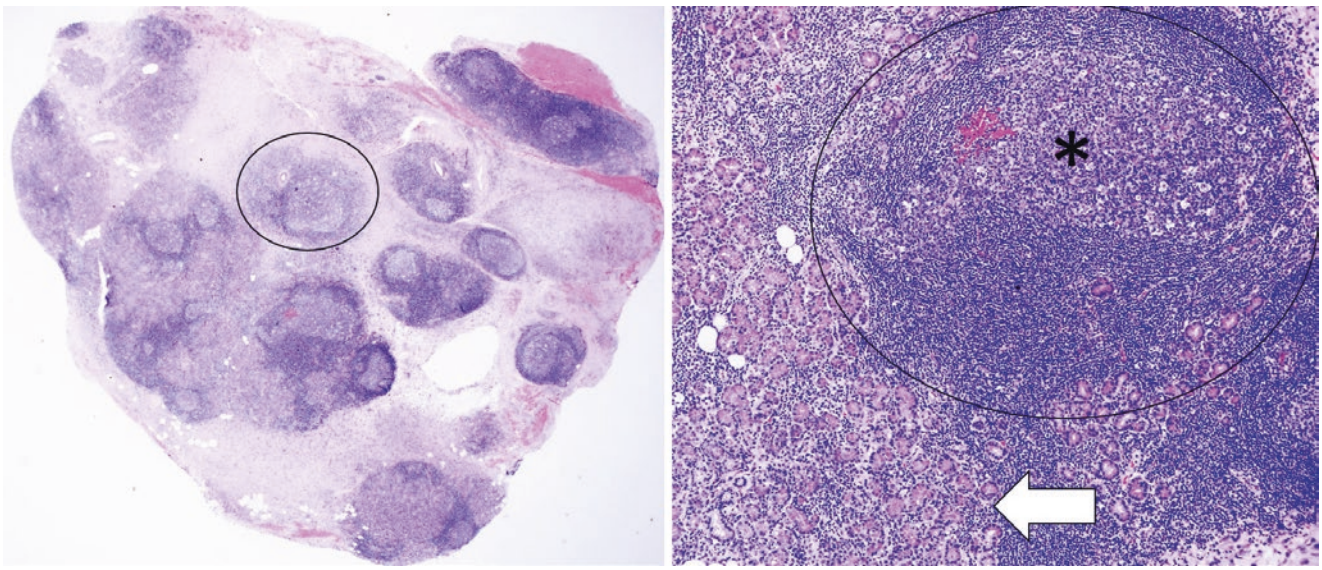

Fig. 34.3 There is a lymphoid infiltrate with follicular pattern (black circles). The lymphoid follicles exhibit germinal centers (*). Benign seromucinous glands are also present (white arrow). Left: HE stain, 20× magnification. Right: HE stain, 100× magnification

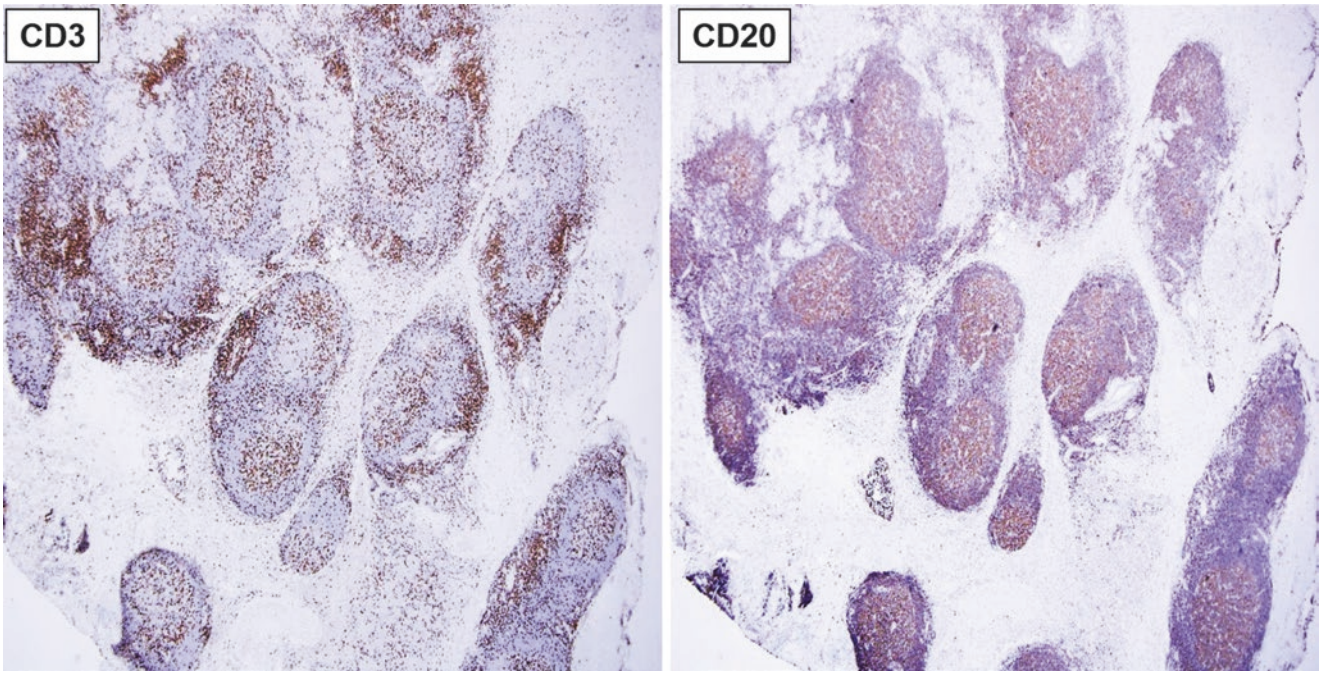

Fig. 34.4 CD3 mainly highlights the T-cells in the inter-follicular region, while CD20 mainly highlights the B-cells in the follicles. Left: Immunohistochemistry (CD3 antibody), 40× magnification. Right: Immunohistochemistry (CD20 antibody), 40× magnification

follicular lymphoma. The features were those of reactive lymphoid hyperplasia.

Management

The patient responded well to a course of oral steroids and was investigated for autoimmune disease. She was advised for close follow-up and re-biopsy should the swelling recur.

Discussion

Reactive lymphoid hyperplasia (RLH) and non-specific orbital inflammatory disorder (NSOID) are two distinct entities. RLH affects most commonly the lacrimal gland. The diagnosis is made mainly from the absence of clonal B-cell population by immunohistochemistry which can be confirmed by additional tests such as flow cytometry and/or molecular techniques. The flow cytometry requires abundant fresh tissue that may be difficult to obtain in orbital biopsies. There has been a shift in diagnostic patterns with the advent of flow cytometry and molecular testing. Some lesions that had been thought to be benign RLH have been reclassified as extranodal marginal zone lymphoma (ENMZL).

The term atypical lymphoid hyperplasia has been used for indeterminate lesions where the amount of tissue available is limited, or the combined results of flow cytometric or molecular investigations are inconclusive.

There has been an increased awareness of IgG4 inflammations in recent years. Some of the RHL can mimic IgG4 inflammation. Therefore, immunohistochemical staining for IgG and IgG4 is recommended for all cases of lymphoid hyperplasia.

A small proportion of RLH cases have been reported to transform into lymphoma at a later date. Therefore, all cases of RHL have to be investigated for coexistence of lymphoma elsewhere in the body and should be followed up closely for relapses and transformation to lymphoma.

Learning Points

Reactive lymphoid hyperplasia (RLH) is one end of the spectrum of lymphoproliferative disorders. Spread of the lesion along the planes in the absence of bony erosion in CT should raise the possibility of OAL. Immunohistochemistry, flow cytometry, and molecular techniques should be used where possible to rule out lymphomas. Thorough systemic evaluation combined with close monitoring for life is necessary in cases of RHL.

Further Reading

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