CASE REPORT

IgG4-related multiorgan disease: report of the first autopsy case

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SUMMARY

IgG4-related disease (IgG4RD) is a chronic recurring fibro-inflammatory pathology that is considered to be of autoimmune origin. Histopathology is considered to be the gold standard method for diagnosis. IgG4RD affects multiple organs. IgG4RD was first identified in the pancreas and was called autoimmune pancreatitis (AIP). During the following years, the disease spectrum was expanded and it was realised that the extrapancreatic lesions can precede, coexist or appear after the diagnosis of AIP. At present, several illnesses such as Mikulicz disease, Küttner tumour, multifocal fibrosclerosis, etc, are considered to be part of the IgG4RD spectrum. The symptoms of the disease tend to appear over months and years and diagnosis is achieved on average 13.5 months (4–60 months) after the onset. The purpose of this report was to provide information about a case that was sadly fatal but that permitted a complete histopathological study of the damaged tissues.

BACKGROUND

IgG4-related disease (IgG4RD) is a chronic recurring fibro-inflammatory pathology that is considered to be of autoimmune origin. It is diagnosed by clinical, radiological, serological, histopathological and immunohistochemical studies, although histopathology is considered to be the gold standard method. Histopathology of this disease reveals inflammatory lymphoplasmacytic infiltration with abundant IgG4-positive plasma cells, storiform fibrosis and obliterative phlebitis.

Patients frequently also have elevated serum IgG4 levels and respond very well to steroid therapy. IgG4RD affects multiple organs, including the pancreaticobiliary tract, liver, salivary glands, nasopharynx, bone marrow, lacrimal gland, extra-ocular muscles and retrobulbar space, kidneys, lungs, lymphatic nodes, meninges, aorta, mammary glands, prostate, thyroid and pericardium.¹

The case presented below is the first autopsy study of multiorgan IgG4RD.

CASE PRESENTATION

This case involved a 50-year-old woman with the following medical history: her father and mother had died of prostate and bone cancers, respectively, and the patient had a haemorrhoidectomy 5 years earlier and had suffered from allergic rhinitis for many years. One year before the onset, the patient began to suffer from haematemesis that was preceded by nausea and accompanied by melena. One week before being hospitalised, she developed

asthenia, adynamia, generalised weakness and weight loss of 2 kg. Haemorrhage of the upper digestive tract was diagnosed. An endoscopy revealed a vascular neoformation in the gastric antrum. A physical examination showed that the patient looked older than her chronological age, her blood pressure was 100/70 mm Hg, heart rate 110/min and respiratory rate 24/min. She had pallor; dryness of the mucous membranes, pulmonary condensation in both supercapillary regions and a distended abdomen due to adipose panicle.

The laboratory and doctor's office analyses performed 1 week before hospitalisation showed the following: albumin 1.5 g/dl, creatine 4.2 mg/dl, alkaline phosphatase (FA) 173 U/l, total protein 4.4 g/dl, aspartate aminotransferase (TGO) 107 U/l, glucose 60 mg/dl, and lactate dehydrogenase (HDL) 625 U/l. The coagulation times were prothrombin time (PT) 18 s, partial thromboplastin time (PTT) 53.8%, international normalised ratio 1.6, Blood biometry showed: leucocytes $9.7 \times 10^3/\mu\text{l}$, neutrophils 91.4%, lymphocytes 6.9%, macrophages 0.7%, erythrocytes $3.2 \times 10^6/\mu\text{l}$, haemoglobin 10.7 g/dl, haematocrit 30%, platelets $207 \times 10^3/\mu\text{l}$, electrolyte serum Na 183 mmol/l, and Cl 159 mmol/l. Blood biometry performed 3 days later showed: Na 138.6 mmol/l, K 5.5 mmol/l, Cl 109 mmol/l and Ca 7.1 mg/dl. Cranial CT showed diffuse cerebral oedema with partial ventricular collapse, diffuse granulomatous calcifications of probable parasitic origin.

During her hospitalisation, the patient exhibited neurological deterioration, electrolyte imbalances and fever composed of irregular severe febrile episodes. She was managed with sedation. She exhibited lung dysfunction with the presence of basal bilateral subcrepitant stertors, and uresis diminished. Although the hydroelectrolytic imbalance was corrected, the fever continued. She had a poor ventilatory evolution and therefore required mechanical ventilatory support. She then fell into a coma and exhibited cerebral oedema, papilloedema, and severe kidney failure. The patient died during the fifth day of hospitalisation. The combined diagnoses were multiple organ failure, severe kidney failure, pneumonia, corrected hydroelectrolyte imbalance, secondary cerebral oedema and a state of coma.

The postmortem study showed a woman with a distended abdomen, with pallor of the teguments and oedema of the inferior extremities up to the middle third of the legs. The thyroid gland was slightly enlarged in weight and size and adhered to

To cite: Ochoa ML, Gabiño López B, Cabello RR, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009636

the outer surface of the trachea firmly. On being cut, the thyroid was found to be composed of hard and homogeneous pale pink tissue (figure 1). The lymphatic cervical, mediastinal, peripancreatic and paraaortic glands were enlarged and had a hard consistency and clear yellow colour (figure 2). The superior lobes of the lungs exhibited nodes with well-defined borders; they were yellow and had a rigid consistency. In addition, in the superior lobe of the right lung, a vessel was occluded by a blood thrombus (figure 3). The hilum of the spleen contained a $2 \times 1.5 \times 1.0$ cm node that was yellow, well-defined, homogeneous and had a rigid consistency. The oesophagus had two longitudinal $3 \times 2 \times 1$ mm ulcers on the middle third, with well-defined borders and a haemorrhagic background. The stomach contained 1000 ml of coagulated blood and the mucosa of the gastric curvature bore abundant pinpoint erosions with a haemorrhagic background. The pancreas was small, yellow and hard. When it was cut, the tail of the pancreas was found to bear a poorly defined $2.5 \times 1.8 \times 1.5$ cm area that was light yellow, had a rigid consistency and focally penetrated the adjacent adipose tissue (figures 4 and 5). The kidneys and the right suprarenal gland were enveloped in hard, light yellow tissue that was firmly attached to both the underlying renal parenchyma and the suprarenal gland. Both kidneys had nodes with a cortical predominance. Their borders were well-defined and they were light yellow and had a rigid consistency both on the external surface and when cut (figures 6 and 7).

Microscopic analysis of the lesions in the thyroid, lymphatic nodes, lungs, pancreas, spleen, kidneys, retroperitoneal soft tissues and the serosa and muscular layer of the gallbladder was then performed. It revealed that all of these tissues had similar changes that reflected a chronic inflammatory disease where normal tissue became substituted with an inflammatory infiltration with a predominance of lymphocytes and plasma cells. This resulted in varying levels of fibrosis with steriiform patterns and the thickening of the walls of small-caliber veins due to connective tissue and inflammatory cells. This in turn reduced the diameter of the affected vessels (figures 8–10). Some organs, such as the thyroid gland and lymphatic glands, also had nodular clusters of lymphocytes that were dispersed in the connective tissue that was extensively sclerotised and had a steriiform pattern.

Immunohistochemistry to identify CD3, CD20, IgG, and IgG4 was then performed. CD3 and CD20, which identify T and B lymphocytes, respectively, were detected. The sections

Figure 1 Cut surface of thyroid gland completely replaced by fibrous yellow tissue.

Figure 2 Lymph node tissue replaced by light yellow, homogeneous tissue.

were also positive for IgG and IgG4, which were observed in the cytoplasm of plasma cells (figure 11).

The anatomopathological diagnoses were disease related to systemic IgG4 that affected the thyroid, pancreas, gallbladder, kidneys, lungs, lymphatic glands and retroperitoneal soft tissues; acute and chronically ulcerated oesophagitis; acute erosive gastritis; right pulmonary thromboembolism and right pulmonary infarct.

DISCUSSION

IgG4RD was first identified in the pancreas and was therefore initially called AIP. It was discovered in 1961 and the first description of the histopathological data was published in 1991.^{2,3} In 2001, AIP was found to relate to elevated IgG4 levels in the serum.⁴ The observation that extrapancreatic tissues of patients with AIP can also have marked fibro-inflammatory lesions that contain multiple IgG4-positive plasma cells led to the concept of IgG4RD in 2003.⁵ During the following years, the disease spectrum was expanded to include the biliary ducts, retroperitoneum and salivary glands and it was realised that the extrapancreatic lesions can precede, coexist or appear after the diagnosis of AIP. At present, illnesses such as Mikulicz disease, Küttner tumour, multifocal fibrosclerosis, inflammatory pseudotumour, Riedel's thyroiditis, inflammatory aneurism of the aorta, cutaneous pseudolymphoma and

Figure 3 Lung nodular lesions in both upper lobes. In the right lung thromboembolism is observed with recent infarction.

Figure 4 Pancreas decreased in size with a focal tail injury.

eosinophilic angiocentric fibrosis are considered to be part of the IgG4RD spectrum.

IgG4RD is currently known as an IgG4-related systemic disease, an IgG4-related sclerotic disease, a disease associated with the hyperproduction of IgG4 and an IgG4 syndrome, among others. The name IgG4RD was proposed in 2012, and was later approved by an international committee of experts.⁶

Elevated serum levels of IgG4 should arouse suspicion of IgG4RD as many patients can have 25 or more times the normal levels of IgG4. However, between 20% and 40% of patients have normal IgG4 serum concentrations, even though they meet the histopathological criteria of the disease.⁷ The IgG4 concentrations tend to be higher in patients with multiorgan disease and are not indicators of the activity of the disease nor of its response to treatment. Patients in the last stages of the disease, which is characterised by prominent sclerosis on histology, tend to have low concentrations of IgG4. Other diseases, such as atopic dermatitis, parasitic infections, pemphigus vulgaris, pemphigus foliaceus and pancreatic carcinoma, can also be associated with elevated levels of IgG4.^{8,9}

IgG4RD is more frequent in men over 50 years of age than in other demographic groups and has a tendency to form nodular lesions on organs that are frequently confused with malignancies, as happened in the present case. The pseudotumours can appear in the eye-socket, salivary glands, lungs, kidneys, lymphatic glands, retroperitoneum and other organs. Diffuse infiltrating lesions can also develop in the meninges, skin, aorta or peripheral nerves. Sometimes only one or two organs are affected; in other cases, multiple organs are affected.^{10,11} The largest case-series analysis to date (n=114) revealed that 31% had systemic or multiorgan disease, 24% had pancreaticobiliary

Figure 5 Nearing the tail of the pancreas with a yellow lesion extending to the peripancreatic fat tissue.

Figure 6 Cut surface of the kidney showing yellow nodules predominantly cortical.

disease, 20% had the disease in the head or neck, 14% had thoracic disease and 11% had retroperitoneal disease.¹² Patients with IgG4RD also often have a history of allergic rhinitis, sinusitis, asthma and other allergies. Some patients exhibit elevated serum IgE levels and peripheral eosinophilia. The symptoms of the disease tends to appear over months and years and diagnosis is achieved on average 13.5 months (4–60 months) after the onset.¹³ The majority of patients feel fine, although when the disease is systemic, some patients feel severely ill with general symptoms, fever and elevated acute phase reactants in the serum.⁶

To diagnose IgG4RD, IgG4-positive plasma cell numbers should be elevated and three histopathological criteria should be met, namely, inflammatory lymphoplasmacytic infiltration, fibrosis with a storiform pattern and obliterative phlebitis. These changes cause atrophy and loss of specialised structures of different tissues.¹⁴ All tissues undergo similar changes, irrespective of which an organ is affected.^{15,16}

It was believed that the elevation of IgG4-positive plasma cell numbers is a highly specific marker of the disease. However, it is now known that this finding is non-specific because other diseases can also exhibit it, including vasculitis associated with ANCA, rheumatoid arthritis, inflammatory intestinal disease, Rosai-Dorfman disease, autoimmune atrophic gastritis,

Figure 7 Right adrenal. Retroperitoneal soft tissue fibrosis and chronic inflammatory infiltrate. Haematoxylin and eosin.

Figure 8 Retroperitoneal soft tissue nodular sclerosis and lymphocyte accumulations. Haematoxylin and eosin $\times 40$.

Castleman disease, primary sclerosing cholangitis, perforating collagenosis, inflammatory myofibroblastic tumour and some carcinomas.^{17 18} It is recommended that the plasma cells in the different organs are quantified and compared to the cut-off points established by experts in 2012.^{17 18} These cut-off points vary from more than 10 IgG4-positive plasma cells in pancreas, liver or kidney biopsies to more than 200 IgG4-positive cells in skin biopsies. It should be emphasised that the number of positive cells should not be used as a diagnostic criterion in isolation as other diseases can exhibit elevated IgG4-positive plasma cell numbers, particularly when there is considerable sclerosis. Some researchers suggest that if the proportion of IgG4-positive and IgG-positive plasma cells exceeds 40%, IgG4RD can be diagnosed.¹⁴ However, the consensus among experts is that this criterion is not acceptable itself because there are cases with IgG4-positive/IgG-positive ratios that exceed 50%¹⁸ yet do not meet the histopathological criteria of IgG4RD. Examples are rheumatoid arthritis and Castleman disease, which are characterised by elevated serum concentrations of interleukin-6.¹⁹

While the gold standard for the diagnosis of IgG4RD is the combination of histopathological data and elevated IgG4-positive plasma cell numbers, the presence of tissues that exhibit particular characteristics in the appropriate context is considered to be sufficient evidence for the clinicopathological diagnosis of IgG4RD.²⁰ Three categories of evidence have been

Figure 9 Steriorm fibrosis associated with lymphoplasmacytic inflammatory infiltrate. Masson staining $\times 100$.

Figure 10 Pancreas with obliterative phlebitis. Elastic fibre staining $\times 100$.

proposed. The first is characterised by histological data that are highly suggestive of IgG4RD, as at least two of the three histological results are obtained. In addition, there should be high IgG4-positive plasma cell counts in accordance with established parameters and an IgG4-positive/IgG-positive plasma cell ratio that exceeds 40%.¹⁸ The second category is characterised by histological data that indicates probable IgG4RD, where one histopathological criterion is met (generally inflammatory lymphoplasmacytic infiltration) along with an adequate IgG4-positive plasma cell count. In such cases, clinical, radiological and serological evidence is required to confirm the diagnosis. This can include IgG4 serum levels that exceed 135 mg/dl and radiological or pathological evidence showing that another organ is affected. The third category is characterised by insufficient histological data to diagnose IgG4RD. Here, the biopsies exhibit inflammatory lymphoplasmacytic infiltration but without a concomitant elevation in the plasma cell number or the presence of fibrosis without a storiform pattern.^{17 18}

The affliction of the thyroid is recognised most often because some patients exhibit hyperthyroidism and elevated levels of antithyroglobulin antibodies. Indeed, Riedel thyroiditis has been identified as a manifestation of IgG4RD.²¹ At the beginning of the IgG4RD illness, thyroid biopsies exhibit histopathological characteristics of IgG4RD but when the illness is advanced, only fibrosis is present, as occurred in the present case. Recently, a variant of Hashimoto thyroiditis that is

Figure 11 Reaction positive for IgG4 immunoperoxidase $\times 400$.

responsible for hypothyroidism in some patients was suggested to be part of the IgG4RD spectrum.²²

IgG4RD-related lymphadenopathy can appear earlier, at the same time or after the diagnosis of the disease. Generally, various groups of lymph nodes are affected, such as the mediastinal, abdominal and axillaries lymph nodes. Patients may exhibit polyclonal hypogammaglobulinaemia, elevated serum concentrations of IgG4 and elevated serum IgE and IgG levels. In such cases, it is common for biopsies to be performed because of a presumptive diagnosis of lymphoma, Castleman disease or metastatic carcinoma. Five patterns have been described in these cases: (I) similarity to Castleman disease, (II) follicular hyperplasia, (III) interfollicular expansion, (IV) progressive transformation of germinal centres and (V) similarity to an inflammatory pseudotumour. In the case presented here, the last pattern was present. All patterns are associated with an elevated number of IgG4-positive cells and an IgG4-positive/IgG-positive ratio exceeding 40%.^{8 23 24} Half of the patients with IgG4-related pulmonary disease exhibit cough, haemoptysis, dyspnoea, pleural effusion and thoracic pain. In others, the disease is asymptomatic and is discovered by imaging studies. There are six morphological patterns that are based on the radiological and histopathological viewpoints: (1) nodules present, as in the case presented here, (2) thickening of the hilum; (3) interstitial/ alveolar disease with a honeycomb pattern, diffuse images in polished glass and bronchiectasis; (4) rounded opacities in polished glass; (5) pleural thickening or effusions; and (6) extrinsic compression of the superior airways because of fibrosing mediastinitis.^{8 23 25}

The symptomatology of patients with AIP differs from that found in other forms of pancreatitis. Typically, the patients exhibit obstructive jaundice. However, this did not develop in this case because the sclerosing lesion was in the tail of the pancreas. There is also weight loss, as in this case, and mild or moderate abdominal discomfort, which was also very evident and developed over a long time in the case presented here. The clinical and radiological data (which indicate invasive masses) lead to the suspicion of pancreatic carcinoma. The typical tomographic findings that show a pancreas with a sausage-like appearance is confirmed by a fine-needle biopsy or by retrograde endoscopic cholangiopancreatography.^{8 23 26}

In the kidneys and the urinary tract, IgG4RD can be manifested by tubulointerstitial nephritis (TIN). Only 7% of patients with renal disease exhibit membranous glomerulonephritis (MGN). The majority of patients with TIN exhibit acute or chronic progressive renal insufficiency (as occurred in this case). In others, it manifests as a renal mass. In some cases, both are present. In patients with TIN, 80% have elevated serum IgG or IgG4 levels. Other findings include a decline in C3 and C4 levels, peripheral eosinophilia, proteinuria, microscopic haematuria and low levels of antinuclear antibodies. In x-rays, the lesions are frequently bilateral, multiple and predominantly in the cortex (as in this case). Diffuse nephromegaly can also be observed. The biopsy or nephrectomy shows inflammatory lymphoplasmacytic infiltration of IgG4-positive plasma cells, fibrosis and tubular atrophy, and the tubular basal membranes show IgG4 deposits. Patients with IgG4-associated MGN exhibit proteinuria in the nephrotic range. The glomerulopathy is probably secondary to the deposit of immune complexes and not the result of the inflammatory process.^{8 23 27}

Retroperitoneal fibrosis is one of the manifestations of IgG4RD. The abdominal aorta is frequently involved in this condition and can adopt two macroscopic patterns: the formation of nodes or masses or the formation of plaques. Depending

on the areas affected by this form of the disease, it can be classified as (1) retroperitoneal fibrosis; (2) inflammatory aneurysm of the aorta; (3) a combination of retroperitoneal and aortic disease and (4) thoracic aortitis.^{8 23 28} In the case presented here, retroperitoneal fibrosis in the form of a plaque that affected the suprarenal glands and surrounded the kidneys was observed.

The majority of cases of IgG4-related cholecystitis are asymptomatic and are detected incidentally. Of the AIP cases, 25% are associated with acalculous lymphoplasmacytic cholecystitis that is rich with IgG4-positive cells and is predominantly an extramural condition.^{8 23}

Gaps in our understanding of IgG4RD remain. The purpose of this report was to provide information about a case that was sadly fatal but that permitted a complete histopathological study of the damaged tissues. The presence of characteristic histopathological data was identified and this correlated with elevated IgG4 levels and clinical and radiological data. These lines of evidence were integrated into a diagnostic algorithm for IgG4-related multiorgan disease.

The optimal treatment approach for IgG4RD has not been established. Data on treatment are derived primarily from previous experience with patients with AIP. Several reports have emphasised that serum IgG4 concentrations decline in most patients after treatment with glucocorticoids, but they still remain above normal levels, in some patients, the disease remains refractory to glucocorticoid tapering. IP appears to relapse in up to one-third of the patients treated with a maintenance dose of glucocorticoids and in more than half of those in whom a maintenance glucocorticoid regimen is not used. B lymphocyte depletion with rituximab is now utilised as a treatment approach in a growing number of conditions associated with autoimmunity. However, the precise mechanisms through which rituximab achieves its effects appear more complex than simply via the elimination of autoantibodies. Koshroshai described four patients with diverse manifestations of IgG4-RSD who underwent B lymphocyte depletion therapy with rituximab. Treatment with rituximab leads indirectly to the disappearance of IgG4-bearing plasma cells within 2 weeks.²⁹

Learning points

- There are no reports in the literature describing the changes that occur with this disease in different organs of the body.
- This is a disease that is not diagnosed and not thought of as the primary diagnosis.
- Since it is a condition that can be controlled by drug therapy, it is important to take into account the various symptoms which may present for diagnoses, and treatment may be started early.

Contributors Dr Raul Romero Cabello and Raul Romero Feregrino were the physicians in charge of the patient, Dra Minerva Lazos Ochoa and Dra Belem Gabiño Lopez were the pathologists who conducted the autopsy and prepared the histochemistry tests.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Hirabayashi K, Zamboni G. IgG 4- related disease. *Pathologica* 2012;104:43–55.
- 2 Sarles H, Sarles J, Muratore R, *et al.* Chronic inflammatory sclerosis of the pancreas—an autonomous pancreatic disease? *Am J Dig Dis* 1961;6:688–98.
- 3 Kawaguchi K, Koike M, Tsuruta K, *et al.* Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. *Hum Pathol* 1991;22:387–95.
- 4 Hamano H, Kawa S, Horiuchi A, *et al.* High serum IgG4 concentrations in patients with sclerosing pancreatitis. *N Engl J Med* 2001;344:732–8.
- 5 Kamisawa T, Egawa N, Nakajima H. Autoimmune pancreatitis is a systemic autoimmune disease. *Am J Gastroenterol* 2003;98:2811–2.
- 6 Umehara H, Okazaki K, Masaki Y, *et al.* A novel clinical entity, IgG4 related disease (IgG4RD): general concept and details. *Mod Rheumatol* 2012;22:1–14.
- 7 Kamisawa T, Okamoto A, Funata N. Clinicopathological features of autoimmune pancreatitis in relation to elevation of serum IgG4. *Pancreas* 2005;31:28–31.
- 8 Mukul D, Sun A, Jae Y. IgG4 related sclerosing disease, an emerging entity: a review of a multi-system disease. *Yonsei Med J* 2012;53:15–34.
- 9 Weiss L, O'Malley D. Benign lymphadenopathies. *Mod Pathol* 2013;26:588–96.
- 10 Kamisawa T, Zenimoto M, Obayashi T. IgG4 related sclerosing disease. *Rhinsho Byori* 2009;57:113–19.
- 11 Ebbo M, Grados A, Daniel L, *et al.* IgG4 related systemic disease: emergence of a new systemic disease? Literature review. *Rev Med Interne* 2012;33:23–34.
- 12 Zen Y, Path F, Nakanuma Y. IgG4-related disease. A cross-sectional study of 114 cases. *Am J Surg Pathol* 2010;34:1812–19.
- 13 Bosco J, Suan D, Varikatt W, *et al.* Extra-pancreatic manifestations of IgG4 related systemic disease: a single centre experience of treatment with combined immunosuppression. *Intern Med J* 2012;26:65–71.
- 14 Cheuk W, Chan JK. IgG4 related sclerosing disease: a critical appraisal of an evolving clinicopathologic entity. *Adv Anat Pathol* 2010;17:303–32.
- 15 Khosroshahi A, Stone JH. A clinical overview of IgG4 related systemic disease. *Curr Opin Rheumatol* 2011;23:57–66.
- 16 Hirabayashi K, Zamboni G. IgG4 related disease. *Pathologica* 2012;104:43–55.
- 17 Deshpande V. The pathology of IgG4 related disease: critical issues and challenges. *Sem Diagn Pathol* 2012;29:191–6.
- 18 Deshpande V, Yoh Z, Chan J, *et al.* Consensus statement on the pathology of IgG4 related disease. *Mod Pathol* 2012;25:1181–92.
- 19 Strehl J, Hartman A, Agaimy A. Numerous IgG4 positive plasma cells are ubiquitous in diverse localized non-specific chronic inflammatory conditions and need to be distinguished from IgG4 related systemic disorders. *J Clin Pathol* 2011;64:237–43.
- 20 Culver EL, Bateman A. IgG4-related disease: can non-classical histopathological features or the examination of clinically uninvolved tissues be helpful in the diagnosis? *J Clin Pathol* 2012;65:963–9.
- 21 Pusztaszeri M, Triponez F, Pache JC. Riedel's thyroiditis with increased IgG4 plasma cells: evidence for an underlying IgG4-related disease? *Thyroid* 2012;22:964–8.
- 22 Yaqiong L, Gengyin Z, Takahashi O, *et al.* Distinct histopathological features of Hashimoto's thyroiditis with respect to IgG4-related disease. *Mod Pathol* 2012;25:1086–97.
- 23 Stone J. IgG4-related disease: nomenclature, clinical features and treatment. *Semin Diagn Pathol* 2012;29:177–90.
- 24 Cheuk W, Chan J. Lymphadenopathy of IgG4-related disease: an underdiagnosed and overdiagnosed entity. *Sem Diagn Pathol* 2012;29:226–34.
- 25 Eunhee S, Sekiguchi H, Peikert T, *et al.* Pathologic manifestations of Immunoglobulin (Ig) G4- related lung disease. *Sem Diagn Pathol* 2012;29:219–25.
- 26 Shinagare Sh, Shingare A, Deshpande V. Autoimmune pancreatitis: a guide for the histopathologist. *Sem Diagn Pathol* 2012;29:197–204.
- 27 Cornell L. IgG4-related kidney disease. *Sem Diagn Pathol* 2012;29:245–50.
- 28 Zen Y, Path F, Kasashima S, *et al.* Retroperitoneal and aortic manifestations of immunoglobulin G4-related disease. *Sem Diagn Pathol* 2012;29:212–18.
- 29 Khosroshahi A, Bloch DB, Deshpande V, *et al.* Rituximab therapy leads to rapid decline of serum IgG4 levels and prompt clinical improvement in IgG4-related systemic disease. *Arthritis Rheum* 2010;62:1755–62.

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