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Original article

Clinical characteristics of immunoglobulin G4–related disease: a prospective study of 118 Chinese patients

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Abstract

Objective. To characterize the clinical features of IgG4-related disease (IgG4-RD) in China.

Methods. A prospective cohort study of IgG4-RD was carried out in Peking Union Medical College Hospital between 2011 and 2013. Patients with newly diagnosed IgG4-RD were enrolled.

Results. A total of 118 patients with IgG4-RD were enrolled, including 82 males and 36 females, aged 53.1 (S.D. 13.6) years. The most common symptom at onset was lacrimal gland swelling (38/32.2%). A range of organs were involved: 77 patients (65.3%) had lymphadenopathy, 76 (64.4%) had sialadenitis, 60 (50.8%) had dacryoadenitis, 45 (38.1%) had autoimmune pancreatitis, 32 (27.1%) had pulmonary involvement, 31 (26.3%) had periaortitis/retroperitoneal fibrosis, 29 (35.4% of male patients) had prostatitis and 29 (24.6%) had renal involvement. In addition, there were 21 (17.8%) cases of sclerosing cholangitis, 15 (12.7%) of sinusitis and 10 (8.5%) of inflammatory pseudotumour. Uncommon manifestations included mediastinal fibrosis, skin involvement, sclerosing thyroiditis, hypophysitis, orchitis and colitis. Multiple organ involvement was observed in 93 patients, whereas only 4.2% had only a single organ involved. A history of allergy was reported in 73 (61.9%) patients. The serum IgG4 level was elevated in 97.5% and was correlated with the number of organs involved. Most patients were treated with glucocorticoids alone or in combination with immunosuppressive drugs, and the majority usually improved within 3 months.

Conclusion. IgG4-RD is a systemic inflammatory and sclerosing disease. Parotid and lacrimal involvement (formerly called Mikulicz's disease), lymphadenopathy and pancreatitis are the most common manifestations. Patients with IgG4-RD showed favourable responses to treatment with glucocorticoids and immunosuppressive agents.

Key words: IgG4-related disease, autoimmune pancreatitis, Mikulicz's disease, prospective cohort, IgG4.

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CLINICAL SCIENCE

Rheumatology key messages

- IgG4-related disease is a systemic inflammatory and sclerosing disease with multiple organ involvements.
- Salivary glands, pancreas and lymph nodes are the most commonly affected organs in IgG4-related disease.
- Patients with IgG4-related disease showed favourable response to glucocorticoid and immunosuppressive agents.

Introduction

IgG4-related disease (IgG4-RD) is a newly recognized entity characterized by tumour-like swelling in multiple sites caused by lymphoplasmacytic infiltration and sclerosis, and is associated with elevated serum IgG4 levels and infiltration of IgG4-positive plasma cells in the organs and tissues involved [1–4].

The association of increased serum IgG4 levels with this condition was initially suggested by its presence in patients with sclerosing pancreatitis [5]. IgG4-RD was proposed as a systemic condition in 2003 [6] and as a distinct clinical entity in 2010 [7]. Patients with IgG4-RD show various clinical symptoms, depending on which organs are affected. IgG4-RD mainly affects the salivary and lacrimal glands, with the clinical phenotype formerly referred to as Mikulicz's disease [8], and the pancreas, manifesting as autoimmune pancreatitis (AIP) [9]. In the past decade, the number of target organs of IgG4-RD has expanded considerably, and the disease spectrum now not only includes the salivary glands, lacrimal glands, pancreas, parotid glands, lymph nodes, lung, and kidney, but also the thyroid gland, bile ducts, retroperitoneum, skin and pituitary gland [10–21]. In addition, a history of allergic disease is one of the clinical features of this disease.

Most of the descriptions of IgG4-RD have been reported from Japanese and Caucasian populations. Recently, we reported 28 Chinese patients who fulfilled the 2011 comprehensive diagnostic criteria for definite IgG4-RD (probable and possible IgG4-RD patients were not included) [22]. This preliminary evaluation initially characterized the clinical spectrum of IgG4-RD patients in China [23]. As the tertiary referral centre in China, Peking Union Medical College Hospital (PUMCH) has evaluated many newly diagnosed IgG4-RD patients nationwide in the past 2 years. To define the characteristics of Chinese patients with IgG4-RD more completely, we investigated the clinical, laboratory and histological characteristics of this prospective cohort of 118 cases of IgG4-RD.

Patients and methods

Patients

A prospective cohort study of IgG4-RD patients was conducted in PUMCH from January 2011 to December 2013. Newly diagnosed IgG4-RD patients were recruited from throughout China.

Patients with definite, probable or possible IgG4-RD according to the 2011 comprehensive diagnostic criteria for IgG4-RD [22] were recruited. Briefly, definite IgG4-RD must have the following: (i) organ enlargement, mass or nodular lesions, or organ dysfunction; (ii) a serum IgG4 concentration >135 mg/dl; and (iii) histopathological findings of >10 IgG4$^+$ cells per high power field (/HPF) and an IgG4$^+$/IgG$^+$ cell ratio of $>40\%$. Possible IgG4-RD required (i) and (ii), but with negative results on histopathology or without histopathological examination. Probable IgG4-RD required (i) and (iii), but without increased serum IgG4. Patients with malignancy or other autoimmune diseases were excluded. Demographic data, initial symptoms, disease duration, history of allergy and physical examination were recorded. This study was approved by the Medical Ethics Committee of PUMCH (Beijing, China). All patients signed informed consent forms.

Laboratory tests, imaging studies and histological examination

Complete blood count, liver and renal function tests, ESR, CRP, serum Ig level, IgG subclasses, total IgE level, complement and autoantibodies (including RF and ANAs) were tested.

All patients underwent imaging examinations, including ultrasonography, CT or MRI; ^{18}F-fluorodexoyglucose PET/CT (^{18}F-FDG PET/CT) was performed in some patients.

Sixty-eight patients underwent tissue biopsies. Samples were stained with haematoxylin and eosin. Antibodies against CD3, CD20, CD138, CD38, IgG and IgG4 were used for immunohistochemical staining.

Statistical analysis

All parameters are described in the standard summary statistics, including mean, S.D., minimum and maximum. Comparisons between groups were performed using the chi-square or Fisher's exact test. The correlations of serum IgG4 levels and various parameters were analysed by Pearson's rank test. All statistical analyses were performed by SPSS version 17.0 (SPSS, Chicago, IL, USA) and GraphPad Prism software version 5.0 (Graph-Pad, San Diego, CA, USA). A P-value < 0.05 was considered statistically significant.

Results

Patient demographic characteristics

A total of 118 IgG4-RD patients, 82 males and 36 females (M: F 2.3:1), were enrolled in this prospective cohort study between January 2011 and December 2013. The mean age at diagnosis was 53.1 (13.6) years, ranging from 19 to 80, and mean disease duration was 26.8 (35.0) months. According to the 2011 comprehensive diagnostic criteria for IgG4-RD, 64 (54.2%), 3 (2.5%) and 51 (43.2%) cases were diagnosed as definite, probable and possible IgG4-RD, respectively.

Clinical manifestations

The most common initial presentation was lacrimal gland swelling (32.2%), followed by submandibular gland swelling (23.7%), and abdominal pain (19.5%). Less common manifestations at onset included parotid gland swelling (9.3%), enlarged lymph nodes (8.5%), jaundice (7.6%), low back pain (7.6%), nasal congestion (2.5%), and nausea and vomiting (1.7%). Throughout the disease course, 63 (53.4%) patients experienced salivary gland swelling, 59 (50%) patients exhibited lacrimal gland swelling, 62 (52.5%) developed lymphadenopathy, 45 (38.1%) had abdominal pain, 27 (22.9%) had parotid gland swelling, 24 (20.3%) had nausea and vomiting, 23 (19.5%) had a cough, 19 (16.1%) had jaundice, and 15 (12.7%) had low back pain. Notably, as many as 73 (61.9%) patients reported a history of allergy, including 33 (45.2%) with allergic rhinitis or asthma, 24 (32.9%) with allergic reactions to drugs, 10 (13.7%) with skin sensitivity or urticaria, and 6 with food allergy.

Organ involvement

Organ involvement was evaluated by symptoms, signs, radiographic or other imaging examination or tissue biopsies. The majority of patients ($n = 93$, 78.8%) manifested involvement of more than two organs, including 9 (7.6%) patients with more than seven involved organs; only 4.2% ($n = 5$) had only one organ involved. Throughout the course of IgG4-RD, lymphadenopathy was the most common manifestation, present in 77 (65.3%) patients; sialadenitis and dacryoadenitis occurred in 76 (64.4%) and 60 (50.8%) patients, respectively. In addition, there were 45 (38.1%) patients with AIP, 31 (26.3%) with periaortitis/retroperitoneal fibrosis, 29% (35.4 of male patients) with prostatitis, 32 (27.1%) with pulmonary involvement, 29 (24.6%) with kidney disease and 21 (17.8%) with sclerosing cholangitis. Less common manifestations included sinusitis (15/12.7%), inflammatory pseudotumour (10/8.5%), skin involvement (5/4.2%), mediastinal fibrosis (4/3.4%), thyroiditis (2/1.7%), hypophysitis (2/1.7%), orchitis (1/1.3% of male patients) and colitis (1/0.8%).

Compared with reports from other groups, as shown in Table 1, IgG4-RD patients in this cohort presented with a wider disease spectrum. The prevalence of dacryoadenitis was significantly higher in this study than in the French and Japanese [24, 25] groups (50.8% *vs* 12% and 12.3%, respectively). Lymphadenopathy, sialadenitis as well as AIP and prostatitis were significantly more common in our study than in the Japanese cohort (65.3% *vs* 41.2%, 64.4% *vs* 34.2%, 38.1 *vs* 24.6%, respectively), whereas, lymphadenopathy, sialadenitis and AIP were comparable to the French cohort (65.3% *vs* 76%, 64.4% *vs* 44%, 38.1% *vs* 52%, respectively). Renal involvement was rarer in our group than in the French cohort (24.6% *vs* 44%), but more common than in Japanese cases (24.6% *vs* 8.8%). Pulmonary involvement was comparable between the three groups. An allergic history was more common in this study than in the other two studies (61.9% *vs* 24% and 19.3%).

Laboratory findings

The mean baseline ESR, CRP, serum IgG level, total IgE level and serum IgG4 level were all elevated in this group [38.5 (31.5) mm/h, 6.6 (11.2) mg/l, 23.0 (10.1) g/l, 784.2 (1053.0) KU/l and 1521.8 (1678.5) mg/dl, respectively]. At entry into the study, 74 patients (62.7%) had an elevated ESR, 52 patients (44.1%) had an elevated CRP level, 79 patients (66.9%) had an increased serum IgG level and 65/72 patients (88.9%) exhibited an increase in IgE. Notably, among 118 patients, only 3 cases (2.5%) had a normal IgG4 level. Low titre ANAs were detected in 13 patients, none of whom was positive for anti-extractable nuclear antibodies. Table 2 shows the baseline laboratory findings for the group of IgG4-RD patients.

Histopathological features

Sixty-eight patients underwent tissue analysis, including biopsies of lachrymal gland, salivary gland, lymph node, paranasal sinus, kidney, lung, retroperitoneal tissue, brain and pancreas.

Of these, 64 patients fulfilled the pathological diagnostic criteria of IgG4-RD. The most common findings were lymphocytic and plasma cell infiltration (100%). Ectopic germinal centre formation and fibrosis/sclerosis were documented in 15.6% ($n = 10$) and 67.2% ($n = 43$) of samples, respectively. In some patients with AIP, obliterative phlebitis was observed as well. The characteristic histopathological finding was infiltration of $IgG4^+$ plasma cells ($IgG4^+$ plasma cells/IgG^+ plasma cells $>40\%$ and/or >10 $IgG4^+$ plasma cells/HPF in organ biopsies, and $IgG4^+$ plasma cells/IgG^+ plasma cells $>40\%$ and/or >50 $IgG4^+$ plasma cells/HPF for lymph nodes). Fig. 1 illustrates typical histological features of IgG4 patients.

Imaging study

The typical imaging of IgG4-RD patients demonstrates organ enlargement of involved tissues (Fig. 2). Lacrimal and salivary gland enlargement were commonly observed (Fig. 2A and B). Diffuse soft tissue occupying the paranasal sinuses and/or nasal polyps were routinely seen in patients with chronic sinusitis (Fig. 2D). Radiological findings in the lung included honey-combing or ground-glass opacification, pulmonary nodules, bronchovascular thickening (Fig. 2G–I) and pleural nodules (Fig. 2J). Typical features of AIP were local or diffuse pancreatic gland enlargement (Fig. 2K), occasionally with pseudocyst formation (Fig. 2L). Gall bladder enlargement and bile duct dilatation or thickening was seen in patients with sclerosing cholangitis (Fig. 2M). Diffuse kidney swelling and peripheral cortical nodules of the kidney were found in IgG4-related kidney disease (Fig. 2N and Q). Retroperitoneal tissue involvement was found with soft tissue lesions surrounding the aorta or masses around the ureters (Fig. 2N and O). Other patterns of organ involvement included prostate swelling (Fig. 2R) and swelling of the pituitary stalk (Fig. 2F).

Table 1 Comparison of clinical features in different studies

	Current Cohort ($n = 118$)	French Study ($n = 25$)	Japanese Study ($n = 114$)	*P*-value[a]	*P*-value[b]
Age, mean (range), years	53.1 (19–80)	58.1 (24–83)	64 (42–79)	–	–
Men/women, *n* (%)	2.3:1	2.6:1	3.2:1	0.804	0.243
Organ involvement, *n* (%)					
Dacryoadenitis	60 (50.8)	3 (12	14 (12.3)	<0.001	<0.001
Lymphadenopathy	77 (65.3)	19 (76)	47 (41.2)	0.299	<0.001
Sialadenitis	76 (64.4)	11 (44)	39 (34.2)	0.058	<0.001
Autoimmune pancreatitis	45 (38.1)	13 (52)	28 (24.6)	0.200	0.026
Sclerosing cholangitis	21 (17.8)	8 (32)	33 (28.9)	0.109	0.045
Prostatitis	29 (35.4)	–	1 (1.1)	–	<0.001
Retroperitoneal fibrosis/periaortitis	31 (26.3)	14 (56)	23 (20.2)	0.004	0.272
Inflammatory pseudotumour	10 (8.5)	4 (16)	–	0.250	–
Interstitial nephritis	29 (24.6)	11 (44)	10 (8.8)	0.049	0.001
Mediastinal fibrosis	4 (3.4)	–	1 (0.9)	–	0.188
Pulmonary involvement	32 (27.1)	3 (12)	26 (22.8)	0.110	0.448
Skin involvement	5 (4.2)	–	–	–	–
Sinusitis	15 (12.7)	–	–	–	–
Thyroiditis	2 (1.7)	–	–	–	–
Hypophysitis	2 (1.7)	2 (8)	–	0.082	–
Orchitis	1 (1.3)	–	–	–	–
Colitis	1 (0.8)	–	–	–	–
Allergic history, *n* (%)	73 (61.9)	6 (24)	22 (19.3)	0.001	<0.001

[a]Current study *vs* French study; [b]Current study *vs* Japanese study.

Table 2 Baseline laboratory findings in patients with IgG4-RD ($n = 118$)

Parameter	Value
Eosinophilia, *n* (%)	40 (33.9)
Eosinophils, mean (S.D.), %	5.4 (7.0)
ESR, mean (S.D.), mm/1 h	38.5 (31.5)
Elevated ESR, *n*/%	74/62.7
CRP, mean (S.D.), mg/l	6.6 (11.2)
Elevated CRP, *n* (%)	52 (44.1)
IgG, mean (S.D.), g/l	23.0 (10.1)
Elevated IgG, *n* (%)	79 (66.9)
IgA, g/l, mean (S.D.)	2.0 (1.0)
IgM, mean (S.D.), g/l	1.0 (0.6)
IgE, mean (S.D.), KU/l	784.2 (1053.0)
Percentage elevated IgE[a]	88.9% (65/72)
IgG1, mean (S.D.), mg/dl	957.7 (494.8)
IgG2, mean (S.D.), mg/dl	597.1 (360.5)
IgG3, mean (S.D.), mg/dl	75.6 (68.9)
IgG4, mean (S.D.), mg/dl	1521.8 (1678.5)
IgG4/IgG, mean (S.D.), %	38.2 (21.8)
Normal IgG4, *n* (%)	3 (2.5)
ANA (+), *n* (%)	13 (11.0)

[a]Seventy-two patients were tested for serum IgE at baseline.

Correlation of serum IgG4 levels with clinical and laboratory parameters

Since IgG4-RD is characterized by elevated serum IgG4 levels, we analysed the relationships of the baseline serum IgG4 level with clinical features (illustrated in Fig. 3A).

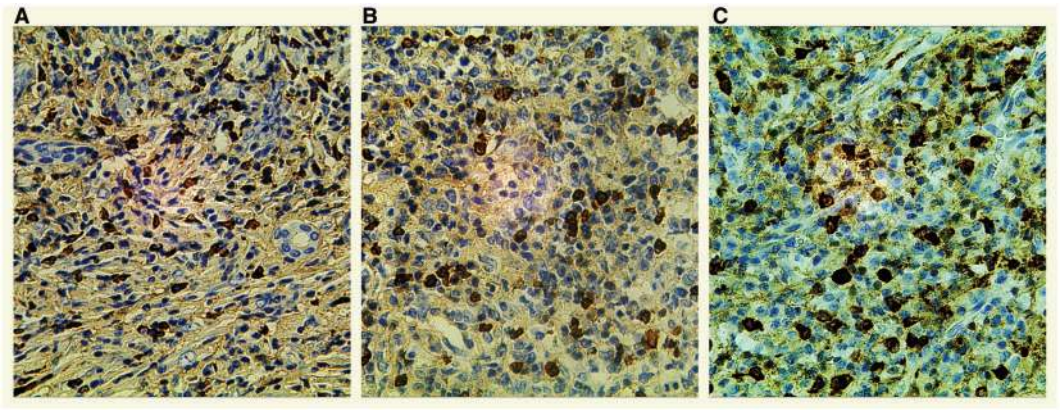
Although there was no statistical correlation between serum IgG4 level and age, disease duration or IgE levels ($r = -0.018$, $P = 0.847$; $r = 0.154$, $P = 0.099$; $r = -0.026$, $P = 0.846$, respectively), the serum IgG4 value was negatively correlated with serum IgA and IgM levels in IgG4-RD patients ($r = -0.380$, $P < 0.001$; $r = -0.265$, $P = 0.006$; respectively; Fig. 3B and C). Moreover, the serum IgG4 value was positively correlated with ESR, IgG, IgG1 levels and IgG4/IgG ratio ($r = 0.392$, $P < 0.001$; $r = 0.743$, $P < 0.001$; $r = 0.343$, $P < 0.001$; $r = 0.841$, $P < 0.001$; respectively; Fig. 3D–G). Notably, the serum IgG4 level correlated positively with the number of involved organs ($r = 0.557$, $P < 0.001$; Fig. 3H).

Response to treatment

Most of the patients (114/118) were treated with glucocorticoids, including 71 patients with combination therapy including immunosuppressive agents. The majority of patients had good responses, with improvement in organ swelling, as well as a decrease in ESR, CRP, IgG and IgG4 levels. One month after treatment, mean ESR decreased from 38.5 (31.5) mm/h to 10.4 (13.4) mm/h, mean serum IgG level decreased from 23.0 (10.1) g/l to 14.7 (6.3) g/l, serum IgG4 decreased from 1521.8 (1678.5) mg/dl to 1096.6 (1409.3) mg/dl and total IgE decreased from 1521.8 (1678.5) KU/l to 1096.6 (1409.4) KU/l. The trends for ESR, IgG, IgG4 and IgE before and after treatment are shown in Fig. 4.

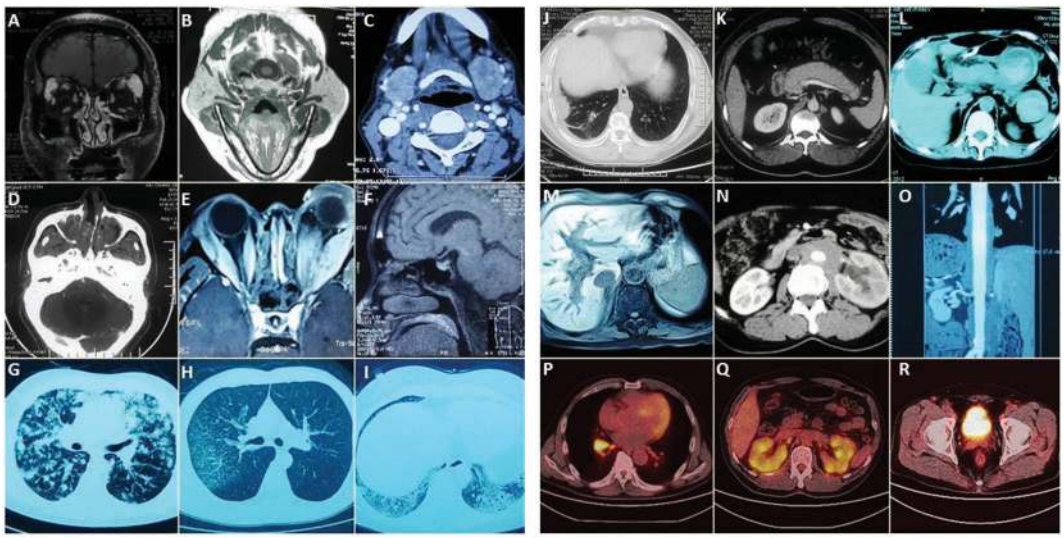
Serum IgG4 levels were significantly decreased within the first 3 months of therapy, with 45.7% of patients showing a decrease to the normal range and 37.1% of patients decreasing by >50% of the baseline level.

Fig. 1 Histopathological features of IgG4-RD



IgG4 immunohistochemistry in salivary gland (**A**), lacrimal gland (**B**) and brain in inflammatory pseudotumour (**C**) from IgG4-RD patients showing prominent $IgG4^+$ plasma cell infiltration. Magnification ×400.

Fig. 2 Typical imaging of IgG4-RD patients



Typical CT imaging findings of various organ involvements in IgG4-RD patients are presented (CT images are shown in (**A**–**O**) and PET/CT images are shown in (**P**, **Q** and **R**); lesions are indicated with arrows). Bilateral lachrymal gland enlargement (**A**); bilateral enlargement of submandibular glands (**B**); bilateral enlargement of the parotid glands (**C**); sinuses filled with soft tissue (**D**); orbital myositis and lacrimal gland enlargement with left eyeball protrusion (**E**); enlargement of the pituitary gland (**F**); diffuse nodules, ground-glass opacity and lung interstitial fibrosis (**G**–**I**); solid nodule near pleura (**J**); diffusely swelling sausage-shaped pancreas (**K**); pancreatic gland swelling with a pancreatic pseudocyst (**L**); dilatation of the intrahepatic bile duct (**M**); retroperitoneal irregular mass-like soft tissue surrounding the aorta with hydronephrosis of the left kidney (**N**); soft tissue lesion surrounding the thoracic and abdominal aorta (**O**); enlarged mediastinal lymph nodes, kidneys and prostate with high uptake values in PET/CT (^{18}F-FDG PET/CT) (**P**–**R**).

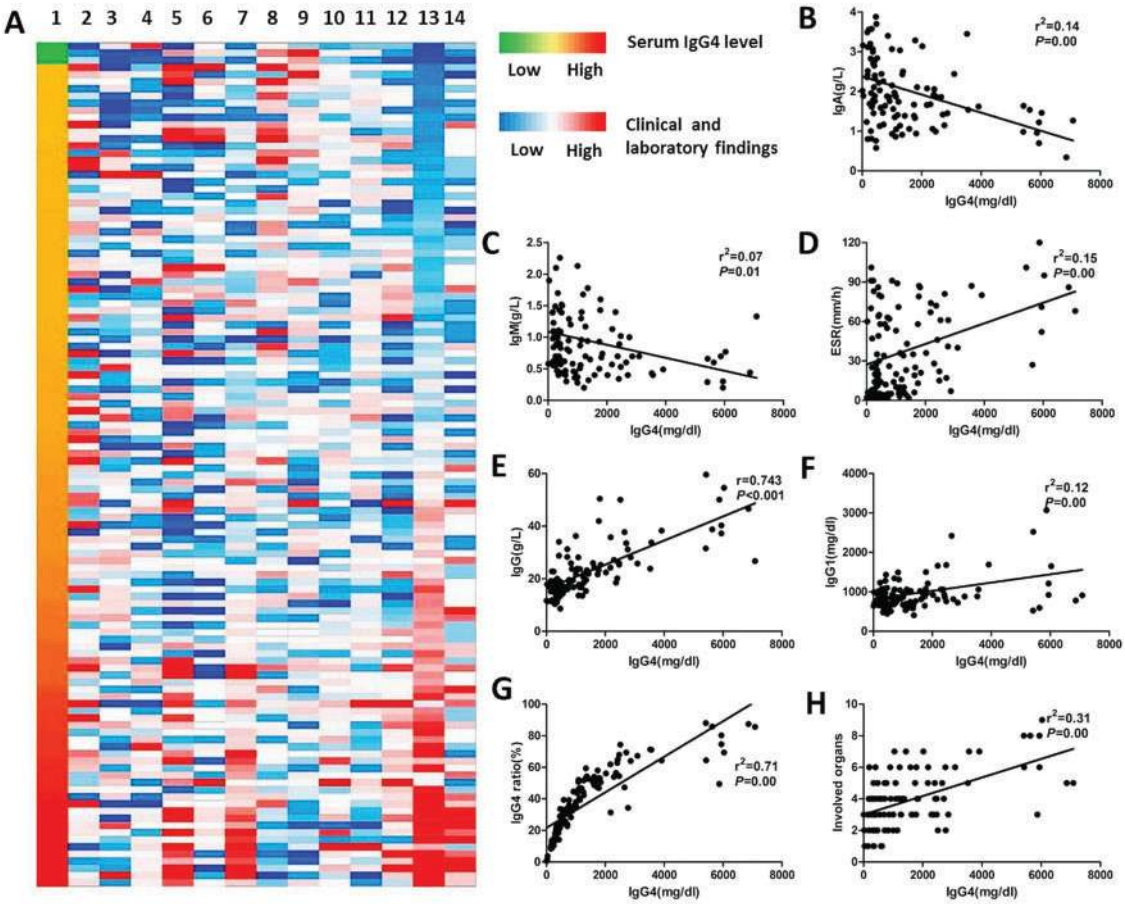
Compared with those with lower baseline IgG4 levels, patients who had higher baseline IgG4 levels were less likely to achieve normal or lower levels after treatment.

Discussion

In this study, we described the clinical, laboratory, histopathological, radiological and imaging features and treatment response of 118 Chinese patients with IgG4-RD. To our knowledge, this is the largest prospective cohort of IgG4-RD patients from China. In this cohort, IgG4-RD patients had a male predominance (ratio, 2.3:1) and a mean age of 53.1 years, which is consistent with other studies [25].

Elevated serum IgG4 levels, as well as hypergammaglobulinaemia, are hallmarks of IgG4-RD. Moreover, elevated

FIG. 3 The relationship between IgG4 levels and clinical and laboratory findings



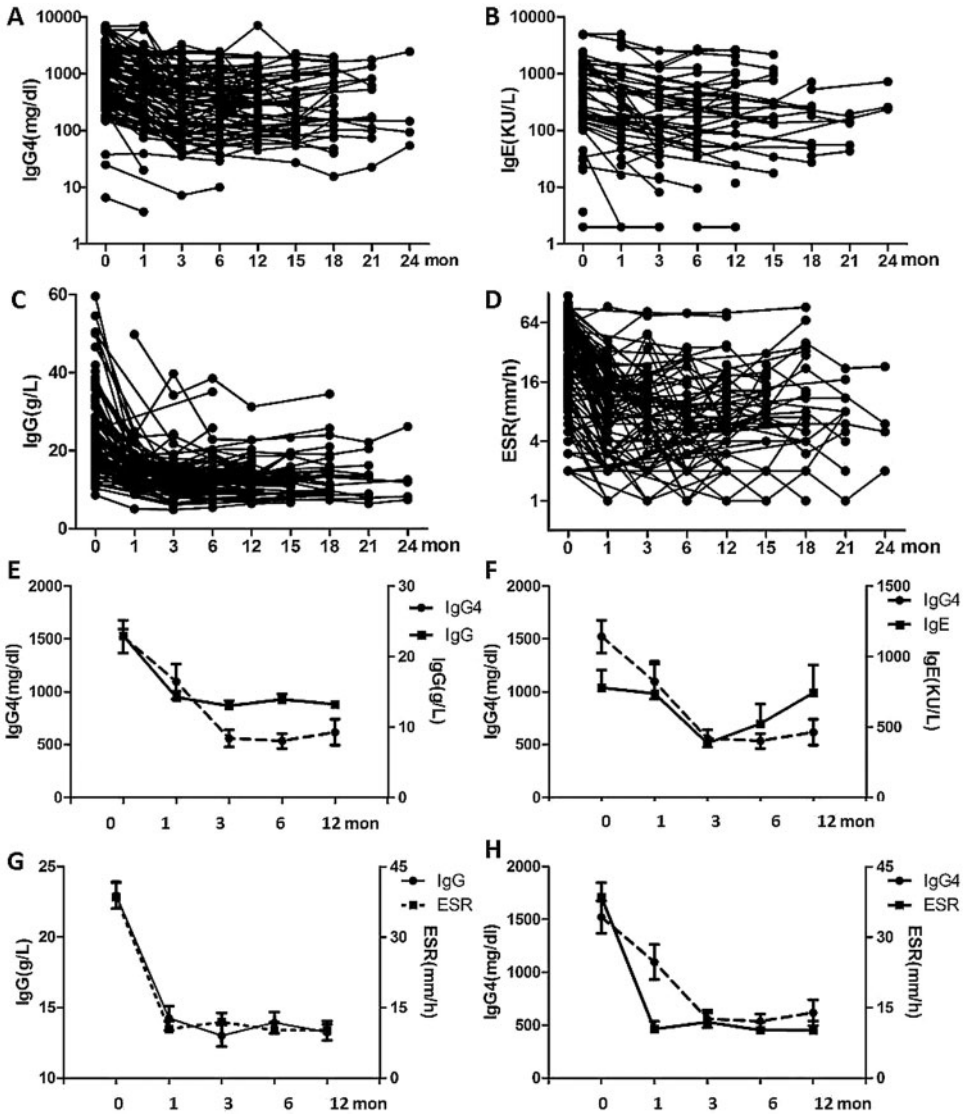
(**A**) Heat map illustrating the clinical features and laboratory findings. Patients were ordered according to their serum level of IgG4, from normal IgG4 level in green to high IgG4 level in red (column 1) (light blue for the lowest to dark red for the highest values of the various parameters). The parameters from columns 2 to 14 are: age, disease duration and percentage of eosinophils, ESR, serum level of CRP, IgG, IgA, IgM, IgG1, IgG2, IgG3, IgG4 ratio, and number of involved organs. (**A**) The serum IgG4 value was negatively correlated with serum IgA and IgM levels (**B**) and (**C**). The serum IgG4 value was positively correlated with ESR, serum IgG and IgG1 levels, the IgG4 ratio and the number of involved organs (**D**–**H**).

serum IgE levels and eosinophilia were commonly observed. In this cohort, eosinophilia and elevated serum IgE levels were observed in 33.9% and 88.9% of patients, respectively. Over half of the patients (56.8%) had a history of allergy, which was also comparable to previous reports from Japan [26]. Della and colleagues [27] reported that eosinophilia and elevated serum IgE levels were observed in 27% and 35% of their overall cohort. Th2 polarization potentially plays an important role in IgG4-RD [28, 29]. However, Mattoo *et al*. proposed that a Th2 immune response in IgG4-RD likely reflected undercurrent allergic conditions rather than a fundamental feature of IgG4-RD [30]. In addition, we found that a subset of CD19+CD24−CD38hi B cells was associated with IgG4-RD [31].

In this study, no correlation was found between serum IgG4, IgE and IgG2 levels. However, there was a positive correlation between IgG4 and IgG1, as well as between IgG4 and IgG3, the IgG4/IgG ratio and the ESR. Additionally, the serum IgG4 level was positively correlated with the number of involved organs. Because of the structure of IgG4, which does not activate the classical complement pathway efficiently [1, 32], our findings suggest that IgG1 or IgG3 may participate in immune complex formation and further activate the inflammatory response. In this context, the elevation in IgG4 may reflect an effort to down-modulate disease activity by switching to a poorly inflammatory IgG4 response.

IgG4-RD is a systemic condition characterized by multiple organ involvement. Similar to other studies [33], the most common lesion in this cohort was lymphadenopathy (64.4%), followed by inflammation of the salivary glands (61.0%) and lacrimal glands (47.5%), and AIP (34.7%).

FIG. 4 Analysis of ESR, serum IgG, IgE and IgG4 levels before and after treatment



The changes in ESR, serum IgG4, IgE and IgG levels during treatment are shown. Levels of serum IgG4, IgE, IgG and ESR in individual patients are shown in (**A**–**D**). Mean levels (S.E.M.) of IgG4, IgG, IgE and ESR are shown in (**E**–**H**).

Other manifestations included interstitial lung disease, periaortitis/retroperitoneal fibrosis, prostatitis, interstitial nephritis, sclerosing cholangitis, paranasal sinusitis, inflammatory pseudotumour, mediastinal fibrosis, prurigo nodularis, sclerosing thyroiditis, hypophysitis, orchitis and colitis. Therefore, systemic evaluation of IgG4-RD should be emphasized before initiating therapy.

Various imaging examinations, including US scanning, CT and/or MRI or FDG-PET/CT, are useful for assessment of organ involvement in IgG4-RD [34]. We previously showed that FDG-PET/CT is superior to other imaging modalities for asymptomatic involvement, as well as for active lesions [35]. Takahashi *et al*. [36] proposed that the diagnosis of IgG4-RD can be made with a characteristic FDG-PET/CT pattern, even in the absence of classic inflammatory involvement. Compared with other studies [24], IgG4-RD patients in this cohort showed a wider disease spectrum and different proportions of involved organs. The differences among these groups may be related to a different focus (prospective *vs* retrospective), more intensive imaging analysis, and evolving knowledge about the full spectrum of disease. In this regard, both French and Japanese studies were retrospective.

In this study, tissue biopsies from the various involved organs, including lachrymal gland, salivary gland, lymph node, kidney, lung, brain and pancreatic gland, showed similar pathological features, which confirmed that IgG4-RD is a systemic disorder presenting with a similar

pathological process in various tissues and organs, regardless of their location.

It is well known that IgG4-RD patients have good responses to glucocorticoids. Patients in this study also experienced positive responses to glucocorticoid therapy. Most patients experienced dramatic improvement within 1–3 months, including reduction of organ swelling, inflammatory parameters, and reduction in serum IgG and IgG4 levels. However, a standard glucocorticoid treatment regimen has not yet been defined. In particular, the activity of disease may fluctuate during glucocorticoid tapering, an observation that is consistent with previous reports [37, 38]. Early intervention and individualized treatment might improve the long-term prognosis. Therefore, more prospective studies are needed to explore the glucocorticoid regimen as well as the potential role of immunosuppressive agents. In addition, long-term follow-up studies are required to define the overall prognosis of the condition.

In conclusion, IgG4-RD is a systemic inflammatory disease with multiple organ involvement. Lacrimal and salivary gland enlargement (formerly called Mikulicz's disease), lymphadenopathy and autoimmune pancreatitis are the most common manifestations. Response to treatment with glucocorticoids and immunosuppressive agents is favourable. Long-term follow-up is underway to explore the prognosis of these patients; however, the nature and pathogenesis of IgG4-RD are still unclear and offer opportunities for further investigation.

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