· Case Report ·

IgG4-related hepatic inflammatory pseudotumor: a case report

Yang Liu[1*], Qian Wang[1], Yanyan Jia[1]

[1]Department of Infectious Diseases, Cangzhou Central Hospital, Hebei Province, China

Abstract

We report the case of a 33-year-old man who was admitted to the hospital with fatigue lasting 1 month and fever lasting 10 days. Contrast-enhanced magnetic resonance imaging of the upper abdomen revealed multiple abnormal signals in the liver, suggestive of infectious lesions. Liver biopsy pathology showed predominantly proliferative fibrous tissue with significant infiltration of plasma cells and neutrophils, raising the possibility of an IgG4-related inflammatory pseudotumor. Following treatment with cefoperazone-sulbactam sodium, the patient's body temperature returned to normal. After further evaluation, the final diagnosis was confirmed as IgG4-related hepatic inflammatory pseudotumor.

Keywords: IgG4-related disease, IgG4-related hepatic inflammatory pseudotumor, glucocorticoids

Introduction

IgG4-related diseases have been increasingly reported in recent years. Because of their involvement of multiple organs, they are often described by various departments, primarily in the form of case reports. When the liver is affected, manifestations may include bile duct inflammation or hepatic inflammatory pseudotumor (IPT), the latter being relatively rare in clinical practice. This report presents a case of IgG4-related hepatic IPT with normal IgG4 levels, initially presenting with fatigue and fever.

Case Report

The patient, a 33-year-old male delivery worker, was admitted on 3 February 2025 because of a 1-month history of fatigue and a10-day history of fever. One month prior, he began experiencing fatigue characterized by general weakness, loss of appetite, and reduced food intake, without nausea, vomiting, abdominal pain, or diarrhea. On 18 January, he visited the Respiratory and Endocrinology Departments of our hospital, where an abdominal computed tomography (CT) scan revealed a low-density shadow in the liver. The Endocrinology Department noted elevated fasting blood glucose but did not confirm diabetes. The patient did not return for follow-up and went home without any medication. Ten days before admission, he developed a fever, with a maximum temperature of 42°C, accompanied by chills but without cough, sputum, chest tightness, shortness of breath, nausea, vomiting, abdominal pain, diarrhea,

***Correspondence:**
Yang Liu; Email: shedu2000@163.com

or muscle pain. He received intravenous and oral medications—including levofloxacin—for 1 week outside the hospital, with no improvement. He then presented to our hospital's fever clinic, where an enhanced CT scan of the upper abdomen revealed a space-occupying lesion in the liver, and magnetic resonance imaging (MRI) was recommended (Figure 1), prompting hospitalization. Since the onset of illness, the patient had experienced poor appetite and sleep and had lost approximately 15 kg in weight.

The patient's medical history was unremarkable. His personal history included a 10-year history of smoking, averaging 3–4 cigarettes per day; his marital status was divorced with no children; and his family history involved both parents being alive and well.

Physical examination

The patient was conscious, with fluent speech and a thin build. No skin rashes were observed. Enlarged lymph nodes were palpable in the neck. Both pupils were equal in size and reactive to light. The lips showed no cyanosis, the pharynx was slightly red, and the tonsils were not enlarged. Lung auscultation revealed clear breath sounds without obvious dry or wet rales. The heart rate was 78 beats per minute, with strong heart sounds and a regular rhythm. No pathological murmurs were heard over any of the heart valves. The abdomen was flat and soft, with no tenderness or rebound pain. The liver was palpable below the costal margin, but the spleen was not. Shifting dullness was negative, and there was no tenderness in the liver or kidney regions. The limbs appeared normal, with no edema in the lower extremities.

Auxiliary examinations

Routine blood tests revealed a platelet count of 364.00 × 10^9/L, absolute neutrophil count of 6.56 × 10^9/L, absolute eosinophil count of 0.01 × 10^9/L, and immature granulocyte count of 0.03/L. C-reactive protein was elevated at 58.58 mg/L. Levels of alpha-fetoprotein, carbohydrate antigen 19-9, and des-γ-carboxy prothrombin were all within normal limits.

Biochemical analysis showed a total protein level of 93.90 g/L, globulin of 54.90 g/L, glucose of 6.52 mmol/L, sodium of 129.20 mmol/L, and chloride of 93.40 mmol/L. Glycated hemoglobin was measured at 6.80%. Interleukin-6 was elevated at 20.90 pg/mL. Procalcitonin was 0.35 ng/mL, and the D-dimer level was 3.60 mg/L. The erythrocyte sedimentation rate was significantly elevated at 100.00 mm/h.

The tuberculosis-specific cell-mediated immune response was negative, and the cryptococcal capsular polysaccharide antigen test was also negative. Fecal occult blood

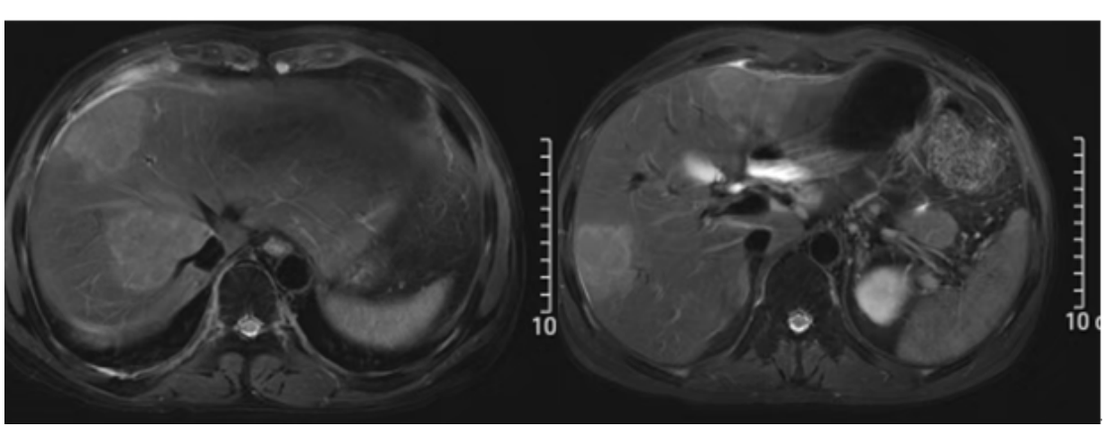


Figure 1. Abdominal magnetic resonance T2-weighted image.

testing was positive (+). Routine urinalysis was normal. The endotoxin quantitative test result was at the upper limit of normal (0.08 EU/mL; normal,<0.08 EU/mL). The fungal (1-3)-β-D-glucan test was 97.04 pg/mL (normal,<70 pg/mL), and the Aspergillus galactomannan test result was 0.05 (normal,<0.5).

A blood cell morphology and classification report showed an increased granulocyte ratio without obvious morphological abnormalities. Mild anisocytosis of mature red blood cells was observed. No nucleated red blood cells were seen among 100 white blood cells. A suboptimal lymphocyte ratio was noted, composed of mature lymphocytes. Platelets appeared scattered but were easily visible.

The PPD test was negative. Electrocardiogram indicated sinus rhythm with a heart rate of 78 beats per minute. Cardiac ultrasound showed mild tricuspid and mitral regurgitation, with normal left ventricular function.

Ultrasound of the thyroid and cervical lymph nodes revealed a normal thyroid structure and visible bilateral cervical lymph nodes.

Enhanced CT of the upper abdomen demonstrated multiple slightly low-density lesions in the liver, with MRI recommended; a dense shadow in the liver; and gas and fecal accumulation in the colon Upper abdominal MRI with contrast revealed multiple abnormal signals in the liver, suggestive of infectious lesions; multiple abnormal signals in both kidneys, suggestive of inflammatory changes; multiple enlarged lymph nodes in the hepatic portal area and retroperitoneum, indicating reactive inflammatory changes; and a small amount of fluid around the liver (Figure 1-4).

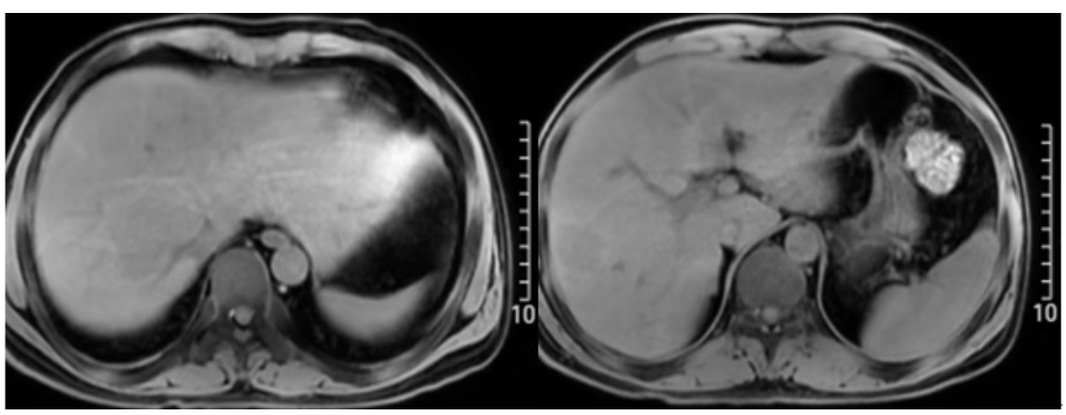


Figure 2. Abdominal magnetic resonance T1-weighted image.

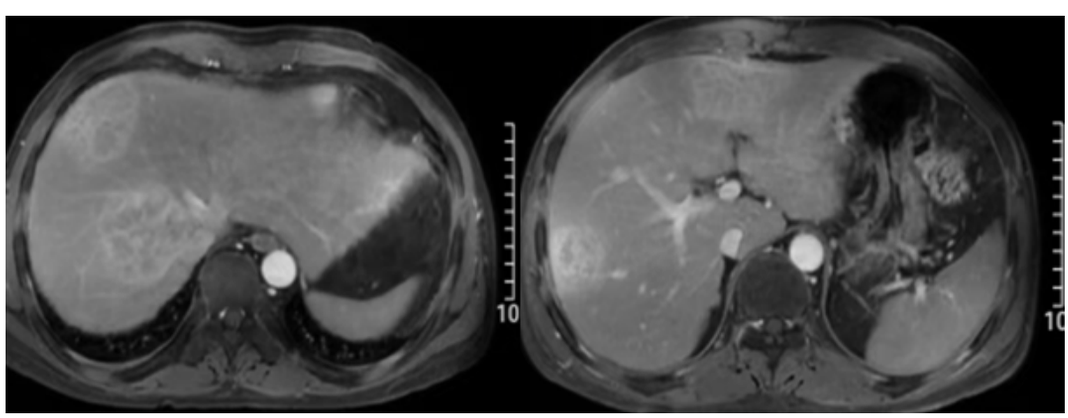


Figure 3. Abdominal magnetic resonance imaging with 5-minute delayed enhancement.

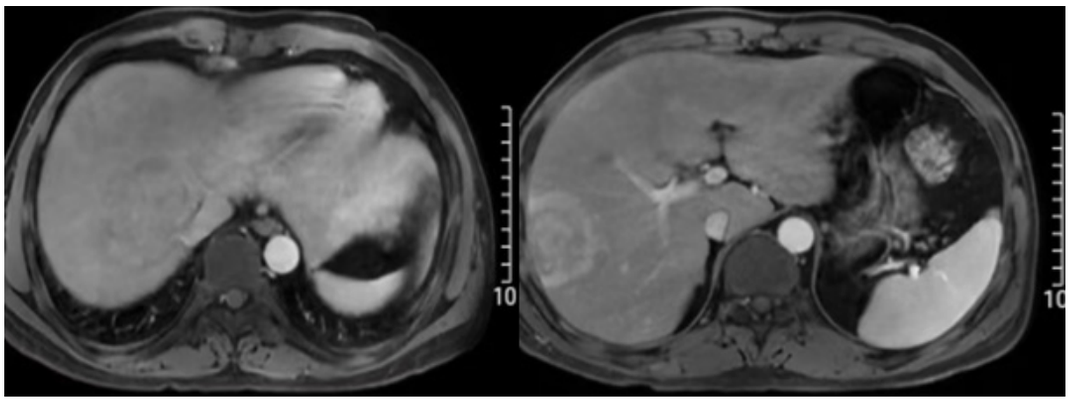


Figure 4. Abdominal magnetic resonance imaging: two-phase contrast enhancement.

Admission diagnoses

The diagnoses upon admission were a space-occupying lesion in the liver, hyponatremia, hypochloremia, and possible diabetes.

Treatment course

After admission, the patient's fasting and postprandial blood glucose levels were monitored. Following consultation with the Endocrinology Department, he was considered to be in the prediabetic stage and was prescribed acarbose 25 mg to be taken with the first bite of food, three times daily. Antibacterial treatment included intravenous cefoperazone-sulbactam sodium at 3 g every 12 hours.

On 7 February, a CT-guided liver biopsy was performed. A repeat fecal occult blood test on February 8 returned a negative result (−).

On 12 February, the liver pathology results were received. Microscopic examination of the liver tissue revealed primarily proliferative fibrous tissue with numerous plasma cells and neutrophils, raising the possibility of an IgG4-related IPT. Additional clinical tests were recommended to support the diagnosis. Immunohistochemical staining showed the following results: CD138(+), CD38(+), Lambda(+), Kappa(+), Ki-67 (30%+), Hepatocyte(−), CK7(−), ALK(1A4)(−) (positive control [+], negative control [−]), CD34(−), and SMA(+), as shown in Figure 5.

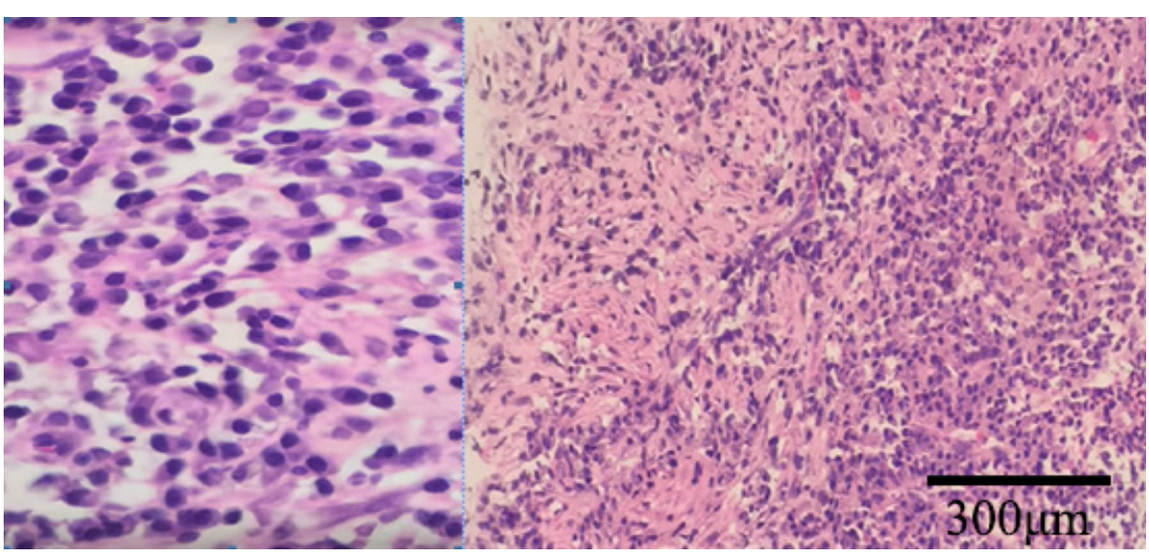


Figure 5. Liver biopsy histopathology showing fibrosis with plasma cell infiltration.

Based on the liver biopsy findings, an IgG4-related hepatic IPT was suspected. However, because our hospital was unable to confirm the diagnosis and the patient had remained afebrile for more than 3 days, he was advised to seek further diagnostic evaluation at a higher-level hospital with the pathological slides. The patient was discharged on 13 February (Table 1-2).

Follow-up

After discharge, the patient visited the Pathology Department of Beijing You'an Hospital. The results were as follows. 27 February, IgG subclass testing showed IgG1 at 21.9 g/L, while IgG2, IgG3, and IgG4 levels were within normal ranges. Total IgG was elevated at 34.4 g/L. Complement components C3 and C4 were within normal limits. Biochemical testing showed a total protein level of 90.9 g/L, albumin of 40.2 g/L, globulin of 50.7 g/L, and gamma-glutamyl transferase of 73 U/L. Autoimmune liver panel results revealed a positive antinuclear antibody at a titer of 1:320, with a nuclear granule and cytoplasmic granule pattern. An ultrasound examination of the liver, gallbladder, spleen, and pancreas revealed multiple heterogeneous hypoechoic areas in the liver, with their nature yet to be determined. Further examination was recommended. The largest lesions measured approximately 63 × 33 mm and 49 × 35 mm.

The patient subsequently borrowed the pathological slides from our hospital and submitted them for further evaluation at Beijing You'an Hospital. Based on the additional analysis, a final diagnosis of IgG4-related liver disease was confirmed. The patient was started on prednisone acetate at a dosage of 30 mg/day, and the dosage had not yet been tapered at the time of this writing.

Discussion

IgG4-related IgG4-related disease is an immune-mediated chronic inflammatory condition characterized by fibrosis and the potential to affect multiple organs and systems. Most patients exhibit elevated serum IgG4 levels, and affected tissues typically show extensive infiltration of IgG4-positive plasma cells along with varying degrees of fibrosis. In recent years, reports of IgG4-related disease have increased; however, there remains a lack of epidemiological data on this condition in China, and its pathogenesis and etiology are still not well understood [1]. Clinically, the disease often pres-

Table 1. Changes in routine blood parameters and C-reactive protein.

Date	1-18	2-3	2-6	2-12
WBC(10^9/L)	19.98	8.99	6.32	6.61
NE(10^9/L)	17.44	6.56	4.55	5.32
RBC(10^{12}/L)	3.32	3.92	3.2	3.58
HB(g/L)	98	118	94	106
PLT(10^9/L)	643	364	327	440
CRP(mg/L)	121.4	58.58	49.83	25.8

Table 2. Changes in abnormal biochemical indicators.

Date	1-18	2-3	2-6	2-12
GLB(g/L)	52.2	54.9	45.3	55.9
ALB(g/L)	30.2	39	31.6	33.8
Na^+(mmol/L)	135	28.2	140.5	134.8
Cl^+(mmol/L)	97.7	93.4	105.2	97.1

ents with a chronic onset. Significantly elevated serum IgG4 levels and the presence of mass-like lesions are among the most common manifestations. Fever is uncommon, although some patients may experience symptoms such as fatigue and weight loss. IgG4-related disease can involve a wide range of organs and tissues, with the most commonly affected sites including the lymph nodes, lacrimal glands, pancreas, lungs, bile ducts, kidneys, large blood vessels, and the heart. Many patients present with or eventually develop lesions in multiple organs, either simultaneously or sequentially.

In China, reports of IgG4-related diseases are increasing, but cases involving IPTs in organs remain rare and are mostly reported as individual cases. Affected organs have included the heart, kidneys, liver, brain parenchyma, orbits, and lungs. Cases of IgG4-related hepatic IPTs presenting primarily as liver masses are still uncommon. In 2016, Fudan University reported a retrospective analysis of MRI features of hepatic IgG4-related IPTs, which although based on only nine cases, provided clinically significant conclusions. The study found that among 11 lesions in 9 patients with hepatic IgG4-related IPT, all lesions exhibited low signal intensity on T1-weighted imaging. On T2-weighted imaging, eight lesions showed high signal intensity. On contrast-enhanced scans, five lesions demonstrated progressive enhancement, four showed persistent enhancement, and two exhibited atypical washout patterns. The main accompanying signs included delayed capsular enhancement in six lesions and central non-enhancing areas in seven. The study concluded that the MRI manifestations of hepatic IgG4-related IPT are diverse, with typical features including low signal intensity on T1-weighted imaging, slightly high signal intensity on T2-weighted imaging, and progressive or persistent high signal intensity on contrast-enhanced scans, often accompanied by delayed capsular enhancement and central non-enhancing areas [2].

Further literature review revealed that in 2024, Jiangxi Children's Hospital reported a case involving a 3-year-old boy—the youngest patient diagnosed with IgG4-related hepatic IPT to date. The patient had an 11-month history of illness, initially presenting with anemia, followed by fever and liver tenderness. Laboratory tests showed elevated inflammatory markers and serum IgG4 levels. An abdominal enhanced CT scan revealed a 7.6-cm low-density mass in the right lobe of the liver. MRI demonstrated mild low signal intensity on T1-weighted images and mild high signal intensity on T2-weighted images, raising suspicion for a malignant liver tumor. A subsequent liver biopsy revealed a fibrotic matrix with dense lymphoplasmacytic infiltration. Immunohistochemical analysis confirmed the presence of IgG4-positive plasma cells, leading to a diagnosis of IgG4-related hepatic IPT [3]. The imaging features of this case were consistent with the MRI characteristics of IgG4-related IPTs described in the aforementioned retrospective analysis.

In this case, the patient initially presented with fatigue, followed by fever, and experienced significant weight loss during the course of the disease. Laboratory tests showed elevated inflammatory markers and globulin levels. Abdominal CT revealed multiple slightly low-density shadows in the liver, and MRI demonstrated multiple patchy, slightly long T1 and T2 signals in the liver, with high signal intensity on diffusion-weighted imaging and low signal intensity on apparent diffusion coefficient imaging. Dynamic contrast-enhanced scans showed honeycomb-like enhancement, with patchy high perfusion around the lesions during the arterial phase. The intrahepatic and extrahepatic bile ducts showed no stenosis or dilation, and the bile signal appeared uniform. The initial differential diagnosis included liver abscess, liver tumor with in-

fection, hematologic disease, and plasma cell disease. Because the patient's inflammatory markers were elevated on admission and imaging findings indicated bilateral renal infiltration, the presence of perinephric infection was confirmed, and treatment with ceftoperazone-sulbactam was initiated for anti-infective therapy.

Primary hepatocellular carcinoma (HCC) is often associated with chronic hepatitis B or C infection. In its early stages, HCC may be asymptomatic, while more advanced disease may present with right upper quadrant pain. Key diagnostic differences include serum alpha-fetoprotein, which is typically elevated in HCC but usually normal in intrahepatic cholangiocarcinoma. Other tumor markers, such as carcinoembryonic antigen and carbohydrate antigen 19-9, may be elevated in intrahepatic cholangiocarcinoma but are less commonly seen in HCC. Imaging findings also differ: HCC usually exhibits arterial-phase hyperenhancement on contrast-enhanced CT or MRI, whereas intrahepatic cholangiocarcinoma often shows peripheral enhancement with progressive central delayed enhancement and portal venous phase imaging that highlights fibrous stroma.

A review of the literature revealed that the liver MRI features in this case were consistent with those previously described for IgG4-related hepatic IPTs, suggesting that the imaging characteristics supported this diagnosis. However, definitive diagnosis required both histopathological evaluation and IgG4 level testing. After discharge, the patient visited Beijing You'an Hospital, where serum IgG4 levels were found to be within the normal range. This did not meet the following diagnostic criteria proposed by Japan in 2011[4]: (1) Clinical presentation of characteristic diffuse or localized swelling or mass formation in one or more organs; (2) Elevated serum IgG4 levels (>1.35 g/L); and (3) Histopathological findings of (a) significant lymphoplasmacytic infiltration and fibrosis and (b) IgG4-positive plasma cell infiltration, defined as an IgG4+/IgG+ plasma cell ratio of>40% and >10 IgG4+ plasma cells per high-power field. A definitive diagnosis requires criteria 1+2+3; a probable diagnosis, 1+3; and a possible diagnosis, 1+2.

In this case, because the patient's serum IgG4 levels were not elevated, a definitive diagnosis of IgG4-related disease could not be made based on the above criteria. However, the literature indicates that while serum IgG4 levels are an important reference for diagnosing and assessing the severity of IgG4-related disease, they lack diagnostic specificity. Some patients may present with normal serum IgG4 levels, and elevated levels can also occur in tumors, chronic infections, and other conditions [5]. Therefore, additional diagnostic tests are necessary. In uncertain cases, patients should be advised to seek further evaluation at a higher-level hospital with their pathological slides. In this case, the patient borrowed the pathological slides from our hospital and submitted them for further analysis at Beijing You'an Hospital, where the final diagnosis confirmed IgG4-related hepatic IPT.

This case represents an atypical presentation of IgG4-related disease, which is easily misdiagnosed for several reasons: (1) the presence of fever, particularly high fever, during the course of illness; (2) laboratory findings showing significant elevations in white blood cells, neutrophils, and C-reactive protein; (3) normalization of body temperature and marked improvement in clinical symptoms following anti-infective treatment; (4) post-treatment decreases in white blood cells, neutrophils, and C-reactive protein, alongside an increase in globulin levels; and (5) evidence of renal exudation with normal urine test results, raising the possibility of IgG4-related kidney disease. Although the patient's symptoms

had improved significantly at discharge, the underlying condition had not yet been addressed. Under prolonged chronic inflammation, the affected organs may gradually develop functional abnormalities [6]. Furthermore, there have been reports of tumors arising in the context of IgG4-related disease [7,8], making timely treatment essential once a definitive diagnosis is established.

Although the involved organs may vary, the treatment approach for IgG4-related diseases is generally consistent and includes both induction and maintenance therapy. Glucocorticoids are the first-line treatment, with prednisone at 30–40 mg/day used to induce remission. After 2–4 weeks of disease control, the dose is gradually reduced to a maintenance level, typically decreasing by 5 mg every 1–2 weeks[9]. However, the optimal duration of maintenance therapy remains unclear. The efficacy of glucocorticoids largely depends on the extent of fibrosis in affected organs—patients with significant fibrosis may not respond well. In cases of poor response, immunosuppressants may be considered. Currently, these are used in patients with glucocorticoid resistance, intolerance to side effects, or recurrent disease [10]. Rituximab has also shown promise in treating refractory IgG4-related diseases [11].

In conclusion, IgG4-related diseases involve multiple organ systems and are prone to misdiagnosis. Clinicians—especially those in primary care settings—should enhance their awareness and understanding of these conditions to provide timely and accurate diagnosis and treatment.

Acknowledgments

We thank Benjamin Knight, MSc., from Liwen Bianji (Edanz) (www.liwenbianji.cn) for editing the English text of a draft of this manuscript.

Author Contributions

Yang Liu: The primary author of the paper and the main attending physician responsible for the patient during hospitalization. Jia Yanyan: Literature review and follow-up. Wang Qian: The supervising physician, who participated in revising the discussion section.

Conflicts of Interest

The authors declare they have no conflicts of interest regarding publication of this case report.

References

[1] Fei Y, Liu Y, Dong L, Yang X, Zhang W, Zhao Y. Recommendations for the diagnosis and treatment of IgG4-related disease in China. Chin J Intern Med. 2023 (62):1161–1171. In Chinese.

[2] Sheng R, Zhai C, Zeng M, JI Y, CHEN C. MRI features of hepatic IgG4-related inflammatory pseudotumor. Chin J Radiol. 2016 (50):432–435. In Chinese.

[3] Qian W, Xu Z, Liu X, Wu Z, Zhong Q, Wu C. A case report of IgG4-related hepatic inflammatory pseudotumor in a 3-year-old boy. Front Immunol. 2024 (15):1376276.

[4] Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Comprehensive diagnostic criteria for IgG4-related disease (IgG4-DR), 2011. Mod Rheumatol. 2012 (22):21–30.

[5] Zhou J, Zhang W. Interpretation of "Chinese Expert Consensus on the Diagnosis and Treatment of IgG4-Related Diseases." J Clin Hepatol. 2021 (37):2062–2065. In Chinese.

[6] Culver EL, Chapman RW. IgG4-related hepatobiliary disease: an overview. Nat Rev Gastroenterol Hepatol. 2016 (13):601–612.

(Continued on page 74)