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HYPERTRANSAMINASEMIA IN A PATIENT WITH ACUTE ABDOMINAL PAIN: AN UNUSUAL CASE REPORT

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ABSTRACT

Background: Hypertransaminasemia associated with acute abdominal pain can be indicative of a broad spectrum of diseases, from benign to life-threatening.

Case description: We present the case of a 72-year-old man reporting abdominal pain, unintentional weight loss and moderately elevated liver enzymes. Imaging revealed multisystem involvement including pancreas, biliary tract, thyroid, and salivary and lacrimal glands. Serological tests showed markedly elevated serum IgG4 levels. Histological findings revealed IgG4-positive lymphoplasmacytic infiltrates. In the absence of exclusion criteria, the patient met the 2019 EULAR/ACR classification criteria for IgG4-related disease (IgG4RD).

Discussion: IgG4RD is a systemic immune-mediated condition characterised by fibro-inflammatory infiltrates that can mimic malignancies or other autoimmune diseases. Its diagnosis requires an integration of clinical, radiological and histopathological data.

Conclusions: This case highlights how non-specific findings, such as hypertransaminasaemia and abdominal pain, may hide rare but treatable conditions such as IgG4RD. Early recognition is crucial to initiate immunosuppressive therapy and prevent irreversible organ damage.

KEYWORDS

IgG4-related disease, hypertransaminasemia, autoimmune pancreatitis, biliary stricture, multisystemic fibroinflammatory disease

LEARNING POINTS

- Hypertransaminasaemia and abdominal pain, although common and non-specific findings, may conceal rare systemic conditions such as IgG4-related disease.
- Multisystem involvement together with markedly elevated serum IgG4 levels are key clues that should prompt consideration of IgG4-related disease.
- Early recognition of IgG4-related disease allows timely initiation of immunosuppressive therapy, which is essential to prevent irreversible organ damage.

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INTRODUCTION

Acute abdominal pain covers a wide spectrum of conditions, ranging from benign and self-limiting to surgical emergencies, to more specialised diagnoses[1]. As challenging as the abdominal pain is the detection of abnormal liver enzyme levels (AST, ALT), which may signal a liver injury or bile flow alteration. The degree of aminotransferases alteration can be classified as mild (<5 ×), moderate (5–10 ×) or marked (>10 ×)[2]. Here, we present a case where non-specific symptoms such as hypertransaminasaemia and abdominal discomfort concealed an uncommon diagnosis: IgG4-RD, showing us how even the most non-specific clinic can hide the most curious diagnosis.

CASE DESCRIPTION

A 72-year-old man came to our Emergency Department due to abdominal pain, nausea, weight loss and fatigue. Past medical history included hyperthyroidism and hypertension, no alcohol use or smoking, and no allergies. On admission he presented conscious, apyretic and with normal vital signs. Physical examination revealed scleral jaundice, swelling of both submandibular glands, a soft and flat abdomen with no tenderness or rebound pain, and normal heart and chest examinations. Laboratory tests revealed AST 163 U/l, ALT 204 U/l, ALP 225 U/l, GGT 382 U/l, total bilirubin 2.31 mg/dl and normal amylase and lipase levels. On suspicion of hepatobiliary pathology, the patient was admitted to the Internal Medicine Department for further investigations. Imaging studies (abdomen ultrasound and CT) showed fluid collections, mild intrahepatic duct dilatation, and thickening of the gastric antrum and pylorus, raising suspicion for malignancy. A total body CT scan with contrast medium revealed thyroid enlargement with mediastinal extension, pulmonary interstitial disease, pericardial effusion, biliary tract dilatation, inhomogeneous omental apron suggesting peritoneal carcinomatosis and a slightly enlarged pancreatic head without focal lesions. A thyroid ultrasound showed signs of thyroiditis and thyromegaly. No focal lesions were seen during oesophagogastroduodenoscopy or colonoscopy, but gastric and colic biopsies were taken nonetheless. Oncological markers were negative. Then, MRI cholangiography showed a vascularised stenosis of the common hepatic duct, thickening of the right and left hepatic duct and the biliary confluence, and dilatation of the upstream biliary tract *(Fig. 1)*. These findings were worthy of further diagnostic investigation by endoscopic retrograde cholangiopancreatography, which highlighted a 'bare tree' appearance of the biliary tract due to its diffuse stenosis, and a rigid and stenotic cystic duct. However, no biopsies were taken because there was no evidence of focal lesions. During the hospital stay a more in-depth anamnesis revealed that from 2013 to 2016 our patient started a diagnostic workup due to the onset of xerostomia and xerophthalmia associated with lacrimal and major salivary glands tumefaction. At that time, he underwent a head and neck MRI which pointed out a retro-orbital pseudotumour and a volumetric increase of lacrimal glands, and a submandibular and lacrimal glands biopsy showed a lymphocyte infiltrate. This new data prompted us to consider the possibility of an autoimmune condition and the suspicion of IgG4RD was beginning to make its way into our diagnostic hypotheses. Autoimmunity assessment was carried out showing increased erythrocyte sedimentation rate, negative ANA, AMA, anti-dsDNA, pANCA and cANCA, and extractable nuclear antigen profile, while quantitation of immunoglobulin subclasses showed IgG4 at surprisingly high levels: 13.9 g/l, seven times higher than the normal value. Thanks to this new data, glucocorticoid (GC) therapy was administered. Finally, the patient underwent a CT-guided biopsy procedure of the suspected peritoneal lesions and oncology counselling, which recommended diagnostic laparoscopy in case of inconclusiveness of the biopsy samples performed, and in the suspicion of autoimmune pathology as well. A few weeks later the histological results of endoscopic examinations were available, which highlighted glandular patrimony reduction and presence of IgG4-positive lymphoplasmacytic infiltrates in the lamina propria of the gastric body and antrum. Unfortunately, a CT-guided biopsy of peritoneal tokens was inconclusive. The patient was discharged and placed in follow-up at our Rheumatology outpatient clinic, continuing corticosteroid therapy with prednisone due to the strong diagnostic suspicion of IgG4RD. This was supported by the high score obtained considering the inclusion criteria for the diagnosis of IgG4RD according to the 2019 EULAR/ACR classification. These criteria were an IgG4 level above 5× ULN, dense lymphoplasmacytic infiltrate on histopathology and immunostaining, involvement of both lacrimal and submandibular glands, pulmonary involvement, pancreas and biliary tree involvement, all combined with the absence of exclusion criteria[3].

DISCUSSION

IgG4-RD is a relatively recent clinical entity; its first recognition as a separate disorder occurred in 2003. It is a systemic immune-mediated disease, characterised by

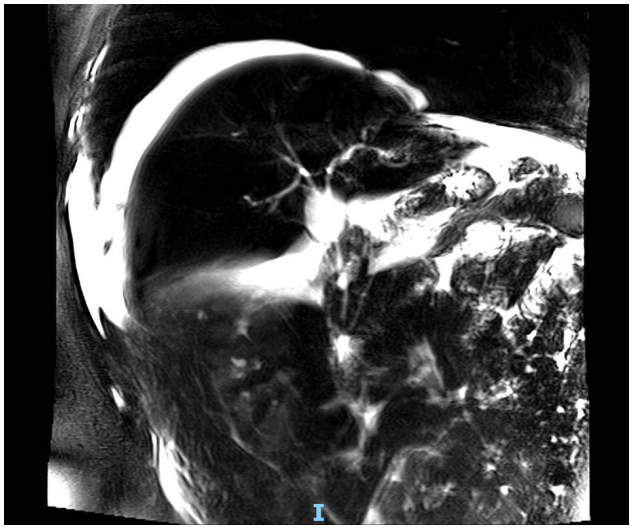


Figure 1. Patient's biliary tract from MRI.

Domain	Criteria	Points
Serum IgG4 concentration	Normal or not checked	0
Serum IgG4 concentration	> Normal but <2 × upper limit of normal	+4
Serum IgG4 concentration	2–5 × upper limit of normal	+6
Serum IgG4 concentration	>5 × upper limit of normal	+11
Bilateral lacrimal, parotid, sublingual and submandibular glands	No set of glands involved	0
Bilateral lacrimal, parotid, sublingual and submandibular glands	One set of glands involved	+6
Bilateral lacrimal, parotid, sublingual and submandibular glands	Two or more sets of glands involved	+14
Chest	Not checked or neither item listed is present	0
Chest	Peribronchovascular and septal thickening	+4
Chest	Paravertebral band-like soft tissue in the thorax	+10
Pancreas and biliary tree	Not checked or none of the items listed is present	0
Pancreas and biliary tree	Diffuse pancreas enlargement (loss of lobulations)	+8
Pancreas and biliary tree	Diffuse pancreas enlargement and capsule-like rim with decreased enhancement	+11
Pancreas and biliary tree	Pancreas (either of above) and biliary tree involvement	+19
Kidney	Not checked or none of the items listed is present	0
Kidney	Hypocomplementaemia	+6
Kidney	Renal pelvis thickening/soft tissue	+8
Kidney	Bilateral renal cortex low-density areas	+10
Retroperitoneum	Not checked or neither of the items listed is present	0
Retroperitoneum	Diffuse thickening of the abdominal aortic wall	+4
Retroperitoneum	Circumferential or anterolateral soft tissue around the infrarenal aorta or iliac arteries	+8

Table 1. IgG4RD inclusion domains and point assignments.

fibro-inflammatory infiltration and potential multi-organ involvement. The wide variety of clinical manifestations make it a diagnostic challenge, because it can be frequently confused with malignancies, infections or other autoimmune diseases[4]. IgG4RD epidemiology is poorly described; its true prevalence is unknown because of lack of recognition and a usual indolent course, which make it underestimated. However, there is a male predominance and an average age of diagnosis of between 50 and 60 years. The only modifiable risk factor recognised is cigarette smoking and occupational exposure to solvents, gases and oils suggests the possibility of chronic antigenic stimulation by environmental triggers in the immunological pathogenesis[4]. Pathophysiology is still an area of active research but its chronic nature and responsiveness to immunosuppressants suggest an underlying autoimmune mechanism. The humoral immune system plays a central role in IgG4-RD pathogenesis. A correlation has been observed between disease clinical activity and clonal expansion of circulating and tissue B cells, plasmablasts, follicular, regulatory and cytotoxic T cells (CTLs)[4]; both CTLs and B cells has been found in lymphocyte infiltrates[4]. Finally, the specific role of IgG4 antibodies is still unknown. Increased serum IgG4 levels and the presence of IgG4+ plasma cells in tissue infiltrates are IgG4-RD hallmarks, but IgG4 has anti-inflammatory activity, so it has been suggested that IgG4 could play both a protective and a pathogenic role[4]. Diagnosis requires a comprehensive evaluation of clinical, radiological and histopathological findings. In 2019, EULAR and ACR jointly approved the classification criteria for IgG4RD to help physicians to identify and diagnose this condition. As basic inclusion criteria *(Table 1)*[3], typical organ involvement affected by IgG4RD in clinical, radiological or histopathological terms must be demonstrated. Typical organs are lacrimal and

major salivary glands, orbits, lungs, paravertebral soft tissues, pancreas, biliary tract, kidneys, retroperitoneum, aorta, meninges and thyroid. If the patient has typical organ involvement, exclusion criteria *(Table 2)*[3] suggesting an alternative diagnosis must not be present. If one of the exclusion criteria is found, an alternative diagnosis should be considered, and the patient should not be classified as being affected by IgG4-RD. A score of 20 points is identified as the cut-off at or above which the majority of investigators consider the patient to be affected by IgG4RD, assuming that the patient has involvement of at least one of the typical IgG4RD organs and has not met any of the exclusion criteria[3]. Clinical manifestations are extremely heterogeneous. The development of the disease is generally indolent, although some more acute manifestations are sometimes observed. Fibro-inflammatory infiltrates in the affected organs may cause dysfunction directly by inflammation of the organ itself or determine organomegaly that may invade or compress local structures. Moreover, proliferation of the soft tissues surrounding organs may form space-occupying lesions often mistaken for malignancies[4]. Among clinical manifestations and areas affected are the following:

- *Atopia:* Allergic symptoms, increased serum IgE and eosinophilia are common[4].
- *Constitutional symptoms:* Fever and weight loss in patients who develop exocrine pancreas failure due to IgG4-related autoimmune pancreatitis[4] – our patient reported unintentional weight loss.
- *Head and neck – ocular and orbital area:* IgG4-RD is now recognised as a cause of orbital inflammation. Orbital and ocular involvement is quite varied: uveitis, orbital pseudotumour, chronic rhinosinusitis. The main differential diagnoses include lymphoma, granulomatosis with polyangiitis and Graves' orbitopathy[5].
- *Head and neck – salivary and lacrimal glands:* Symmetrical, non-painful volume increase of lacrimal, parotid and submandibular glands and symptoms of Sjögren's syndrome may occur[4].
- *Head and neck – thyroid:* Riedel's thyroiditis has recently been shown to be a manifestation of IgG4RD[5]. Thyromegaly often results in compression of local structures such as the trachea and oesophagus[4]. Our patient reported a history of symptoms related to Sjögren's syndrome, detection of retro-orbital pseudotumour and increased volume of lacrimal, major salivary glands and thyroid.
- *Chest:* Pulmonary interstitial disease, infiltrates mimicking bacterial pneumonia, nodules or masses simulating malignancies; pleural effusion with pleural thickening. Pericardial effusion, thickening and constrictive pericarditis are common. Also, coronary artery disease leading to aneurysms or sudden cardiac arrest[4].
- *Pancreas:* Acute pancreatitis responsive to corticosteroid, pancreatic mass mimicking pancreas cancer. Abdominal pain is usually less intense than in acute alcohol-induced or biliary lithiasis pancreatitis. The pancreas may show radiological abnormalities such as loss of normal lobulation or otherwise present radiologically normal. Often, the only manifestation could be exocrine or endocrine pancreatic insufficiency development[4].
- *Biliary tract:* IgG4-related biliary tract disease is linked

Category	Exclusion criteria
Clinical	Fever Unresponsive to glucocorticoids
Serological	Leukopenia and thrombocytopenia Peripheral eosinophilia Positive to PR3, MPO-ANCA, Anti-Ro or La Positive double-stranded DNA, RNP or Sm antibodies Other disease-specific autoantibody Cryoglobulinaemia
Radiological	Known radiological findings suspicious for malignancy or infection not sufficiently investigated Rapid radiologic progression Long bone abnormalities (Erdheim-Chester disease) Splenomegaly
Pathology	Cellular infiltrates suggesting malignancy not sufficiently evaluated Markers consistent with inflammatory myofibroblastic tumour Prominent neutrophilic inflammation Necrotising vasculitis Prominent necrosis Primarily granulomatous inflammation Pathologic features of macrophage/histiocytic disorder Known diagnosis of the following: • Multicentric Castleman's disease • Crohn's disease or ulcerative colitis (if only pancreaticobiliary disease is present) • Hashimoto's thyroiditis (if only the thyroid is affected)

Table 2. *IgG4RD exclusion criteria.*

with primary sclerosing cholangitis[5], associated with older age, male predominance, obstructive jaundice, weight loss and abdominal discomfort[5].

- *Kidney:* Features include tubulointerstitial nephritis, membranous glomerulonephritis and renal pseudotumour[4].
- *Peritoneum and retroperitoneum:* Retroperitoneal fibrosis (RPF) or periaortitis with poorly localised abdominal, back, hips or groin pain, and compression of local structures (ureter compression resulting in hydronephrosis, lower limb oedema)[4]. Our patient had pancreatic and biliary involvement associated with peritoneal fibrosis simulating carcinosis.
- *Nervous system and hypophysitis:* Hypertrophic pachymeningitis presenting with headache and hydrocephalus due to obstruction of cerebrospinal fluid flow. Hypophysitis with enlargement of the adenohypophysis, the neurohypophysis or both and hormone deficiency, or infraorbital nerve perineuritis are other possibilities[4].

Several serum biomarkers correlate with disease activity: a serum concentration of IgG4 is elevated in about 90% of patients with IgG4RD. Pharmacological treatment leads to a reduction of these levels but without ever reaching normal values[4]. However, high IgG4 values should not be considered specific for IgG4RD diagnosis, as these could also be found in other diseases (autoimmune, neoplastic or infectious). Other biomarkers include IgG1 and IgE, eosinophilia, serum levels of C3 and C4 complement proteins (low during active disease), increased erythrocyte sedimentation rate, increased C-reactive protein (less frequent) and specific biomarkers of organ damage[4]. Histopathological findings are also crucial. Main histopathological findings are dense lymphoplasmacytic infiltrates composed of T and B cells, eosinophils and plasma cells with occasional germinal centres, fibrosis and phlebitis. However, some patients do not present the three classical patterns, particularly when a small specimen is obtained from a CT-guided procedure[4]. Some histopathological findings are particularly atypical in IgG4RD and suggest alternative diagnoses (such as granulomatous inflammation, necrosis, neutrophilic inflammation or findings of malignancy) and these represent exclusion criteria according to 2019 EULAR classification. If treatment starts in time, organ damage can be avoided. IgG4RD is a relapsing disease, so therapy aims achieving a remission maintenance strategy and surveillance to identify disease flare-ups[4]. Remission induction is defined as the resolution of symptoms and improvement of most biochemical and radiological abnormalities; it usually occurs from a few days to several weeks[6]. Treatment strategies include GCs: this is the cornerstone of treatment and quite effective, allowing initial control of the disease; non-responsiveness is an exclusion criterion. Starting dosage is prednisone 0.5 mg/kg/d for four weeks, followed by tapering and toxicity monitoring[6]. Once remission is achieved, some centres continue with low-dose prednisone as maintenance, while others prefer steroid-sparing and close monitoring of flare-ups[4].

Disease-modifying anti-rheumatic drugs (DMARDs) such as azathioprine, mycophenolate mofetil, methotrexate, leflunomide and cyclophosphamide are commonly used in combination with glucocorticoids to reduce toxicity[6]. Rituximab, an anti-CD20 monoclonal mediates B cell depletion and reduction of fibrosis[6], inducing disease remission and prevention of flare-ups[4]. Other agents – monoclonal antibodies such as belimumab, a Bruton's tyrosine kinase inhibitor, elotuzumab and an anti-CD19 are undergoing trials[4].

CONCLUSION

Abdominal pain and hypertransaminasaemia are common and non-specific findings but may conceal unusual and investigative diagnoses such as IgG4RD, a systemic immune-mediated disease. This condition is often misdiagnosed as a malignant tumour, lymphoma, Sjögren's syndrome or other diseases[7]. Despite a chronic and indolent course, early recognition and treatment can prevent severe outcomes. Diagnosis requires a comprehensive evaluation of clinical, radiological and histopathological features, and the EULAR/ACR 2019 classification criteria may help physicians to identify it. GCs, DMARDs and rituximab are the most widely used drugs for treatment, but the optimal long-term management of this disease is still actively debated. This case emphasises the importance of comprehensive clinical evaluation, especially when standard investigations remain inconclusive.

REFERENCES

1. Cartwright SL, Knudson MP. Evaluation of acute abdominal pain in adults. *Am Fam Physician* 2008;**77**:971–978.
2. Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. *CMAJ* 2005;**172**:367–379. doi: 10.1503/cmaj.1040752
3. Wallace ZS, Naden RP, Chari S, Choi H, Della-Torre E, Dicaire JF, et al. American College of Rheumatology/European League Against Rheumatism IgG4-Related Disease Classification Criteria Working Group. The 2019 American College of Rheumatology/European League Against Rheumatism classification criteria for IgG4-related disease. *Arthritis Rheumatol* 2020;**72**:7–19. doi: 10.1002/art.41120
4. Katz G, Stone JH. Clinical perspectives on IgG4-related disease and its classification. *Annu Rev Med* 2022;**73**:545–562. doi: 10.1146/annurev-med-050219-034449
5. Stone JH, Khosroshahi A, Deshpande V, Chan JK, Heathcote JG, Aalberse R, et al. Recommendations for the nomenclature of IgG4-related disease and its individual organ system manifestations. *Arthritis Rheum* 2012;**64**:3061–3067. doi: 10.1002/art.34593
6. Zhang W, Stone JH. Management of IgG4-related disease. *Lancet Rheumatol* 2019;**1**:e55–e65. doi: 10.1016/S2665-9913(19)30017-7
7. Umehara H, Okazaki K, Masaki Y, Kawano M, Yamamoto M, Saeki T, et al. Research program for intractable disease by Ministry of Health, Labor and Welfare (MHLW) Japan G4 team. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details. *Mod Rheumatol* 2012;**22**:1–14. doi: 10.1007/s10165-011-0508-6