Recurrent orbital tumor

Joint SS Soft Tissue and Bone Pathology and Ophthalmic Pathology:

More than meets the eye

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CT scan: right lacrimal gland and orbital soft tissue tumor
Case presentation

Female, 38 y

1992 orbital tumor
Idopathic Orbital Inflammation
IOI

Treatment immunosuppression

2012
Recurrence orbital tumor
IgG4 related disease

Orbit 2014;33:388-91
IgG4-Related Disease

- Immune-mediated systemic fibro-inflammatory condition:
  - **Boston Consensus Criteria**
  - Tumor-like lesions
  - Lymphoplasmacytic infiltrate
  - IgG4-positive plasma cells (mean of 3 HPF)
    - >50/HPF (orbit)
    - >100/HPF (lacrimal gland)
    - IgG4/IgG ratio >0.4
  - Storiform fibrosis
  - Obliterative phlebitis
IgG4-Related Orbital Disease

- Lacrimal gland
- Orbital soft tissue
- Extraocular muscles
- Eyelids
- Sclera
- Optical and trigeminal nerves an
- Orbital bones
Spectrum of known diseases

- Mikulicz’s disease
- Küttner’s tumor
- Sclerosing sialadenitis
- Eosinophilic Angiocentric Fibrosis
- Riedel’s thyroiditis
- A subset of idiopathic retroperitoneal fibrosis
- Many cases of (Idiopathic) Orbital Inflammation
  - Adult Onset Xanthogranuloma (AOX)
  - Necrobiotic Xanthogranuloma (NBX)
  - Adult Onset Asthma and Periocular Xanthogranuloma (AAPOX)
Iodiopathic Orbital Inflammation (IOI)

- Retrospective survey 1987-2012
  - Virchows Arch 2014;465 (Suppl 1):S43
- 73 cases of IOI over a 25 y period
- 10/73 = 13.7% proved to be IgG4-RD

- Other studies:
  - 5.4% 3/55 Br J Ophthalmol 2015;99:376–381
  - 27% 21/78 Pathology International 2008; 58: 465–470
  - 45.8% 11-24 Br J Ophthalmol 2015;99:1493–1497

Different criteria used!
23% of systemic IgG4-RD show orbital involvement

Third most frequent location after pancreas and lacrimal gland

May present as localized disease

It pays to review earlier biopsies of any organ involved
Eosinophilic Angiocentric Fibrosis

Rheumatology 2017;56:2245-2247
Eosinophilic Angiocentric Fibrosis

- Tumefactive lesion of the orbit and upper resp. tract

- Histopathological features:
  - Arterioles surrounded by a concentric layers of fibrosis
  - Mixed inflammatory cells
  - Eosinophils
  - Plasma cells

- Elevated IgG4 positive plasma cells >50/HPF
- IgG4/IgG ratio >0.40

Different stages of the disease have different morphology

- Necrosis, giant cells, and overt evidence of vasculitis as common in Wegeners’ disease often are not observed in EAF
Xanthogranulomas

- 16 cases of adult xanthogranulomas (over 25 years)
  - 8/16 cases elevated IgG4 plasma cells
- IgG4 related disease in AOX, AAPOX and NBX?
- No positive staining in ECD (n=2)
- No positive staining in JXG 0/20

Orbit 2014;33:17-22
IgG4 and xanthogranulomas

- Part of the IgG4-RD spectrum?
- Association?
- IgG4 also associated with other neoplasms
- Xanthogranulomas show recurrent BRAF/NRAS and other mutations
  - Not immune diseases but neoplastic
  - Low response rate to glucocorticoids
  - React very well to BRAF inhibitors
“We must conclude … that elevated levels of IgG4-positive plasma cells in orbital xanthogranulomatous disease occurs in 50% of the cases and when not accompanied by storiform fibrosis and/orobliterative phlebitis, is most likely not related to systemic IgG4-related disease.”

 Orbit 2014;33:17-22
Glucocorticoids 0.5-1 mg/kg/day: 89% response rate
  - High relapse rate

DMARD:
  - Rituximab 93% response rate
  - Others: 36-75% response rate
    - Metothrexate
    - Azathioprine
    - Mycophenolate mofetil
Questions?