Correlation between serum immunoglobulin levels and retinal structure in patients with newly diagnosed Vogt-Koyanagi-Harada disease

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Abstract. Immunoglobulins serve immunomodulatory roles in numerous autoimmune diseases. The aim of the present study was to investigate the correlations between serum Ig levels and retinal structural parameters in patients with newly diagnosed acute Vogt-Koyanagi-Harada (VKH) disease. A total of 138 participants were enrolled and the foveal thickness (FT), serous retinal detachment (SRD), sensory retinal thickness, central FT (CFT), cube volume (V) and cube average thickness (AT) were assessed by optical coherence tomography. The patients were divided, according to the extent of SRD, into a high-detachment group (>500 μm) and a low-detachment group (≤500 μm). Rate-scattering turbidimetry was performed to measure the Ig levels. The high-detachment group comprised 51 (36.96%) patients. The proportion of males was significantly greater in the high-detachment group compared with the low-detachment group (58.82 vs. 40.23%; P<0.05) and best-corrected visual acuity was significantly worse in the high-detachment group compared with the low-detachment group (P<0.001). The IgE levels in the high-detachment group were significantly greater compared with the low-detachment group (P<0.05). FT, SRD, CFT, V and AT were significantly greater in the high-detachment group compared with the low-detachment group (P<0.001). The IgE levels were positively associated with SRD, CFT and AT (P<0.05). Multivariate binary logistic regression analysis demonstrated that male sex (B=2.447; P<0.05) and serum IgE levels (B=0.997, P<0.05) may be independent risk factors for severe SRD. The results of the present study demonstrated that males are more likely to develop severe SRD and that serum IgE levels were associated with the extent of detachment. These data suggested that IgE may be involved in the progression of VKH disease.

Introduction

Vogt-Koyanagi-Harada (VKH) disease is an autoimmune disease that is relatively common in China and is characterized by ophthalmic, auditory, dermatologic and neurologic effects. The most common ophthalmic manifestation of VKH disease is granulomatous intraocular inflammation. Serous retinal detachment (SRD) is the most common ocular manifestation in patients presenting in the acute phase of VKH disease (1,2).

The etiology and pathogenesis of VKH disease are still unknown. One putative mechanism may involve an autoimmune response to melanocytes, which is mediated through CD4+ T cells (3). Changes in the ratio of CD4+ lymphocytes and CD4+/CD8+ cells were observed in skin lesions of patients with VKH disease. Histopathology of skin lesions demonstrated that in addition to diffuse infiltration of activated T cells in the choroid membrane, the lesions also contained infiltrations of plasma cells, multinucleated giant cells and other cells, which suggested that humoral immunity may also serve a role in the pathogenesis of VKH disease (4).

Immunoglobulins are globulin proteins with antibody-like structures that exert important immune antibody activities. Upon stimulation by an antigen, B cells proliferate and differentiate into plasma cells, which secrete antigen-relevant Ig antibodies involved in the regulation of humoral immunity. Igs also serve immunomodulatory roles by neutralizing specific antigens and activating the complement system (5). Studies have demonstrated that serum IgG, IgA and IgM also serve important roles in numerous diseases, including autoimmune hemolytic anemia, IgA nephropathy and autoimmune hepatitis (6-8). It has also been reported that the serum IgG, IgA and IgM levels were significantly increased in patients

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with rheumatoid arthritis and the changes in these levels were associated with disease activity (9). Elevated IgE levels were detected in patients with other autoimmune diseases, including systemic lupus erythematosus and bullous pemphigoid, and IgE autoantibodies were also detected in these patients (10,11). Previous studies have also reported higher serum total IgE levels in patients with types of autoimmune uveitis, including acute iridocyclitis, Eales' disease, pars planitis and multifocal choroiditis compared with normal control group patients (12,13).

However, few previous studies have assessed Ig levels in patients with VKH disease or examined the correlation between Ig levels and retinal structural parameters. Therefore, in the present study, the medical records of patients admitted to Shanghai Xuhui Central Hospital with acute VKH disease were reviewed and the serum Ig levels in these patients were analyzed according to the extent of SRD. Correlations between Ig levels and changes in retinal structure in acute VKH disease were also examined.

Materials and methods

Ethics approval. The present study was approved by the Shanghai Xuhui Central Hospital Ethics Committee (Shanghai, China; approval no. 2020-179). These protocols followed the tenets of The Declaration of Helsinki, and written informed consent was obtained from all patients or their guardian after obtaining ethics approval and prior to performing the analysis.

Patients. This was a retrospective clinical study. The authors retrieved the medical records of patients with newly diagnosed acute VKH who were admitted to Shanghai Xuhui Central Hospital (Shanghai, China) between August 2015 and June 2020. Patients who satisfied the diagnostic criteria for acute VKH disease, as previously described (2), were eligible for inclusion in the present study. Once identified, patients were contacted to obtain informed consent. Patients with corneal disease, glaucoma, eye trauma, a history of eye surgery, eye developmental abnormalities or genetic diseases were excluded. Patients with asthma, urticaria, systemic lupus erythematosus, bullous pemphigoid or other systemic immune diseases were also excluded. Furthermore, patients who did not cooperate with the examinations or patients with corneal or lenticular opacity were excluded. The best-corrected visual acuity (BCVA), which was taken as the converted logarithm of the minimum angle of resolution (logMAR), and the interval between the onset of ocular symptoms and initiation of treatment were retrieved from the patients' medical records. Optical coherence tomography (OCT) and serum data, assessed at the same time as BCVA, were also retrieved from the medical records.

OCT examination of the macular area. OCT was performed at the time of admission to hospital. Patients' pupils were dilated with tropicamide (0.5% tropicamide and 0.5% deoxyepinephrine hydrochloride) eye drops before the examination. The macular areas were scanned using a Cirrus HD-OCT 4000 OCT scanner (Carl Zeiss AG) with software version 4.0. All patients were scanned in both the macular cube mode and with a five-line raster.

The macular cube 512x128 mode scanned a 6.0x6.0 mm square region centered on the fovea. The central foveal thickness (CFT; assessed in the central 1 mm subfield), cube volume (V) and cube average thickness (AT) were automatically quantified by the software (Fig. 1A).

In the five-line raster scanning mode, the distance between each line was 0.25 mm and the transverse scans were centered on the fovea. Foveal thickness (FT), SRD and sensory retinal thickness (SRT) were quantified manually using the software's caliper. FT boundaries were set as the internal limiting membrane and the inner boundary of the retinal pigment epithelium (RPE) layer. SRD was defined as the distance from the inner boundary of the sensory layer to the internal boundary of the RPE layer in the fovea. SRT was defined as the distance from the inner boundary membrane in the fovea to the inner boundary of the sensory layer (Fig. 1B). Each measurement was repeated twice and the mean value was recorded. The patients were divided into two groups based on the SRD, a high-detachment group (>500 μm) and low-detachment group (≤500 μm).

Measurement of serum Igs, CRP and TNF-α levels. Fasting venous blood samples were obtained at the time of admission and the sera were separated and stored at -20°C until testing. Ig levels were quantified by rate-scattering turbidimetry on a BN II System automatic analyzer (Siemens Healthineers). CRP and TNF-α levels were assessed using ELISA kits (R&D Systems, Inc.).

Statistical analysis. SPSS version 15.0 (SPSS, Inc.) was used for statistical analyses. Data were tested for a normal distribution using the Kolmogorov-Smirnov test. Data that did not conform to a normal distribution were presented as the median. The Mann-Whitney U test was used for comparisons between the two groups. Pearson's χ^2 test was used to test categorical variables. In all analyses, P<0.05 was considered to indicate a statistically significant difference.

Results

General clinicopathological characteristics of patients. The present study included 138 patients, of whom 67 were male (48.55%). The median age was 41.5 years (range, 14-76 years) and the mean interval between the onset of ocular symptoms and initiation of treatment was 17.71 days (range, 2-90 days). The mean logMAR BCVA was 0.76±0.56.

General clinicopathological characteristics of patients in the two groups are presented in Table I. Of the 138 patients, 51 were included in the high-detachment group, 30 of whom were male (58.82%). The other 87 patients were included in the low-detachment group, of whom 35 were male (40.23%). In the high-detachment group, the median age was 42 years [interquartile range (IQR), 28-52] and the median interval between the onset of ocular symptoms and initiation of treatment was 10 days (IQR, 7-20). The median logMAR BCVA for the high-detachment group was 1.0 (IQR, 0.6-1.3). In the low-detachment group, the median age was 41 years (IQR, 28-50) and the median interval between the onset of ocular symptoms and initiation of treatment was 14 days (IQR, 7-21). The median logMAR BCVA for the low-detachment group was 0.5 (IQR, 0.3-0.7).
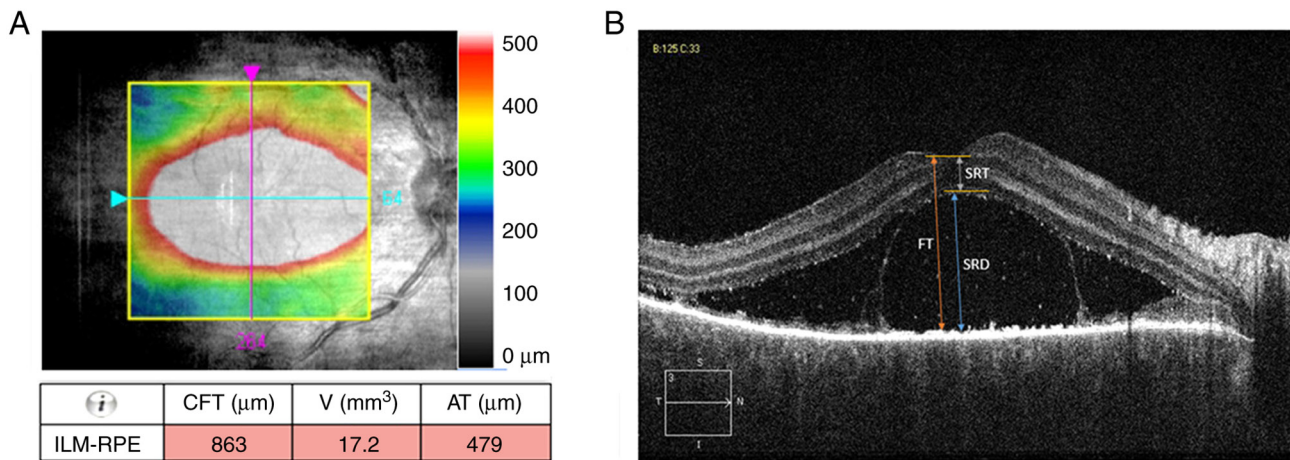
Figure 1. Representative optical coherence tomography images of the fovea. (A) The macular cube 512x128 scan was used to automatically measure the CFT, V and AT. (B) The horizontal B scan was used to manually measure FT, SRD and SRT. AT, cube average thickness; CFT, central fovea thickness; FT, foveal thickness; SRD, serous retinal detachment; SRT, sensory retinal thickness; V, cube volume.

The proportion of males (P=0.035) and the logMAR BCVA (P<0.001) were significantly different in the high-detachment group compared with the low-detachment group. However, there were no significant differences in the age of onset (P=0.841) or the interval between the onset of ocular symptoms and initiation of treatment (P=0.535) between the two groups.

Serum Ig, CRP and TNF-α levels. The serum IgA, IgG, IgM, IgE, CRP and TNF-α levels of the two groups are presented in Table II. There were no significant differences in the serum levels of IgA (P=0.304), IgG (P=0.208), IgM (P=0.865), CRP (P=0.082) or TNF-α (P=0.099) between the high- and low-detachment groups. However, the serum IgE level was significantly greater in the high-detachment group compared with the low-detachment group (P=0.016).

Comparison of Oct macular area morphologic characteristics. The FT, SRD, SRT, CFT, V and AT macular parameters of the high- and low-detachment groups are presented in Table III. FT (P<0.001), SRD (P<0.001), CFT (P<0.001), V (P<0.001) and AT (P<0.001) were significantly higher in the high-detachment group compared with the low-detachment group. However, although SRT was not identified as significantly different between the high- and the low-detachment groups (P=0.052), it was markedly greater in the high-detachment group.

Correlations and associations between IgE, BCVA and OCT macular characteristics. Correlations between IgE or BCVA and OCT assessed macular characteristics are presented in Table IV. The serum IgE levels were weakly positively associated with SRD (r=0.136; P=0.024), CFT (r=0.137; P=0.023) and AT (r=0.125; P=0.038). Moreover, the BCVA was significantly positively correlated with FT (r=0.644; P<0.001), SRD (r=0.618; P<0.001), SRT (r=0.160, P=0.008), CFT (r=0.588; P<0.001), V (r=0.596; P<0.001) and AT (r=0.554; P<0.001).

Analysis of risk factors for severe SRD. Multivariate binary logistic regression was performed using IgA, IgG, IgM, IgE, CRP and TNF-α as the independent variables and severity of SRD (SRD >500 μm=1; SRD ≤500 μm=0) as the dependent variable. Age, sex (male=1; female=2) and interval between ocular symptom onset and initiation of treatment were also included for adjustment. In this analysis, male (P=0.049) and serum IgE level (P=0.014) were identified as putative significant independent risk factors for severe SRD (Table V). The receiver operating characteristic curve analysis demonstrated that the area under the curve for IgE as a diagnosis of severe SRD was 0.623 (P=0.016).

Discussion

All of the patients included in the present study were of Han Chinese ethnicity. The mean age at onset of VKH disease was 41.65 years (range 14-76 years). The percentage of females (51.45%) was lower compared with a previous report (3). Possible explanations may include the differing sample sizes or racial differences (3). However, the proportion of males was significantly greater in the high-detachment group than in the low-detachment group and the regression analysis demonstrated that male sex was a significant risk factor for SRD in this cohort of patients with VKH disease. These results suggest that, among Han Chinese, males with acute VKH disease are more likely than females to present with severe SRD.

VKH disease is a common type of panuveitis. As choroidal inflammation develops, it first affects the adjacent RPE layer, causing it to crease. As choroidal vascular permeability increases, inflammatory choroidal fluid accumulates beneath the neuroepithelium, which causes neuroepithelial detachment. Fluorescein and indocyanine green angiography can be used to detect any leaks from retinal blood vessels that may lead to SRD. SRD is a common manifestation of VKH disease that indirectly reflects the severity of inflammation (1). OCT, a non-invasive imaging modality, can provide clear tomographic images that demonstrate the microstructure of the retina (14). The extent of SRD can be quantified using numerous OCT parameters. In the present study, the age at onset and the interval between ocular symptom onset and initiation of treatment were not significantly different between

Table I. General clinicopathological characteristics of patients with serous retinal detachment.

Clinicopathological characteristic	High-detachment group	Low-detachment group	P-value
n (male; %)	51.00 (30.00; 58.82)	87.00 (35.00; 40.23)	0.035
Age, years[a]	42.00 (28.00, 52.00)	41.00 (28.00, 50.00)	0.841
Interval between onset of symptoms and initiation of treatment, days[a]	10.00 (7.00, 20.00)	14.00 (7.00, 21.00)	0.535
logMAR BCVA[a]	1.00 (0.60, 1.30)	0.50 (0.30, 0.70)	<0.001

[a]Data are presented as median (interquartile range). BCVA, best-corrected visual acuity; logMAR, log of the minimum angle of resolution.

Table II. Comparison of serum IgA, IgG, IgM, IgE, CRP and TNF-α between patients with serous retinal detachment.

Serum component	High-detachment group[a]	Low-detachment group[a]	P-value
IgA, g/l	2.04 (1.77, 2.59)	2.26 (1.74, 3.08)	0.304
IgG, g/l	11.20 (9.74, 13.05)	11.69 (10.20, 13.76)	0.208
IgM, g/l	1.23 (0.92, 1.64)	1.24 (0.86, 1.67)	0.865
IgE, U/ml	83.00 (30.00, 251.00)	53.00 (32.00, 80.00)	0.016
CRP, mg/l	1.04 (0.50, 2.02)	0.67 (0.30, 3.00)	0.082
TNF-α, pg/l	4.60 (4.00, 6.43)	4.21 (4.00, 5.47)	0.099

[a]Data are presented as median (interquartile range).

Table III. Comparison of the OCT parameters FT, SRD, SRT, CFT, V and AT between patients with serous retinal detachment.

OCT parameter	High-detachment group[a]	Low-detachment group[a]	P-value
FT, μm	864.00 (661.00, 1247.25)	324.50 (232.00, 446.25)	<0.001
SRD, μm	701.00 (421.75, 997.25)	162.00 (96.00, 282.00)	<0.001
SRT, μm	141.00 (124.00, 161.25)	134.00 (118.00, 158.50)	0.052
CFT, μm	813.00 (606.75, 1016.25)	362.00 (268.75, 445.50)	<0.001
V, mm^3	17.60 (14.70, 20.38)	11.80 (10.90, 13.00)	<0.001
AT, μm	489.50 (408.00, 566.75)	327.50 (320.75, 360.25)	<0.001

[a]Data are presented as median (interquartile range). AT, cube average thickness; CFT, central fovea thickness; FT, foveal thickness; IQR, interquartile range; OCT, optical coherence tomography; SRD, serous retinal detachment; SRT, sensory retinal thickness; V, cube volume.

the high and low-detachment groups. However, FT, SRD, CFT, V and AT were significantly greater in the high-detachment group than in the low-detachment group, demonstrating that the leakage caused by inflammation was more severe in the high-detachment group. However, SRT was not significantly different between the two groups, which suggested that in the acute stage, the inflammatory process had not caused marked changes in the sensory layer of the retina. Although not statistically significant, SRT was generally greater in the high-detachment group. The BCVA was significantly worse in the high-detachment compared with the low-detachment group, it was significantly positively correlated with FT, SRD, SRT, CFT, V and AT. These findings demonstrated that OCT scans in patients with acute VKH disease not only depicted changes in the retinal structure, but also indirectly reflected the patient's disease severity and BCVA.

The present study demonstrated no significant differences in the serum IgA, IgG, IgM, CRP or TNF-α levels when compared between the high- and low-detachment groups. However, the serum IgE level was significantly greater in the high-detachment group compared with the low-detachment group. IgE synthesis is regulated through a number of factors, including T lymphocytes, B lymphocytes and numerous cytokines (15). The interaction between CD40 on the surface of B lymphocytes and CD40L expressed by CD4$^+$ T lymphocytes is crucial for mediating antigen-specific IgE responses *in vivo*. The IgE response is dependent on T lymphocytes because the activation of B lymphocytes requires the additional T lymphocyte factors IL-4 and IL-3 (16). IgE is highly sensitive to the T cell-derived cytokine environment because it is regulated by cytokines secreted from CD4$^+$ T cells (15). The most widely recognized pathogenesis of VKH disease involves

Table IV. Correlations between IgE, BCVA and optical coherence tomography macular parameters.

Component	IgE	logMAR BCVA	FT	SRD	SRT	CFT	V	AT
IgE								
r-value[a]	1.000	0.067	0.110	0.136	-0.041	0.137	0.113	0.125
P-value		0.269	0.067	0.024	0.500	0.023	0.061	0.038
logMAR BCVA								
r-value[a]	0.067	1.000	0.644	0.618	0.160	0.588	0.596	0.554
P-value	0.269		<0.001	<0.001	0.008	<0.001	<0.001	<0.001

[a]Pearson's correlation coefficient. AT, cube average thickness; BCVA, best-corrected visual acuity; CFT, central fovea thickness; FT, foveal thickness; logMAR, log of the minimum angle of resolution; SRD, serous retinal detachment; SRT, sensory retinal thickness; V, cube volume.

Table V. Multivariate binary logistic regression analysis of risk factors for severe serous retinal detachment.

Item	B-value	Wald-value	P-value	Odds ratio (95%CI)
Sex	2.447	3.876	0.049	1.004-5.964
Age	0.996	0.089	0.766	0.968-1.024
Interval	1.001	0.014	0.906	0.982-1.020
IgA	1.284	1.146	0.284	0.812-2.029
IgG	0.972	0.150	0.698	0.842-1.122
IgM	0.754	0.945	0.331	0.427-1.333
IgE	0.997	6.034	0.014	0.995-0.999
CRP	1.034	0.151	0.698	0.875-1.221
TNF-α	0.917	0.497	0.481	0.719-1.168

autoimmune inflammation mediated by CD4^{+} T cells targeting melanocytes (3). Therefore, it may be hypothesized that elevated IgE levels may also be involved in the autoimmune inflammation mediated by CD4+ T cells.

IgE is recognized as the antibody that mediates parasitic immunity and type I hypersensitivity. Previous studies have reported that the serum IgE level is elevated in patients with certain autoimmune diseases; IgE autoantibodies are also detected in a number of patients (10,12). A retrospective study of 1,583 patients reported that allergic diseases (53.14%) and autoimmune diseases (47.37%) were the most common disease groups associated with patients assessed as having elevated serum IgE levels (17). The correlation between the serum total IgE level and autoimmune disease severity has been reported as being the same as that for specific IgE autoantibodies (10). Moreover, several previous studies have reported that elevated serum total IgE levels were closely associated with the activity of diseases, including systemic lupus erythematosus and bullous pemphigoid (18-20). Permin and Wiik (21) also reported that, although immune complexes comprised IgE autoantibodies, IgE itself increased vascular permeability by mediating the release of vasoactive amines. In the present study, the serum IgE levels in the high-detachment group was significantly higher compared with that in the low-detachment group, and it was weakly positively associated with SRD, CFT and AT. Logistic regression analysis demonstrated that serum IgE level was an independent risk factor for severe SRD. We hypothesized that high IgE levels may lead to a marked increase in vascular permeability, which then progressed to severe SRD, and that high serum IgE levels may have contributed to the severe condition of patients with acute VKH disease.

To the best of our knowledge, the present study is the first to investigate the relationship between SRD and Igs in patients with acute VKH disease. However, the present study has certain limitations; owing to the limitations of the Cirrus OCT-HD 4000 scanner, the images of the choroid were unclear and disease inflammation also made it difficult to quantify the relevant choroid parameters. Furthermore, the serum total IgE level was quantified but the IgE autoantibody levels were not assessed in patients with acute VKH disease.

In conclusion, males with acute VKH disease were more likely to present with severe SRD. Furthermore, the severity of SRD was associated with high serum IgE levels, which suggested that IgE may be involved in the pathogenesis and/or progression of VKH disease.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

ZJ and NZ analyzed and interpreted data and wrote the manuscript. HJ and MLZ collected and analyzed the data and confirm the authenticity of all the raw data. JD and MZ were responsible for the conception and design of the work. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by The Shanghai Xuhui Central Hospital Ethics Committee (Shanghai, China; approval no. 2020-179). Written informed consent was obtained from all patients after obtaining ethics approval and prior to performing the analysis.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Rao NA, Gupta A, Dustin L, Chee SP, Okada AA, Khairallah M, Bodaghi B, Lehoang P, Accorinti M, Mochizuki M, *et al*: Frequency of distinguishing clinical features in Vogt-Koyanagi-Harada disease. Ophthalmology 117: 591-599, 599.e1, 2010.
2. Yang P, Zhong Y, Du L, Chi W, Chen L, Zhang R, Zhang M, Wang H, Lu H, Yang L, *et al*: Development and evaluation of diagnostic criteria for Vogt-Koyanagi-Harada disease. JAMA Ophthalmol 136: 1025-1031, 2018.
3. O'Keefe GA and Rao NA: Vogt-Koyanagi-Harada disease. Surv Ophthalmol 62: 1-25, 2017.
4. Patil YB, Garg R, Rajguru JP, Sirsalmath M, Bevinakatti VA, Kumar M and Sharma S: Vogt-Koyanagi-Harada (VKH) syndrome: A new perspective for healthcare professionals. J Family Med Prim Care 9: 31-35, 2020.
5. Turula H and Wobus CE: The role of the polymeric immunoglobulin receptor and secretory immunoglobulins during mucosal infection and immunity. Viruses 10: 237, 2018.
6. Ajmi H, Mabrouk S, Hassayoun S, Regaieg H, Tfifha M, Jalel C, Skouri H, Zouari N and Abroug S: Success of anti-CD20 monoclonal antibody treatment for severe autoimmune hemolytic anemia caused by warm reactive immunoglobulin A, immunoglobulin G, and immunoglobulin M autoantibodies in a child: A case report. J Med Case Rep 11: 321, 2017.
7. Wyatt RJ and Julian BA: IgA nephropathy. N Engl J Med 368: 2402-2414, 2013.
8. Pape S, Schramm C and Gevers TJ: Clinical management of autoimmune hepatitis. United European Gastroenterol J 7: 1156-1163, 2019.
9. Smolen JS, Aletaha D and McInnes IB: Rheumatoid arthritis. Lancet 388: 2023-2038, 2016.
10. Sanjuan MA, Sagar D and Kolbeck R: The role of IgE in autoimmunity. J Allergy Clin Immunol 137: 1651-1661, 2016.
11. Messingham KA, Holahan HM and Fairley JA: Unraveling the significance of IgE autoantibodies in organ-specific autoimmunity: Lessons learned from bullous pemphigoid. Immunol Res 59: 273-278, 2014.
12. Romero MD, Muiño JC, Bianco GA, Ferrero M, Juarez CP, Luna JD and Rabinovich GA: Circulating anti-galectin-1 antibodies are associated with the severity of ocular disease in autoimmune and infectious uveitis. Invest Ophthalmol Vis Sci 47: 1550-1556, 2006.
13. Muiño JC, Juárez CP, Luna JD, Castro CC, Wolff EG, Ferrero M and Romero-Piffiguer MD: The importance of specific IgG and IgE autoantibodies to retinal S antigen, total serum IgE, and sCD23 levels in autoimmune and infectious uveitis. J Clin Immunol 19: 215-222, 1999.
14. Gupta V, Gupta P, Singh R, Dogra MR and Gupta A: Spectral-domain Cirrus high-definition optical coherence tomography is better than time domain stratus optical coherence tomography for evaluation of macular pathologic features in uveitis. Am J Ophthalmol 145: 1018-1022, 2008.
15. He JS, Narayanan S, Subramaniam S, Ho WQ, Lafaille JJ and Curotto de Lafaille MA: Biology of IgE production: IgE cell differentiation and the memory of IgE responses. Curr Top Microbiol Immunol 388: 1-19, 2015.
16. Turqueti-Neves A, Otte M, Prazeres da Costa O, Höpken UE, Lipp M, Buch T and Voehringer D: B-cell-intrinsic STAT6 signaling controls germinal center formation. Eur J Immunol 44: 2130-2138, 2014.
17. Wang J, Liu N and Zhang M: The detection results of total IgE in patients with different types of diseases. Labeled Immunoassays Clin Med 26: 1452-1460, 2019 (In Chinese).
18. Cozzani E, Gasparini G, Di Zenzo G and Parodi A: Immunoglobulin E and bullous pemphigoid. Eur J Dermatol 28: 440-448, 2018.
19. Atta AM, Sousa CP, Carvalho EM and Sousa-Atta MLB: Immunoglobulin E and systemic lupus erythematosus. Braz J Med Biol Res 37: 1497-1501, 2004.
20. Lamb PM, Patton T and Deng JS: The predominance of IgG4 in prodromal bullous pemphigoid. Int J Dermatol 47: 150-153, 2008.
21. Permin H and Wiik A: The prevalence of IgE antinuclear antibodies in rheumatoid arthritis and systemic lupus erythematosus. Acta Pathol Microbiol Scand C 86C: 245-249, 1978.