IgG4-related disease in Israel: A retrospective, single-center cohort.

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Background: IgG4-related disease (IgG4-RD) is an increasingly recognized systemic fibro-inflammatory condition that can affect almost every organ system. Pathological hallmarks of the disease include lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis. Over the past decade, only a dozen of cohort studies has been published.

Aim: To characterize the clinical and pathological features as well as disease outcome of an Israeli incident cohort.

Methods: We conducted a retrospective single-center study between 2010 and 2020 to describe the characteristics, treatment, and outcome of IgG4RD. IgG4-RD was classified as 'definite', 'probable' or 'possible' according to international consensus guidelines and comprehensive diagnostic criteria for IgG4-RD or if patients fulfilled organ-specific criteria as well as the 2019 ACR/EULAR classification criteria. Disease activity was assessed by means of the IgG4-RD Responder Index (IgG4-RD RI). Baseline demographic, clinical, laboratory, imaging and histopathological features, as well as treatment and disease outcome were systematically retrieved from the electronic charts.

Results: Thirty-six consecutive patients (30.6% female) with a median age of 54.9 years were included in the study: 11 patients (30.56 %) with "definite", 10 patients (27.77) with possible, and 15 (41.67%) with "probable" IgG4RD, and 22 patients (61.1%) fulfilled the 2019 ACR/EULAR classification criteria. 19 patients (52.8%) had a single-organ disease, 8 patients (22.2%) had involvement of two organs, and 9 patients (25%) had 3 or more organs involved. The most involved organs were lymph nodes (36%) and retroperitoneal fibrosis (25%), followed by pancreas (16.7%), lacrimal or salivary glands (13.9%) liver and bile ducts (13.9%), and orbit (13.9%). The median follow-up was 28 months (IQR 13.2-40.7). Thirty-three patients (91.67%) had biopsies available for analysis. Lymphoplasmacytic infiltrate was found in 88.9%, fibrosis in 61.1%, and obliterative phlebitis in 11.1%. Thirty-four patients (94.4%) were treated with prednisone, whereas 38.9% were treated with methotrexate, 27.8% with azathioprine, 5.6% with mycophenolate mofetil and 47.2% with rituximab. The median IgG4-RD RI at the last encounter was 1.0 (IQR 0.0-2.0). Six patients died (16.7%) and

malignancy was diagnosed in 8 patients (22.2%) after the time of diagnosis of IgG4RD. At the time of charts review, sixteen patients (44.4%) were in remission after a median time of 16 months (IQR 6.0-30.0). Only two patients (5.6%) relapsed. Disease remission was associated with higher serum C3 level ($p=0.09$), lower ACR/EULAR criteria index at diagnosis ($p=0.01$), as well as lower IgG4-RD RI at the last encounter ($p<0.001$). Neither serum IgG4 level at diagnosis, nor type of organ involvement nor immunosuppressive/biologic drugs were associated with disease remission. Death ($p=0.03$) and malignancy ($p=0.01$) were negatively associated with remission.

Conclusion: This is the first descriptive study of an Israeli cohort of patients with IgG4RD that is in accordance with previous studies from other regions of the world.