

SUPPLEMENTARY TABLES

Supplementary Table 1. Number of cases with a serum IgG4 level above varying thresholds.

Serum IgG4 Threshold	n (%)
>1x ULN and \leq 2x ULN	2159 (6.7)
>2x ULN and \leq 3x ULN	475 (1.5)
>3x ULN and \leq 4x ULN	150 (0.5)
>4x ULN and \leq 5x ULN	57 (0.2)
>5x ULN and \leq 10x ULN	112 (0.3)
>10x ULN or above assay	86 (0.3)

ULN = upper limit of normal. A total of 32,206 cases had serum IgG subclasses tested between January 1, 2005 and January 1, 2021.

Supplementary Table 2. Characteristics of probable, atypical, and possible IgG4-RD cases.

	Total Cohort (n = 15)	Stanford Cohort (n = 4)	Mass General Brigham Cohort (n = 11)
Age, median [IQR]	67 [54, 71]	55 [46, 64]	68 [60, 71]
Sex, n (%)			
Female	8 (53)	2 (50)	6 (55)
Male	7 (47)	2 (50)	5 (45)
Race/Ethnicity, n (%)			
White	4 (27)	0 (0)	4 (36)
Black	1 (7)	0 (0)	1 (9)
Hispanic*	1 (7)	1 (25)	0 (0)
Asian	5 (33)	0 (0)	2 (18)
Unknown	3 (20)	3 (75)	3 (27)
Other	2 (13)	1 (25)	1 (9)
BMI, mean (SD)			
<25 kg/m ² , n (%)	6 (40)	2 (50)	4 (36)
25-29.9 kg/m ² , n (%)	5 (33)	0 (0)	5 (45)
≥30 kg/m ² , n (%)	4 (27)	2 (50)	2 (18)
Unknown, n (%)	0 (0)	0 (0)	0 (0)
Smoking, n (%)			
Never	9 (60)	3 (75)	6 (55)
Former	5 (33)	1 (25)	4 (36)
Current	0 (0)	0 (0)	0 (0)
Unknown	1 (7)	0 (0)	1 (9)
Atopic disease, n (%)	5 (33)	3 (75)	2 (18)
Sinusitis, n (%)	3 (20)	1 (25)	2 (18)
Receiving allergy immunotherapy, n (%)	0 (0)	0 (0)	0 (0)

IgG4 = immunoglobulin G4; ULN = upper limit of normal; IQR = interquartile range; BMI = body mass index.

*Ethnicity is recorded separately from race in the Stanford cohort, and thus cases may appear twice in this column.

Supplementary Table 3. Pathology findings for probable, atypical, and possible IgG4-RD cases.

Case	Classification	Total Points	Classification Features	Pathology Findings
Case 1	Atypical	N/A	Breast lesion with biopsy-proven IgG4-RD, serum IgG4 > 5x ULN.	Breast biopsy with dense fibroinflammatory infiltrate with elevated IgG4+ plasma cells.
Case 2	Atypical	N/A	Mesentery and breast mass, both biopsied and consistent with IgG4-RD, serum IgG4 > 5x ULN.	Mesenteric mass and L axillary lymph node. Biopsy showed elevated IgG4+ plasma cells and fibrosis.
Case 3	Possible	15	Lymph node with supportive features, serum IgG4 > 5x ULN.	L iliac lymph node biopsy showed reactive follicular hyperplasia with numerous IgG4+ plasma cells.
Case 4	Possible	15	Lymph node with supportive features, serum IgG4 > 5x ULN.	L supraclavicular lymph node showed sinus histiocytosis and increased IgG4+ plasma cells.
Case 5	Possible	15	Lymph node with supportive features, serum IgG4 > 5x ULN.	L cervical lymph node showed follicular hyperplasia, capsular fibrosis, and increased IgG4+ plasma cells.
Case 6	Probable	15	Lacrimal gland enlargement with lymphoplasmacytic infiltrate (4 points) and serum IgG4 > 5x ULN.	R lacrimal gland showed few IgG4+ plasma cells.
Case 7	Probable	15	Remote history of pancreatitis (pathology unavailable). Pharyngeal mass. Lymphadenopathy with fibrosis, lymphoplasmacytic infiltrate. Serum IgG4 > 5x ULN.	R submandibular lymph node showed reactive follicular and paracortical lymphoid hyperplasia with increased IgG4+ plasma cells.
Case 8	Probable	17	Bilateral lacrimal gland enlargement with serum IgG4 > 5x ULN.	Right axillary lymph node showed reactive lymphoid hyperplasia.
Case 9	Probable	11	Pancreas biopsy with chronic pancreatitis and atrophy, CT with biliary strictures, serum IgG4 > 5x ULN.	Pancreas biopsy showed chronic pancreatitis with atrophy, no tumor seen. Bile duct with no tumor seen. Gallbladder with acute and chronic inflammation. Liver with portal inflammation and bile duct proliferation.
Case 10	Probable	19	CT showed renal pelvis thickening and soft tissue, serum IgG4 > 5x ULN.	Kidney biopsy showed features of membranous nephropathy.
Case 11	Probable	19	Clinical pancreatitis with diffuse pancreatic enlargement on CT and serum IgG4 > 5x ULN.	No pathology.
Case 12	Probable	19	Marked periaortic and periliac stranding which extends to involve the mesentery and retroperitoneum in the abdomen and serum IgG4 > 5x ULN.	No pathology.
Case 13	Probable	11	Pulmonary mass with serum IgG4 > 5x ULN, never biopsied, then developed large coronary aneurysms.	No pathology.
Case 14	Probable	19	Classic retroperitoneal fibrosis with circumferential soft tissue around the infrarenal aorta and serum IgG4 > 5x ULN.	No pathology.
Case 15	Probable	17	Bilateral lacrimal gland enlargement with serum IgG4 > 5x ULN.	No pathology.

IgG4 = immunoglobulin G4; IgG4-RD = IgG4-related disease.

Supplementary Table 4. Characteristics of IgG4-RD cases with a serum IgG4 level >5x ULN.

IgG4-RD Patient Characteristics	n (%)
Age, median [IQR]	67 [57, 75]
Sex, n (%)	
Female	36 (25)
Male	108 (75)
Race/Ethnicity, n (%)	
White	79 (54.9)
Black	8 (5.6)
Hispanic*	7 (4.9)
Asian	38 (26.4)
Unknown	8 (5.6)
Other	9 (6.3)
BMI, mean (SD)	26.8 (5.8)
Number of organs involved, median [IQR]	3 [2.0, 4.0]
Single-organ involvement**	16 (11.1)
Multi-organ involvement	128 (88.9)
Lacrimal gland	48 (33.8)
Salivary gland	71 (50.0)
Orbital	25 (17.6)
Pancreas	73 (51.4)
Biliary	34 (23.9)
Liver	14 (9.9)
Renal	44 (31.0)
Retroperitoneal fibrosis	13 (9.2)
Aorta/large vessel	9 (6.3)
Total IgG, elevated (n = 105)	93 (88.6)
IgG1, elevated (n = 130)	54 (41.5)
IgG2, elevated (n = 132)	49 (37.1)
IgG3, elevated (n = 130)	39 (30.0)
IgE, elevated (n = 84)	65 (77.4)
AEC, above 500 k/uL (n = 111)	43 (38.7)
ESR, elevated (n = 81)	52 (64.2)
CRP, elevated (n = 80)	31 (38.8)
SPEP or UPEP, abnormal (n = 63)	6 (9.5)
Kappa:lambda FLC ratio, elevated (n = 33)	18 (54.5)

ULN = upper limit of normal; IgG4 = immunoglobulin G4; IgG4-RD = IgG4-related disease;

IQR = interquartile range; IgE = immunoglobulin E; AEC = absolute eosinophil count;

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; SPEP = serum protein electrophoresis;

UPEP = urine protein electrophoresis; FLC = free light chain.

*Ethnicity is recorded separately from race in the Stanford cohort, and thus cases may appear twice in this column.

**Single-organ involvement included: pancreas (5), lacrimal gland (2), renal (2), pulmonary (2), lymphadenopathy (2), paraspinal mass (1), breast (1), prostate (1).