LACRIMAL GLAND ROSAI DORFMAN DISEASE (RDD)

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EOPS MEMBER: DR HARDEEP SINGH MUDHAR

ADDRESS: NATIONAL SPECIALIST OPHTHALMIC PATHOLOGY SERVICE (NSOPS), DEPT OF HISTOPATHOLOGY, E-FLOOR, ROYAL HALLAMSHIRE HOSPITAL, SHEFFIELD, S10 2JF, ENGLAND UK

CONTACT DETAILS: hardeep.mudhar@nhs.net Tel (office) 0044 114 226 8967

History

A 35-year-old female presented to the Orbital clinic with a lump in the right upper outer eyelid over, getting larger over a duration of 8 months. It was initially painful but became less so in time.

The patient has the following active medical conditions:

-SLE (diagnosed in her teenage years with positive anti-double stranded DNA autoantibodies. Currently joint pain treated with hydroxychloroquine);

-Antiphospholipid syndrome (Warfarin anticoagulation);

-Raised body mass index (BMI).

A CT Orbit with contrast confirmed homogenous lacrimal gland enlargement (Right >Left). This was clinically thought to be due to her SLE. She underwent a debulking and intralesional steroid injection to the right lacrimal gland.

Histology of Lacrimal Gland:

At low power, the striking feature is dark and light patches in the lacrimal gland tissue. The darker areas comprise lymphoid tissue with reactive germinal centres and prominent mature plasma cells. The lighter areas that interface with the darker areas, comprise of eosinophilic to clear histiocytic cells, with ample bubbly cytoplasm. Emperipolesis is readily identified. The surrounding stroma shows fibrosis. There is no vasculitis or granuloma formation, no necrobiosis or xanthogranulomatous infiltrate. More than 40% of IgG staining plasma cells stain for IgG4 and there are more than 50 IgG4 plasma cells per high power field (x40 lens BX51 Olympus microscope). The histiocytic cells are positive for S100 and negative for CD1a and Langerin. No molecular analysis has been performed yet on the Rosai-Dorfman. Serum IgG4 was marginally raised at 1.4 g/L (upper limit 1.3g/L).

Follow up course:

The lacrimal gland histology showed classical extranodal Rosai-Dorfman disease. She underwent further MRI imaging that revealed bilateral parotid and submandibular gland enlargement and a left-side inferior pole renal mass 5cm in maximum dimension with associated para-aortic lymphadenopathy. Whole body PET FDG scans showed cervical, axillary and inguinal lymph nodes and increased FDG activity in the lacrimal glands, salivary glands and left kidney mass. A submandibular biopsy showed a chronic sialadenitis without increased IgG4 plasma cells or S100 positive histiocytes. A biopsy of the renal mass was judged to be peri-lesional and the patient is waiting for a repeat biopsy.

Discussion

1. In the Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages, RDD is classified as group ‘R’ non-Langerhans cell histiocytosis [1].

2. RDD subtypes include: Familial, Classical (nodal), Extranodal, Neoplasia related, and Immune disease associated**.** In the nodal and extranodal types these can be with or without IgG4 disease. The immune associated subtype lists SLE as one of the key immune syndromes [1]

3.Possible role for human herpes virus [2], parvovirus B19 [3], and Epstein-Barr virus [4] in the pathogenesis of the disease have been suggested. However, no definite etiology has been established.

5. Orbital involvement is rare and can be an isolated extranodal manifestation or associated with systemic disease. In the largest case series of RDD, 13 / 113 cases (11%) had periocular infiltration [5], with 11/13 cases involving the orbital soft tissues. Involvement of orbital soft tissues and the eyelids is the most common

ophthalmic manifestation. Involvement of the lacrimal gland (unilateral [6,7] or bilateral [8), conjunctiva [9], uvea [10], cornea [11], and retina [10] has been described. Orbital disease is associated with a higher risk of involvement of other extranodal sites[5].

6. Lacrimal gland involvement has been reported in 18 cases. [6-8; 12-22]).Median age of these patients is 32 years (range 4–78). 13/18 (72%) cases are male. The commonest presentationsisa painless orbital mass, swelling of the eyelids and proptosis. 6/ 18 patients (33%) show isolated lacrimal gland disease with no systemic involvement. The most common type of systemic involvement is cervical lymphadenopathy. 7/18 patients show bilateral lacrimal gland involvement (39%), Bony involvement in RDD is rare (23-24).

7. The histopathology shows an accumulation of histiocytes with enlarged, round to oval hypochromatic nuclei and abundant “watery-clear” or “foamy” cytoplasm, containing engulfed intact inflammatory cells known as emperipolesis. There is associated fibrosis and inflammation of plasma cells and lymphocytes. Occasional neutrophilic infiltrates are present. The histiocytes are positive for S100, Fascin, CD68, Cyclin D1 and negative for Langerin and CD1a [1].

8. Recent studies have identified NRAS, KRAS, MAP2K1, and ARAF mutations in RDD[25-29]

9. Some forms of orbital RDD, have been associated with an increased number of Ig4-positiveplasma cells,No clear evidence suggests that the 2 disorders share the same pathogenesis; however, the most recent classification of histiocytoses recommends evaluating the IgG4/IgG ratio in all patients with RDD [30-31].

10. In this case, notable features include:

-The clear diagnostic histology for extra-nodal RDD from the lacrimal gland compared to the salivary glands and kidney.

-The elevation of the IgG4 plasma cells (>40% IgG4 and >50 IgG4 plasma cells per HPF), which may or may not indicate IgG4RD.

-The presence of active SLE.

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