**Title:** The Clinicopathological Spectrum of IgG4-Related Disease in North West London

**Background**

Immunoglobulin-G4 related disease (IgG4-RD) is a rare, multisystem fibro-inflammatory disorder, characterised by clinical evidence of tumefactive lesions with a raised serum IgG4 level and/or lymphoplasmacytic infiltrates with positive IgG4 immunostaining on histopathological specimens. IgG4-RD may present with variable symptoms which can masquerade as other conditions, presenting diagnostic and treatment challenges for a number of clinical specialties. Here, we report our multi-disciplinary experience of this complex disease in North West London.

**Methods**

We conducted a retrospective review of patients with IgG4-RD presenting to multiple medical specialties across North West London. IgG4-RD was defined in this population by the presence of IgG4-rich plasma cells in histopathological specimens and/or elevated serum IgG4 levels along with suggestive clinical features. Patients were identified through clinical and laboratory databases. Demographic, clinical, serological and histological data were recorded through a review of casenote and electronic reports.

**Results**

A total of 43 patients were identified, of which 39 fulfilled our inclusion criteria for IgG4-RD (median age at diagnosis: 59 years (IQR 25); 61.5% male). Four patients with presumed IgG4-RD were excluded due to insufficient data to support the diagnosis. Our cohort comprised a predominantly Asian population (53.8%), followed by Caucasians (30.8%) and Afro-Caribbeans (5%). 7 (18%) had a smoking history. 16 (44%) patients had a history of atopy (12 asthma, 9 rhinosinusitis, 2 eczema, 1 nasal polyps) while 9 had peripheral eosinophilia. While 3 patients had autoimmune disease unrelated to IgG4-RD (vitiligo, psoriasis and primary sclerosing cholangitis), autoantibodies were detected in 10 (32%) patients.

Pain was the predominant symptom on clinical presentation in 14 (36%), and 19 (49%) presented with constitutional symptoms such as weight loss, fever, anorexia and arthralgia. Serum IgG4 levels were elevated in 25 (64%) patients (mean = 4.78 gl-1, range: 0–25.1 gl-1) (NR <1.35 gl-1), and initial IgG4 levels correlated with the number of organ involvement (Pearson’s R = 0.416, p <0.05). The mean number of organs involved were 2.3 (range: 1–6), where the most common sites involved lymph nodes (13, 33%), kidneys (9, 23%), pancreas (9, 23%), lung (8, 21%), and pituitary (6, 15%). Of those who had renal dysfunction, 4 were attributed to obstructive retroperitoneal fibrosis and 4 had biopsy-proven tubulointerstitial nephritis. 32 (82%) patients had histopathological evidence of positive IgG4 staining plasma cells (mean IgG4/hpf = 50, IgG4/IgG ratio ranged from 20 to 75% where available) with the other common findings of lymphoplasmacytic infiltrates (83%), focal fibrosis (47%) and scattered eosinophilic infiltrates (17%). 3 specimens had granulomas identified on histology.

**Treatment and outcomes**

Corticosteroids formed the mainstay of treatment (n=31, 79%); with variable administration of adjuvant therapy (n=24, 62%) and interventional/surgical procedures (n=11, 28%). Of those who received steroid-sparing immunosuppressive therapy, 12 received rituximab, 8 azathioprine, 2 mycophenolate mofetil, 1 tacrolimus, 4 methotrexate, 1 sulfasalazine, and 1 hydroxychloroquine. Clinical outcomes are being prospectively evaluated to assess long-term treatment response.

**Conclusion**

Here, we report the characteristics of the first multi-ethnic population of patients with IgG4-RD in North West London. Our data are consistent with previous reports with respect to heterogeneity in clinical presentations and characteristics. This presents a number of challenges in the diagnosis and management of IgG4-RD. For these reasons, we would advocate a multi-disciplinary approach to the management of IgG4-RD in specialist tertiary referral centres.