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Contents

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OPINION REVIEW

- 2363 eHealth, telehealth, and telemedicine in the management of the COVID-19 pandemic and beyond: Lessons learned and future perspectives

Giocalone A, Marin L, Febbi M, Franchi T, Tovani-Palone MR

MINIREVIEWS

- 2369 Developing natural marine products for treating liver diseases

Wei Q, Guo JS

ORIGINAL ARTICLE

Case Control Study

- 2382 Analysis of bacterial spectrum, activin A, and CD64 in chronic obstructive pulmonary disease patients complicated with pulmonary infections

Fei ZY, Wang J, Liang J, Zhou X, Guo M

Retrospective Cohort Study

- 2393 Computed tomography perfusion imaging evaluation of angiogenesis in patients with pancreatic adenocarcinoma

Liu W, Yin B, Liang ZH, Yu Y, Lu N

Retrospective Study

- 2404 Epidemiological features and dynamic changes in blood biochemical indices for COVID-19 patients in Hebi

Nie XB, Shi BS, Zhang L, Niu WL, Xue T, Li LQ, Wei XY, Wang YD, Chen WD, Hou RF

Clinical Trials Study

- 2420 Identification and predictive analysis for participants at ultra-high risk of psychosis: A comparison of three psychometric diagnostic interviews

Wang P, Yan CD, Dong XJ, Geng L, Xu C, Nie Y, Zhang S

- 2429 Prognostic significance of peritoneal metastasis from colorectal cancer treated with first-line triplet chemotherapy

Bazarbashi S, Alghabban A, Aseafan M, Aljubran AH, Alzahrani A, Elhassan TA

Observational Study

- 2439 Effect of intraoperative cell rescue on bleeding related indexes after cesarean section

Yu YF, Cao YD

Prospective Study

- 2447 Effectiveness of the combination of workshops and flipped classroom model to improve tube fixation training for nursing students
Wang YC, Cheng HL, Deng YM, Li BQ, Zhou XZ

META-ANALYSIS

- 2457 Mortality in patients with COVID-19 requiring extracorporeal membrane oxygenation: A meta-analysis
Zhang Y, Wang L, Fang ZX, Chen J, Zheng JL, Yao M, Chen WY

CASE REPORT

- 2468 Escitalopram-induced hepatitis: A case report
Wabont G, Ferret L, Houdre N, Lepied A, Bene J, Cousein E
- 2474 Fatal community-acquired bloodstream infection caused by *Klebsiella variicola*: A case report
Long DL, Wang YH, Wang JL, Mu SJ, Chen L, Shi XQ, Li JQ
- 2484 Endoscopic extraction of a submucosal esophageal foreign body piercing into the thoracic aorta: A case report
Chen ZC, Chen GQ, Chen XC, Zheng CY, Cao WD, Deng GH
- 2491 Severe tinnitus and migraine headache in a 37-year-old woman treated with trastuzumab for breast cancer: A case report
Liu YZ, Jiang H, Zhao YH, Zhang Q, Hao SC, Bao LP, Wu W, Jia ZB, Jiang HC
- 2497 Metastatic urothelial carcinoma harboring *ERBB2/3* mutations dramatically respond to chemotherapy plus anti-PD-1 antibody: A case report
Yan FF, Jiang Q, Ru B, Fei XJ, Ruan J, Zhang XC
- 2504 Retroperitoneal congenital epidermoid cyst misdiagnosed as a solid pseudopapillary tumor of the pancreas: A case report
Ma J, Zhang YM, Zhou CP, Zhu L
- 2510 Immunoglobulin G4-related kidney disease involving the renal pelvis and perirenal fat: A case report
He JW, Zou QM, Pan J, Wang SS, Xiang ST
- 2516 Fluoroscopic removal of fractured, retained, embedded Z self-expanding metal stent using a guidewire lasso technique: A case report
Bi YH, Ren JZ, Li JD, Han XW
- 2522 Treatment and five-year follow-up of type A insulin resistance syndrome: A case report
Chen YH, Chen QQ, Wang CL
- 2529 Effective response to crizotinib of concurrent *KIF5B-MET* and *MET-CDR2*-rearranged non-small cell lung cancer: A case report
Liu LF, Deng JY, Lizaso A, Lin J, Sun S

- 2537** Idarucizumab reverses dabigatran-induced anticoagulation in treatment of gastric bleeding: A case report
Jia Y, Wang SH, Cui NJ, Liu QX, Wang W, Li X, Gu YM, Zhu Y
- 2543** Immunoglobulin G4-related disease involving multiple systems: A case report
An YQ, Ma N, Liu Y
- 2550** Daptomycin and linezolid for severe methicillin-resistant *Staphylococcus aureus* psoas abscess and bacteremia: A case report and review of the literature
Hong XB, Yu ZL, Fu HB, Cai ZH, Chen J
- 2559** Isolated scaphoid dislocation: A case report and review of literature
Liu SD, Yin BS, Han F, Jiang HJ, Qu W
- 2569** Dual biologic therapy with ocrelizumab for multiple sclerosis and vedolizumab for Crohn's disease: A case report and review of literature
Au M, Mitrev N, Leong RW, Kariyawasam V
- 2577** Cardiac rehabilitation in a heart failure patient after left ventricular assist device insertion and subsequent heart transplantation: A case report
Yang TW, Song S, Lee HW, Lee BJ
- 2584** Large retroperitoneal atypical spindle cell lipomatous tumor, an extremely rare neoplasm: A case report
Bae JM, Jung CY, Yun WS, Choi JH
- 2591** Hepatocellular carcinoma effective stereotactic body radiotherapy using Gold Anchor and the Synchrony system: Two case reports and review of literature
Masuda S, Tsukiyama T, Minagawa Y, Koizumi K, Kako M, Kinbara T, Haruki U
- 2604** Mantle cell lymphoma with endobronchial involvement: A case report
Ding YZ, Tang DQ, Zhao XJ
- 2610** Fatal systemic emphysematous infection caused by *Klebsiella pneumoniae*: A case report
Zhang JQ, He CC, Yuan B, Liu R, Qi YJ, Wang ZX, He XN, Li YM
- 2616** Takotsubo cardiomyopathy misdiagnosed as acute myocardial infarction under the Chest Pain Center model: A case report
Meng LP, Zhang P
- 2622** Cystic teratoma of the parotid gland: A case report
Liu HS, Zhang QY, Duan JF, Li G, Zhang J, Sun PF
- 2629** Silver dressing in the management of an infant's urachal anomaly infected with methicillin-resistant *Staphylococcus aureus*: A case report
Shi ZY, Hou SL, Li XW
- 2637** Drain-site hernia after laparoscopic rectal resection: A case report and review of literature
Su J, Deng C, Yin HM

- 2644** Synchronized early gastric cancer occurred in a patient with serrated polyposis syndrome: A case report

Ning YZ, Liu GY, Rao XL, Ma YC, Rong L

- 2650** Large cystic-solid pulmonary hamartoma: A case report

Guo XW, Jia XD, Ji AD, Zhang DQ, Jia DZ, Zhang Q, Shao Q, Liu Y

LETTER TO THE EDITOR

- 2657** COVID-19 pandemic and nurse teaching: Our experience

Molina Ruiz JC, Guerrero Orriach JL, Bravo Arcas ML, Montilla Sans A, Escano Gonzalez R

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Immunoglobulin G4-related disease involving multiple systems: A case report

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Abstract

BACKGROUND

IgG4-related disease (IgG4-RD), an immune-mediated chronic progressive fibroinflammatory disease, can affect the functions of several organs. Some common characteristics can be observed in different IgG4-RDs, such as higher prevalence in middle-aged and elderly male patients, raised serum IgG4 levels, abundant infiltration of IgG4-positive cells and fibrosis, diffuse or localized swelling of the affected organs, and good response to glucocorticoids treatment.

CASE SUMMARY

A 72-year-old man complained of left upper abdominal pain 3 mo ago, and he was diagnosed with acute onset of chronic cholecystitis and acute pancreatitis in the local hospital. Pain improved after relevant treatment. Several days ago, his abdominal pain worsened, and he was admitted to our hospital for further treatment. Doppler ultrasound showed that the pancreas presented with sausage-like swelling and the parenchymal echo was diffusely reduced. Gallbladder volume was increased, while the wall was rough and thickened with bilateral signs. Furthermore, the left submandibular gland was enlarged, accompanied with significantly increased blood flow signals. Finally, we found that the adventitia of the abdominal aorta and right iliac artery was thickened locally. Serum IgG4 was elevated to 12600 mg/L. Therefore, the patient was diagnosed with IgG4-RD. After treatment with methylprednisolone, he had an uneventful course and was discharged in good condition.

CONCLUSION

IgG4-RD can involve almost any organs. Ultrasound has a significant role in timely and accurately diagnosis.

Key Words: Immunoglobulin G4; Autoimmune pancreatitis; Cholecystitis; Arteritis; Ultrasound; Case report

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Core Tip: Immunoglobulin G4-related disease (IgG4-RD) can involve multiple organs and sites, such as the glands and ductal tissues. However, it is rare that a patient with more than three organs are involved at the same time, as well as the arterial lesions. In our case, we report a patient with the autoimmune inflammation, his four organs and tissues are involved, they are the aorta, pancreas, gallbladder, and submandibular gland. Meanwhile, the involved abdominal aorta and iliac artery presented as IgG4-related periarteritis. Finally, we made a comprehensive diagnosis according to the clinical histology, imaging, serology, and the response to the therapy.

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INTRODUCTION

IgG4-related disease (IgG4-RD) is an immune-mediated chronic progressive fibroinflammatory disease, which can involve multiple organs or tissues, such as pancreas, biliary tract, salivary glands, lacrimal glands, lung, kidney, and retroperitoneum[1-4]. IgG4-RD has a higher prevalence in male patients with age over 50 years[5,6] and it is easily confused with malignant tumor, infection, and other autoimmune diseases. Histopathology plays a key role in the diagnosis of IgG4-RD, and the typical pathological manifestations include lymphoplasmacytic infiltration, storiform fibrosis, and obliterative phlebitis[7,8]. The affected organs present as localized or diffused swelling, while the serum IgG4 concentration is often significantly elevated[9]. A comprehensive diagnostic criterion was established by the Japan College of Rheumatology in 2011[9] and the corelative classification criteria for IgG4-RD was also developed by the American College of Rheumatology/European League Against in 2019[10]. Besides, most patients have a good response to the steroids or rituximab therapy within a short time, but it is common for this disease to recur.

Although IgG4-RD can involve multiple organs and sites, it is still rare that a patient with more than three organs are involved at the same time and most of the affected sites are glands and ductal tissues. Meanwhile, the arterial lesions are less common in IgG4-RD. In our case, the autoimmune inflammation involved four organs and tissues, including the aorta, pancreas, gallbladder, submandibular gland, and the abdominal aorta and iliac artery presented with IgG4-related periarteritis. Finally, a comprehensive diagnosis is made, according to the clinical histology, imaging, serology, the appearance of the affected organs, and response to therapy.

CASE PRESENTATION

Chief complaints

A 72-year-old man was admitted to the gastroenterology department with pain in the left upper quadrant for 3 mo.

History of present illness

The patient had left upper abdominal pain 3 mo ago, accompanying with symptoms of anorexia, yellow urine, chills, nausea, vomiting, abdominal distention, and diarrhea, but no cough, expectoration, hemoptysis and other lung symptoms. Thus, he was referred to the local hospital. After the relevant laboratory and imaging examinations, the patient was diagnosed with acute onset of chronic cholecystitis and acute pancreatitis. The pain symptom improved after liver protective and anti-infective treatment, resolving tetany, pain relief, and fluid rehydration. Three days ago, his abdominal pain worsened and he was admitted to the Department of Gastroenterology in our hospital for further treatment.

History of past illness

He has a history of chronic hepatitis B > 30 years and hypertension for 10 years treated with nifedipine.

He underwent excision of the right mandible mass 5 mo ago, and pathological results showed massive lymphocyte infiltration with fibrous tissue hyperplasia.

Personal and family history

His father and daughter are both carriers of hepatitis B virus.

Physical examination

There was tenderness in the upper abdomen, no rebound pain and muscle tension, and no mass was touched in the whole abdomen. A surgical scar of 3-4 cm was seen in his right mandible. The others showed no obvious abnormality.

Laboratory examinations

Biochemical examinations showed that ESR was 25 mm/h (normal range 0-15 mm/h). Tumor marker carbohydrate antigen 15-3 was 24.3 U/L. Hepatitis B surface antigen (HBsAg) was 1.06 IU/mL, hepatitis Be antigen (HBeAg) was 0.02 S/CO, hepatitis B core antibody (HBcAg) was 10.07 S/CO. Finally, serum IgG4 was elevated to 12600 mg/L. The routine urine tests and renal function tests were all normal.

Imaging examinations

Abdominal ultrasound revealed that the pancreas was diffusely enlarged and sausage-shaped, in which the anteroposterior diameters of the pancreatic head, body and tail were 3.1 cm, 2.7 cm and 2.2 cm, respectively. The pancreatic parenchyma echo was diffusely reduced and the boundary was not clear (Figure 1A). The gallbladder volume was enlarged, and the wall was rough and thickened with bilateral signs. Silt-like deposits were found in the gallbladder with a range of 5.6 cm × 2.0 cm (Figure 1B). Contrast-enhanced ultrasound (CEUS) revealed that the pancreatic lesions were uniformly enhanced in the arterial phase (Figure 1C). Computed tomography scan indicated that the pancreas was enlarged, and its head had spotty, high-density foci. The gallbladder was enlarged and the cyst wall was thickened (Figure 1D). Furthermore, there were no obvious abnormalities in the lung and kidneys. Thus, autoimmune pancreatitis with gallbladder involvement was considered.

Salivary gland ultrasound showed that the right submandibular gland was almost completely removed, and the left submandibular gland was enlarged with a size of 2.5 cm × 1.4 cm. We found that the parenchymal echo was not uniform, and accompanied with reticular separation and scattered flake-like hypoecho (Figure 2A). Color doppler flow imaging suggested that the blood flow signal was significantly increased (Figure 2B). There was no obvious abnormality in the bilateral parotid and sublingual glands.

Abdominal arterial ultrasound showed that the adventitia of the abdominal aorta and right iliac artery was locally thickened with a maximum up to 5.0 mm (Figure 3A and B). CEUS demonstrated that extensive new blood vessels were distributed in the adventitia, while the intensity of imaging was evaluated to grade III (Figure 3D). These results were similar to the inflammatory activity of periarteritis. Multiple strong echogenic plaques were seen on the arterial wall, suggesting atherosclerosis of the abdominal aorta and iliac artery. Additionally, ulceration was observed in the plaque of the posterior wall of the abdominal aorta (Figure 3C).

FINAL DIAGNOSIS

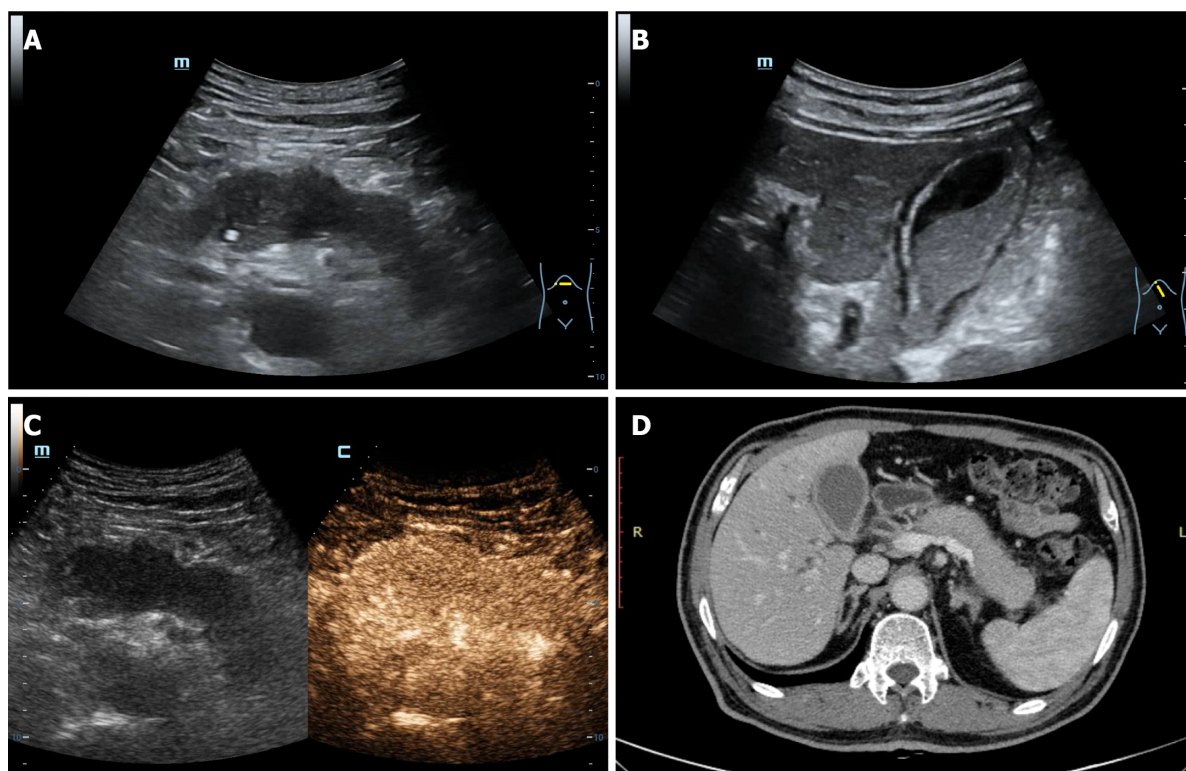
Combined with the clinical manifestations, pathological results, laboratory examinations, and imaging results, IgG4-RD simultaneously affects the pancreas (autoimmune pancreatitis), gallbladder (cholecystitis), salivary gland (submandibular adenitis), and aorta (pancreatitis).

TREATMENT

After excluding the relative contraindications for glucocorticoids, such as tumors and tuberculosis, the patient was injected intravenously with methylprednisolone and supplemented with antihypertensive and hypoglycemic treatment, gastric mucosa protection, liver protection and other treatments.

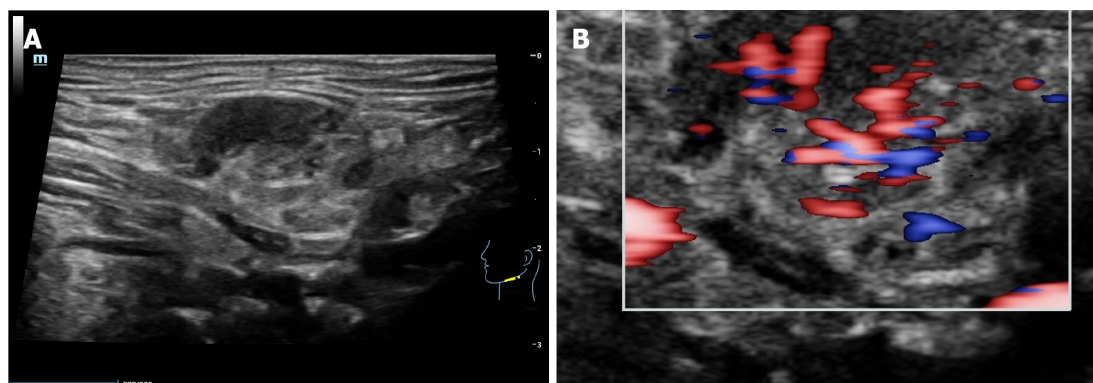
OUTCOME AND FOLLOW-UP

The patient had an uneventful course and was discharged in good general condition. The patient was instructed to take prednisolone on time and closely monitor blood pressure and blood glucose. One month later, there was no obvious abnormality when re-examined by the ultrasound and biochemical tests.



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Figure 1 The ultrasound and computed tomography images of pancreas and gallbladder. A: The pancreas is diffusely enlarged with unclear boundary and the parenchyma echo is reduced; B: The gallbladder volume is enlarged and the wall is rough, accompanying with the silt-like deposits; C: The pancreatic lesions area is uniformly enhanced in arterial phase after the intravenous ultrasound contrast-enhanced; D: Contrast-enhanced computed tomography image revealing that both the pancreas and gallbladder are enlarged and the gallbladder wall is thickened, which are consistent with the ultrasound results.

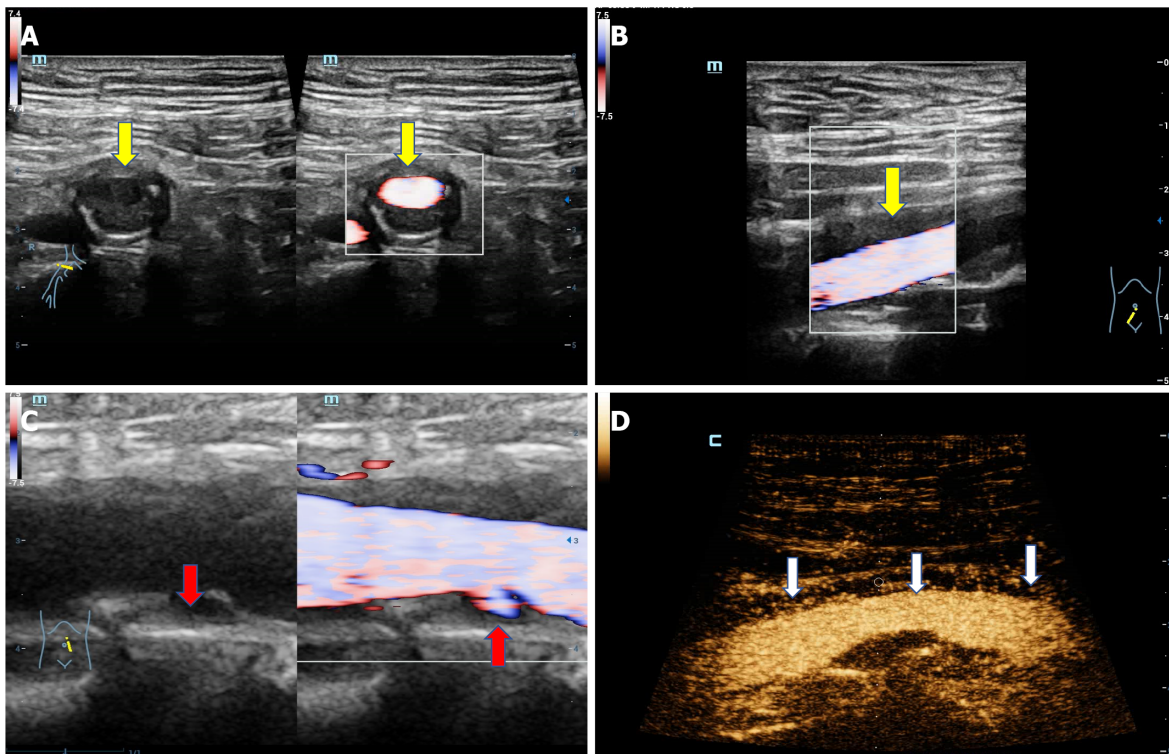


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Figure 2 The ultrasound image of the left submandibular gland. A: The submandibular gland is enlarged and its parenchyma echo is not uniform; B: Color doppler flow imaging suggesting that the blood flow signal is significantly increased.

DISCUSSION

IgG4-RD is a rare disease that can involve multiple organs at the same time[1,11,12], which is similar to many malignant, infectious, and inflammatory diseases[13]. The epidemiological data of IgG4-RD have not been completely established due to rarity and misdiagnosis[14,15]. The clinical manifestations of IgG4-RD mainly depend on the affected organs and lack specificity, which is challengeable for making correct diagnosis[16]. According to the comprehensive diagnostic criteria published in 2012[9], IgG4-RD patients must have (1) A compatible clinical presentation (swelling or masses in single/multiple organs); (2) Serum IgG4 concentration > 135 mg/dL; and (3) Histopathological evidence of marked lymphocytic and plasmocytic infiltration (IgG4-plasma cells/high-power field > 10 with IgG4/IgG-positive cell ratio > 40%). The patient in our case initially presented with epigastric pain similar to pancreatitis and was misdiagnosed with acute pancreatitis in another hospital. However, it was later



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Figure 3 The ultrasound images of the artery. A: The transverse ultrasound image of iliac artery shows that the adventitia is obviously thickened; B: The longitudinal ultrasound image of iliac artery shows that the adventitia is obviously thickened (yellow arrow); C: The longitudinal section of iliac artery, in which multiple plaques can be clearly seen on the arterial wall, and there is an ulceration in the plaque of the posterior wall (red arrow); D: Contrast-enhanced ultrasound demonstrates that extensive new blood vessels in the adventitia (white arrow).

found that the lesions involved multiple sites, and the volume of the affected organs, such as the pancreas, gallbladder, and submandibular gland increased significantly, and serum IgG4 increased to 12600 mg/L (> 1.35 g/L). The pathological results of the previous operation on the submandibular gland suggested that lymphocyte infiltration was accompanied by fibrous tissue hyperplasia. Our case fulfilled all the comprehensive diagnostic criteria, so we made the diagnosis of multisystem IgG4-RD.

If patients present with any typical clinical, serological or radiographic results, the clinical diagnosis sometimes can be made without pathological biopsy examinations[17]. If the patient has typical imaging findings of IgG4-RD, such as sausage-shaped pancreas[3,18] and periarteritis affecting the aorta below the renal artery, combined with relevant clinical manifestations and serological data, clinical diagnosis of IgG4-RD should be considered[10]. For our patient, most of the characteristic manifestations of IgG4-RD were found (such as the lesion involved the pancreas and salivary gland), along with typical imaging findings (such as sausage-shaped swollen pancreas). In addition, periarteritis affecting the abdominal aorta and iliac artery, with inflammatory thickening of the arterial wall, supported the diagnosis of IgG4-RD[19].

The 72-year-old patient presented with multiple sclerotic plaques in the abdominal aorta and iliac artery. There was ulceration on the surface of the sclerotic plaque. At that time, we suspected that the autoimmune inflammation stimulated the arterial wall for a long time and IgG4-RD caused the sclerotic plaques to rupture and ulcerate. It has been shown that IgG4-RD retroperitoneal fibrosis usually occurs around the aorta, suggesting that the adventitia of the arterial vessels may also be a target of this disease [20]. Doppler ultrasound and CEUS revealed that the adventitia of the abdominal aorta and iliac artery were thickened with multiple neovascularization, which also suggested that IgG4-RD mainly involved the adventitia. It has also been reported that IgG4-RD arteritis can lead to aneurysm formation[20], suggesting that inflammation may stimulate diffuse thickening of the arterial wall, narrow the arterial lumen, and cause aneurysm formation[19]. Therefore, if the multisite lesion does not respond to conventional treatments, IgG4-RD should be considered. More attention should be paid to the lesions involving large vessels and aneurysm formation.

Glucocorticoid therapy is the best choice after diagnosis of IgG4-RD[21], while the surgery, radiotherapy and chemotherapy should be avoided as far as possible. Before using glucocorticoids, contraindications to corticosteroids (such as tuberculosis and tumor) should be excluded[22]. For patients with the arteritis, it is important to be aware of the risk of the artery wall becoming thinner or even rupturing during glucocorticoid therapy, which requires real-time monitoring and appropriate intervention.

CONCLUSION

In our case, IgG4-RD involved several anatomical sites and multiple tissues and organs. A comprehensive diagnosis of IgG4-RD, including clinical history, imaging results, and pathological features, should be made. Doppler ultrasound as a noninvasive and convenient method plays an important role in the diagnosis of IgG4-RD. Timely and effective diagnosis could prevent serious organ injury, tissue fibrosis, and even death.

FOOTNOTES

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