**Introduction**

IgG4 related disease (IgG4-RD) is often missed by clinicians. Recognition of the disease has recently started to improve although, the exact prevalence remains unclear.\(^1\) This disease still has not been assigned its own ICD 10 code. The lack of a code hinders epidemiologic studies. As an immune mediated fibroinflammatory condition, that can affect multiple organs, it can be categorized in several systems. It frequently masquerades as lympho-proliferative neoplasm, plasma cell dyscrasia or other autoimmune conditions. We describe a patient with this condition. His clinical presentation and disease course illustrate the challenges clinicians face in making the right diagnosis. This is followed by a brief review, highlighting clinical clues that can help direct us to the right diagnosis.

**Case History**

SF is a 78-year-old male presented initially with 5-10 lb. weight loss, eosinophilia and small peripheral adenopathy. He had diabetes mellitus, hypertension, and hyperlipidemia but otherwise had been active. CT scan showed 1-1.5 cm mediastinal adenopathy, subcentimeter submandibular and cervical nodes. SPEP showed monoclonal gammaglobulinemia, 0.7gm/dl. Bone marrow biopsy was unremarkable and submandibular gland aspirate revealed only sialadenitis. The patient was then lost to follow-up for one year.

During that time he developed bilateral lacrimal gland swelling and continued weight loss. He also noted progressive enlargement of submandibular glands and cervical adenopathy. Repeat CT PET scan showed diffuse hypermetabolism in lacrimal glands, cervical, submandibular, hilar and retroperitoneal nodes. Lacrimal gland biopsy by ophthalmology revealed granulomas with multinucleated giant cells. AFB and fungal stains and cultures were unremarkable. Excisional biopsy of his left submandibular gland showed features highly suggestive of IgG4 Related Disease: presence of extensive chronic lymphoplasmacytic inflammation with fibrosis of the submandibular gland, and marked increased IgG4 plasma cells. Repeat SPEP showed a band-like pattern in the upper gamma region consistent with IgG4. IgG4 level was elevated at 1245.

His clinical presentation including eosinophilia, hypergammaglobulinemia, swelling in lacrimal glands, salivary glands and lymph nodes, high IgG4 level with characteristic histopathology findings were diagnostic of IgG Related Disease.

Patient was started on prednisone 0.6mg per kg with gradual slow taper. He experienced excellent clinical response, with weight gain, and resolution of adenopathy, and lacrimal gland swelling. His IgG4 level decreased to 246 after 2 months. After 6 months treatment, his prednisone has been tapered to 2.5 gm daily and remains asymptomatic with complete resolution of lacrimal gland, lymph nodes and submandibular gland swelling.

**Discussion**

IgG4 related disease, is an immune related fibro-inflamatory disorder that could involve many different organ systems.\(^2\) Initial diagnosis could easily be missed by hematologists, as its clinical presentation tends to mimic lymphoproliferative disorders, plasma cell dyscrasia and/or autoimmune conditions.

As in our case the initial presentation of adenopathy, “monoclonal gammopathy” and eosinophilia lead to the impression of possible lymphoma.

Serum IgG4 typically runs in the fast gamma region on the serum protein electrophoresis, though typically polyclonal, high IgG4 levels can be mistaken as monoclonal gammopathy. Histologic diagnosis can also be misinterpreted if obtained with aspiration only.

As in our case only after excision biopsy of the submandibular gland and discussion with pathology, regarding possible IgG4RD, was the typical pattern identified. Repeat SPEP showed band like pattern in the upper gamma region consistent with IgG4, which was previously confused as M spike. Confirmatory IgG4 level was marked elevated. The subsequent response to steroids served to confirm the diagnosis.

It is useful to consider the clinical symptoms and presentations that could guide us to consider IgG4-RD. It is important to remember that IgG4-RD can affect almost any organ.\(^2\) The most recognizable forms include: autoimmune pancreatitis, orbital disease, salivary gland involvement and retroperitoneal fibrosis. Adenopathy is also common, present in 30-60% of patients in large series. Weight loss, present in 40-50%, may indicate exocrine pancreatitis from autoimmune pan-
In summary IgG4 RD is an important condition for clinicians, especially hematologists, to recognize. The presentation of adenopathy, weight loss, eosinophilia and hypergamma-globulinemia can lead to erroneous diagnosis of neoplastic disease. IgG subclass measurements can frequently guide us to the correct diagnosis. Confirmation requires histology, an adequate biopsy specimen and discussion with the pathologist.

Once the appropriate diagnosis is made, treatment response is frequently gratifying.

REFERENCES


2. Chen LYC, Mattman A, Seidman MA, Carruthers MN.

