Table 1. Clinical profiles of the 31 patients with IgG4-RD

Demographics:	
Age, yrs; average ± SD	67.0 ± 8.0
Males:females	21:10
Affected organs:	
Pancreas	23 (74.2%)
Salivary/lacrimal gland	12 (38.1%)
Lung	11 (35.4%)
Retroperitoneum	8 (25.8%)
Kidney	7 (22.5%)
Upper portion of extrahepatic bile duct	5 (16.1%)
Lymph node	5 (16.1%)
Pituitary gland	3 (9.6%)
Orbit	2 (6.4%)
Prostate	2 (6.4%)
Breast, mediastinum, mesentery, stomach	1 each (3.2%)
Numbers of affected organs:	
1	11 (35.4%)
2	5 (16.1%)
3	7 (19.3%)
4	3 (9.6%)
5	2 (6.4%)
6	3 (9.6%)
Serum IgG4 levels at diagnosis:	30 (96.7%)
≥135 mg/dL	24/30 (80%)
<135 mg/dL	6/30 (20%)
Corticosteroid administration:	
Never treated	25 (80.6%)
Receiving treatment	4
After the first biopsy	2
Number of biopsies or endoscopic resections in each patient	(total 53 specimens)
1	22
2	5
3	1
4	1
7	2

SD, standard deviation

Table 2. IgG4-positive plasma cells, *HP*, and corticosteroid therapy status by inflammatory patterns

	Inflammatory patterns				Total (31)
	BHP (9 cases)	Transmural (14 cases)	Superficial (2 cases)	Minimal (6 cases)	
IgG4-IHC					
High	6 (66%)	4 (28.5%)	0	0	10
Low	1 (11%)	8 (57.1%)	0	6 (100%)	15
Insufficient	2 (22%)	2 (14.2%)	2 (100%)	0	6
HP status					
Positive	2 (22%)	11 (78.5%)	0	1 (16.7%)	14
Negative	7 (78%)	2 (14.2%)	2 (100%)	5 (83.3%)	16
Unknown	0	1 (7.1%)	0	0	1
Corticosteroid administration					
Never treated	7 (78%)	12 (85.7%)	1 (50%)	5 (83.3%)	25
Receiving treatment	1 (11%)	1 (7.1%)	1 (50%)	1 (16.7%)	4
After the first biopsy	1 (11%)	1 (7.1%)	0	0	2

BHP, bottom-heavy plasmacytosis; IHC, immunohistochemistry; *HP*, *Helicobacter pylori*

Table 3. IgG4-high cases

Case	Age at diagnosis of IgG4-RD /Sex	Affected organs	Duration of disease before biopsy (months)	Corticosteroid administration	Serum IgG4 level at biopsy (mg/dL)	Biopsy site and endoscopic findings	*HP* status	Inflammatory pattern	Number of IgG4-plasma cells			IgG4/IgG-positive ratio (%)	Number of eosinophils (/HPF)
									S (/20000 μm^2)	D (/20000 μm^2)	(/HPF)§		
1	61/M	LN, Panc, BD, RP, Lung, Mes	4	After the biopsy	3680	GB/RB of normal mucosa	-	BHP	0	16	70	64.2	19
2	60/M	LN, Lung, Panc	0	Never	1100	GB/Ulcer scar Angle and antrum/ Erosion	-	BHP	11	‡	54	81.8	68
3	72/F	Kid	0	Never	817	Antrum/Ulcer scar	-	BHP partly transmural	0	‡	72	100	59
4	68/F	Panc	0	Never	507	GB/Erosion	-	BHP	0	15	60	109	86
5	48/F	SG/LG, Panc, Breast, Kid	1	Never	564	GB/Red spot	-	BHP	0	‡	42	53.1	62
6	70/F	Panc	4	Never	791	GB/RB of non-tumoral mucosa	+	BHP	3	49	37	92.5	15
7	59/F	Panc, SG/LG, Lung	0	Never	667	RB of atrophic gastritis	+	Transmural	‡	‡	13	44.8	53

8	78/M	Lung, Kid, LN	8	Never	703	GB/RB of normal mucosa Fornix/SMT	+	Transmural	0	13	69	127.7	50
9†	77/M	Stomach	-2	Never	936	GB/RB of non-tumoral mucosa	+	Transmural	3	10	59	62	
			-1		936	GB/Erosion and RB of non-tumoral mucosa	+	Transmural	2	16	71	82.5	63
10	71/M	Panc, BD, SG/LG, Lung, PG, Prostate	0	Never	1170	GB/Elevation with redness	+	Transmural	0	6	21	51.2	31

†, Each of two gastric biopsies that fulfilled criteria are indicated for case 9.
‡, Immunostaining was insufficient at the applicable area.
§, Area per high-power field is about 344,716 μm^2 (the ocular field number of objective lens is 26.5).
BD, bile duct; BHP, bottom-heavy plasmacytosis; D, deeper portion of the mucosal lamina propria; GB, gastric body; *HP*, *Helicobacter pylori*; HPF, high-power field; Kid, kidney; LN, lymph node; Mes, mesentery; Panc, pancreas; PG, pituitary gland; RB, random biopsy; RP, retroperitoneum; S, superficial portion of the mucosal lamina propria; SG/LG, salivary gland/lacrimal gland; SMT, submucosal tumor

Table 4. Cases that revealed BHP in the routine gastric biopsy series

	Age/Sex	Clinical indication of endoscopy	Endoscopic finding	Histological finding	*HP* infection	PH	IgG4+PCs (/HPF)	IgG4/IgG-positive ratio (%)	Eosinophils (/HPF)
R1	77/M	GI bleeding	Ulcer	necrosis, neutrophils	+	HT, COPD	0	0	80
R2	83/F	Chronic gastritis, ulcer follow up	Red spot	granulation, neutrophils	PE	DLBCL	0	0	32
R3	45/F	Upper abdominal pain	Erosions and ulcers	granulation, neutrophils, cytomegalovirus infection	+		41	45.5	52
R4	64/F	Chronic gastritis, follow up	Erosion and ulcers	granulation, neutrophils	+	FL	2	3.0	26
R5	47/F	Chronic gastritis, follow up	Red spot	intestinal metaplasia, atrophy	PE		0	0	78

COPD, chronic obstructive pulmonary disease; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; GI, gastrointestinal tract; *HP*, *Helicobacter pylori*; HT, hypertension; IgG4+PCs, IgG4-positive plasma cells; PE, post-eradication; PH, past history

Figure legends

Figure 1. IgG4-high cases. (a) Bottom-heavy plasmacytosis (BHP): Numerous plasma cells were observed on the muscularis mucosae but not under the foveola. Eosinophilic infiltration was marked (case 4). (b) Numerous IgG4-positive plasma cells were identified at the deeper area. (c) Transmural inflammation: Plasma cells were numerous both on the muscularis propria and under the foveola. (d) IgG4 stain highlighting the BHP pattern. The sub-foveolar area was spared. (e) Lymphoplasmacytic infiltration involving the muscularis mucosae. Plasma cell aggregation was evident between the smooth muscle cells. Eosinophilic infiltration was observed (case 6). (f) Plasma cells were permeating between the non-atrophic fundic glands without much destruction of the glands. Eosinophilic infiltration was observed (case 8). ((a) (c) (e) (f): Hematoxylin and eosin stain, (b) (d): IgG4)

Figure 2. (a) Transmural inflammation (IgG4-low case): Intraepithelial infiltration of neutrophils was characteristic for active chronic gastritis. (b) IgG4-positive plasma cells were rarely detected. (c) Superficial inflammation: Plasma cells were numerous at the superficial part but not on the muscularis mucosa. (d) IgG4-positive plasma cells were not detected. ((a) (c): Hematoxylin and eosin stain, (b) (d): IgG4)

Figure 3. Routine gastric biopsy case with BHP pattern. (a) Gastric mucosa with granulation incorporated with lymphoplasmacytic infiltration. Plasma cell aggregation in the deeper portion was regarded as BHP. Neutrophils were also intermingled. (b) IgG4-positive cells revealed a patchy distribution. There were more than 10 IgG4-positive cells/HPF, and the IgG4/IgG-positive ratio was over 40% at this spot. (c) IgG-positive

plasma cells displaying diffuse infiltration. ((a): Hematoxylin and eosin statin, (b): IgG4, (c): IgG)

Supplementary Table 1. IgG4-low cases

Case	Age at diagnosis of IgG4-RD/Sex	Affected organs	Duration of disease before biopsy	Corticosteroid administration	Serum IgG4 level at biopsy (mg/dL)	Biopsy site and endoscopic findings	*HP* status	Inflammatory pattern	Number of IgG4-plasma cells			IgG4/IgG-positive ratio (%)	Number of eosinophils (/HPF)
									S (/20000 μm^2)	D (/20000 μm^2)	(/HPF) ‡		
L1	76/M	Kid, LN	147	Receiving	396	Antrum/Depression with redness Fornix/SMT	+	BHP partly transmural	5	†	12	30.7	67
L2	64/M	Panc	-14	Never		Angle/Elevation with redness	+	Transmural	2	5	9	34.6	Artifact
L3	67/M	BD, Panc, RP	3	After the biopsy	111	Antrum/ Depression with redness GB/Flat elevation GB/SMT	-	Transmural	0	0	0	0	33

L4	71/M	Panc	0	Never	36	Fornix/Depression	-	Transmural	0	0	8	13.1	32
L5	59/M	Panc	-104	Never		Antrum/Red spot	+	Transmural	0	0	0	0	20
L6	77/F	Panc, BD	-82	Never		Angle/Elevation GB/Polyp	+	Transmural	0	0	2	3.5	36
L7	76/M	Panc	-41	Never		GB/ESD scar	+	Transmural	0	†	1	14.2	42
L8	76/F	Panc, SG/LG, Lung, RP	0	Never	698	RB of atrophic gastritis	+	Transmural	0	3	3	10	37
L9	62/M	Orbit	6	Receiving	137	RB of atrophic gastritis	+	Transmural	0	0	0	0	37
L10	61/F	Panc, SG/LG	42	Receiving	24.4	Cardia/Hyperplastic polyp	-	Minimal	0	†	0	0	12
L11	54/M	RP	0	Never	113	Antrum/Depression with	-	Minimal	0	†	0	0	Artifact

						redness							
L12	68/M	Panc, BD	2	Never	339	Antrum/Erosion	-	Minimal	0	†	0	0	0
L13	74/M	Panc, RP, SG/LG	0	Never	1100	GB/Polyp with redness	-	Minimal	1	†	6	300	1
L14	67/M	Panc, LN	7	Never	69.5	Angle/Elevation with redness Antrum/Depression with redness	+	Minimal	0	0	0	0	29
L15	69/F	Kid	-22	Never		Antrum and cardia/Erosion	-	Minimal	0	†	0	0	3

†, Immunostaining was insufficient at the deeper area.

‡, Area per high power field is about 344716 μm^2 (the field number of objective lens is 26.5).

BD, bile duct; BHP, bottom-heavy plasmacytosis; D, deeper portion of the mucosal lamina propria; ESD, endoscopic submucosal dissection; GB, gastric body; *HP*, *Helicobacter pylori*; HPF, high power field; Kid, kidney; LN, lymph node; Panc, pancreas; RB,

random biopsy; RP, retroperitoneum; S, superficial portion of the mucosal lamina propria; SG/LG, salivary gland/lacrimal gland; SMT, submucosal tumor