IGG4-RELATED SYSTEMIC DISEASE: UNDER RECOGNIZED ENTITY

Muataz Yaziji[1], Riffat Jafrin[2], Sadia Abbasi[2], Monica P. Revelo[2], Nand Wadhwa[1]

[1]Stony Brook Medicine, Stony Brook, NY, and [2]University of Utah, Salt Lake City, Utah

Introduction

▪IgG4-related systemic disease (IgG4-RSD) is newly recognized conditions characterized by tumor-like masses in multiple organs with infiltrates of IgG4 positive plasma cells associated elevated serum IgG4. accompanied by fibrosis, and increased serum IgG4 concentrations. It has been described in nearly every organ, First recognized at autoimmune pancreatitis,

▪We report a case with IgG4-RSD with renal, CNS, ophthalmic, lacrimal and lung involvement where the diagnosis was delayed (30 day hospital stay) and misdiagnosed leading to treatment with anti TB medications.

Case Report

51-year-old female PMH of anemia p/w:

- severe diffuse headaches.
- progressively painless vision loss over 3 weeks.
- 10lb unintentional weight loss.
- Lightheadedness, nausea w/ associated vomiting.

▪Outpatient MRI/MRA of brain, showed b/l ICA aneurysm, for which she was referred to ED.

▪On examination he was afebrile, with blood pressure 140/80 mmHg, HR of 103, pupils not reactive to light, + swelling eyelids, unable to see Bright light perception. Reduced b/l upper and lower strength 2/5, reflexes nl.

▪On labs: Hb: 11.5 g/dL, WBC 19K/mm3 (80% n), plt count 607,000/mm3, Cr: 0.6 mg/dL, ESR 69

▪MRI brain w/o contrast showing interval enlargement of the pituitary gland with suprasellar extension and contact of the optic chiasm and bilateral enlargement of lacrimal glands.

▪CT head without contrast showed 3mm aneurysm of right ICA

▪Ophthalmology evaluation noted multiple subretinal infiltrates in the bilateral retina and serous retinal detachment,

▪MRI of the orbits/pituitary protocol showed irregularly-shaped leptomeningeal masses in the posterior cranial fossa, soft tissue mass in the right orbital apex.

▪LP (Day 2) showed CSF protein 64.4. LDH 128. WBC of 26 No lymphocytosis on differential, cytology negative.

▪NEGATIVE: JAK2 mutation, BCR/ABL, HIV, Hepatitis panel, EBV PCR (resulted 1st week) Flow Cytometry: Day 3: did not detect any immunophenotypes.

▪CT chest/abd/pel with contrast (day 6): Multiple small lung nodules bilaterally predominantly in the lung apices, left kidney enlarged with infiltrative appearance, multiple b/l solid-appearing small masses, Pelvis: Uterus is enlarged with multiple masses identified. No lymphadenopathy.

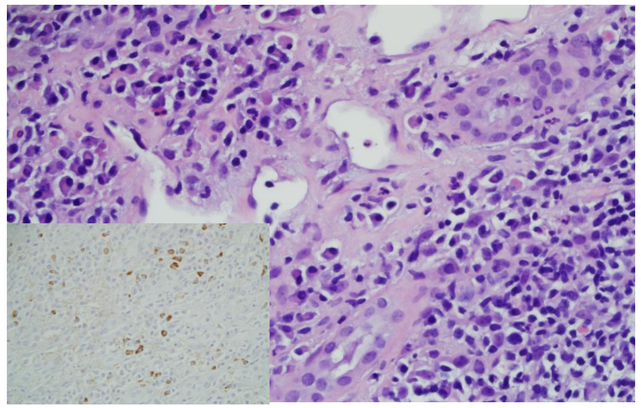
▪Rheumatology work up: NEGATIVE: ANA, dsDNA, C3, C4, SSA/B, Smith, RNP, UA, ANCA, Anti-MPO, Anti-PR3, anti-GBM

▪Lacrimal gland biopsy: Benign chronic inflammation. Acute inflammation involving ducts. Immunohistochemical staining demonstrated a mixed population of T and B cells.

▪Patient was treated with broad spectrum Abx ~ started day 14, All cultures and staining were negative, subsequently Abx d/ced at day 20.

▪Treatment: Patient started on Dexamethasone 4mg q8h on day 10 -> 30 for thalamic edema, Her vision improved, started on 4 drug regimen for treatment of latent TB (day 29)

▪Repeat read of kidney biopsy read: Marked interstitial inflammatory infiltrate with numerous IgG4 positive plasma cells, No significant glomerular abnormalities, Mild arteriolosclerosis. most consistent with IgG4-related tubulointerstitial nephritis.



▪Follow up: Switched to prednisone upon discharge with taper, TB treatment discontinue 1 week after discharge, Started on CellCept 1000 mg once a day 1 month after discharge

▪ F/u brain MRI (6 weeks after discharge) showed Interval resolution of previously seen masses bilateral thalamus and posterior limb of internal capsule. Stable sub-centimeter enhancing right intra coronal lesion abutting the optic nerve on the right.

▪ f/u CT chest and abdominal with IV contrast (8 wks after discharge) showed resolution of kidney masses and pulmonary masses.

▪Her eyesight has been improving steadily and she was able to walk independently

▪Her headache also improved

Discussion

▪IgG4-RD diagnosis can be challenging, because it has multiple clinical manifestations and a wide spectrum of differential diagnosis. The confirmation of diagnosis is based on histopathological findings of the affected organ with immunohistochemical staining, along with elevated serum IgG4 level.

▪Hallmarks of IgG4-RD are lymphoplasmacytic tissue infiltration of mainly IgG4-positive plasma cells and small lymphocytes, which may be accompanied by fibrosis, in the majority of patients, elevated serum levels of IgG4.

•This case report illustrates a common clinical situation of missed and delayed diagnosis of IgG4-RD. It also illustrates a unique presentation of IgG4-RSD with renal, CNS, ophthalmic, lacrimal and lung involvement.

▪Apart from that, as seen in this case the excellent short-term response to the therapy with glucocorticoid and MMF highlights the need to recognize IgG4-RD as treatment may lead to remission and prevent significant morbidity and mortality.

Stony Brook University