

ORIGINAL ARTICLE

Medicine Science 2020;9(3):526-9

The investigation of clinical and radiological findings of igG4-related autoimmune pancreatitis

 Mustafa Koc

Firat University, Faculty of Medicine, Department of Radiology, Elazig, Turkey

Received 14 April 2020; Accepted 08 May 2020

Available online 17.05.2020 with doi: 10.5455/medscience.2020.09.9242

Abstract

This study aims to investigate the clinical and radiological findings of IgG4-related autoimmune pancreatitis diagnosed in our clinic. The data of patient files diagnosed as IgG4-related autoimmune pancreatitis in our hospital between March 2015 and February 2020 were reviewed retrospectively. 17 cases were included in the study. 10 of the cases were male (59 %) and 7 were female (41 %). Their ages ranged between 47 and 72, and the mean age was 61 ± 4.5 . Clinical and laboratory findings with radiological imaging findings of the cases were investigated. The most common symptoms seen during admission to the clinic were obstructive jaundice (65 %), weight loss (53 %) and diabetes mellitus (29 %) that occurred recently. In laboratory examination, there was an increase in CEA and CA 19-9 in 9 patients (53 %). Increased IgG4 was measured in 11 patients (65 %). Some of the patients were accompanied by retroperitoneal fibrosis (3 cases), thyroiditis (2 cases), cholangitis (2 cases) and cholecystitis (1 case). In computed tomography (CT) and Magnetic Resonance Imaging (MRI) examination, diffuse increase in the size of the pancreas was observed in 14 cases (82 %). The focal increased size was most frequently observed in the pancreatic head. Recurrence developed in 5 of the patients (29 %) who received steroid treatment. As a Conclusion, autoimmune pancreatitis is a rare form of chronic pancreatitis that occurs with autoimmune mechanisms. It can be confused clinically with pancreatic cancer. Other extrapancreatic pathologies associated with IgG4 may accompany. Although IgG4 is helpful in diagnosis, the positive predictive value is low. The diagnosis of the disease is very important in terms of treatment. Clinical and radiological findings have an important role in the diagnosis of the disease.

Keywords: Autoimmune pancreatitis, computed tomography, magnetic resonance imaging

Introduction

Autoimmune pancreatitis is a special form of chronic pancreatitis caused by autoimmune mechanisms. It is a rare disease and its true prevalence is unknown. In a large series of chronic pancreatitis patients, autoimmune pancreatitis was found in 2-6 % of patients [1]. Considering its clinical, serological, morphological and histological features, it is divided into two types. Type 1 autoimmune pancreatitis is an IgG4-related form in which a large number of organs are affected, with pancreatic involvement, and is more common in the Asian population. It is also called lymphoplasmocytic sclerosing pancreatitis. Type 2 autoimmune pancreatitis (idiopathic chronic pancreatitis) is limited to the pancreas and is more common in young people and Western countries. IgG4 is usually normal in type 2. [2,3].

In the literature, no statistical difference was found between abdominal pain, weight loss, jaundice, serum CEA and CA19-9 elevations in autoimmune pancreatitis and pancreatic cancer patients [4,5]. Because of that can be confused clinically, the diagnosis of autoimmune pancreatitis can be made in some cases with only postoperative histopathological findings [6]. Serum IgG4 level is increased in two-thirds of Type 1 autoimmune pancreatitis patients. However, the positive predictive value of IgG4 is low. Because, IgG4 level can also be increased in pancreatic cancer, cholangiocarcinoma, and primary sclerosing cholangitis.

In the treatment of IgG4 related autoimmune pancreatitis, steroid therapy is used. Its fast diagnosis is of great importance in terms of survey and mortality. At this time, radiological evaluations of the patient become a very important role. This study aims to review our knowledge of IgG4 related autoimmune pancreatitis and to try to accelerate the diagnosis.

Materials and Methods

After obtaining approval for the study from the Institutional Ethics Committee of University, the data of patient files diagnosed as

*Corresponding Author: Mustafa Koc, Firat University, Faculty of Medicine, Department of Radiology, Elazig, Turkey,
E-mail: mustafa23468@outlook.com

IgG4-related autoimmune pancreatitis in our hospital between March 2015 and February 2020 were reviewed retrospectively. 17 cases were included in the study. 10 of the cases were male (59 %) and 7 were female (41 %). Their ages ranged between 47 and 72, and the mean age was 61 ± 4.5 . Clinical and laboratory findings with radiological imaging findings of the cases were investigated (Table 1). The study was conducted in accordance with the principles of the Declaration of Helsinki. Statistical analysis was performed using SPSS for Windows© software, version 22.0 (Armonk, NY, USA).

Table 1. Primary Characteristics of igG4 related autoimmune pancreatitis

Age (years)	61 $\pm$ 4.5
Gender (F/M)	7/10
Clinical presentation	Obstructive jaundice, Weight loss, Diabetes mellitus
CT/MRI presentation	Diffuse increases the size of the pancreas (82 %)
Recurrence	n: 5, (29 %)

CT examination

All patients were examined by MDCT using a Toshiba Aquilion 64 Toshiba Medical Systems, Tokyo, Japan. The scanning area was identified between the diaphragm and the iliac crest. Images were of kVp 120, mAs 150-200 value, and 0.5 mm collimated cross-section thickness, 0.5 mm reconstruction interval, diameter FOV (30 cm), and with a pitch value between 1-1.5. Investigations were initiated one hour before the examination every 15 min, following a total of 1000–1500 mL oral consumption of water. All examinations were performed with the patients in the supine position and automatic injection of 1mL/kg iopromide or iohexol at a rate of 3 mL/sec through the right antecubital vein, through single breath-holding at 65 sec.

MRI examination

The 1.5T (Ingenia, Philips) MRI device was used for MRI analysis. All patients were analyzed using the 32-channelled body coil and under respiratory monitoring. Diffusion analyses were performed on all patients with the b 400 and b 1000 values, and ADC mappings were obtained from these analyses. The ADC mappings and other measurements were performed by a radiologist with experience in abdominal radiology.

The following parameters were used in the T2A fast spin-echo images obtained from the patients: Matrix: 288x251, Number of Excitations (NEX): 1.0, Field of view (FOV): 40x35 cm, cross-sectional thickness: 5 mm, space between cross-sections: 0.5 mm, Repetition Time (TR): 441 msn, TE: 80 msn.

The following parameters were obtained from the DW images: Matrix: 132x114, Number of Excitations (NEX): 2.0, Field of view (FOV): 40x35 cm, cross-sectional thickness: 5 mm,

space between cross-sections: 0.5 mm, Diffusion direction: All directions, Repetition Time (TR) and Echo Time (TE): minimum. The ADC mapping of all the patients was drawn via diffusion analysis of b-400 and b-1000 values.

A dynamic series consisted of one pre-contrast series followed by early arterial, late arterial and portal phase imaging with 32-second intervals for the start of each phase imaging.

Results

The most common symptoms seen during admission to the clinic were obstructive jaundice (65 %), weight loss (53 %) and diabetes mellitus (29 %) that occurred recently. In laboratory examination, there was an increase in CEA and CA 19-9 in 9 patients (53 %). Increased IgG4 was measured in 11 patients (65 %). Some of the patients were accompanied by retroperitoneal fibrosis (3 cases), thyroiditis (2 cases), cholangitis (2 cases) and cholecystitis (1 case). The clinical findings are summarized in table 2. In ultrasonography, routine radiological findings were identified in terms of acute pancreatitis and no contribution was made to differential diagnosis. In computed tomography (CT) and Magnetic Resonance Imaging (MRI) examination, diffuse increase in the size of the pancreas was observed in 14 cases (82 %). The focal increased size was most frequently observed in the pancreatic head. In enhanced upper abdomen CT, diffuse or focal in the main pancreatic duct stenosis was observed. Minimal peripancreatic heterogeneity was present (Figure 1). Pancreatic parenchymal calcifications and pseudocysts were not observed. Major pancreatic vascular involvement also was not observed. In 4 cases where the pancreatic head was involved, there was stenosis in the choledochal duct. In the abdomen MRI, the affected areas were generally hypointense in the T1-weighted sequence and mild hyperintense in the T2-weighted sequence (Figure 2a, b). Diffusion restriction was present in the diffusion-weighted MRI sequence (Figure 3). In enhanced dynamic abdomen MRI, progressive enhancement was observed portal venous and late venous phase due to fibrosis (Figure 4). Steroid treatment was applied in all patients supported by clinical and radiological findings for IgG4-related autoimmune pancreatitis. Recurrence developed in 5 of the patients (29 %) who received steroid treatment.

Table 2. The clinical findings of igG4 related autoimmune pancreatitis

Increased amylase level	n: 15 (88 %)
Increased CEA	n: 7 (41 %)
Increased CA19-9	n: 9 (53 %)
Increased IgG4	n: 11 (65 %)
Retroperitoneal fibrosis	n: 3
Thyroiditis	n: 2
Cholangitis	n: 2
Cholecystitis	n: 1

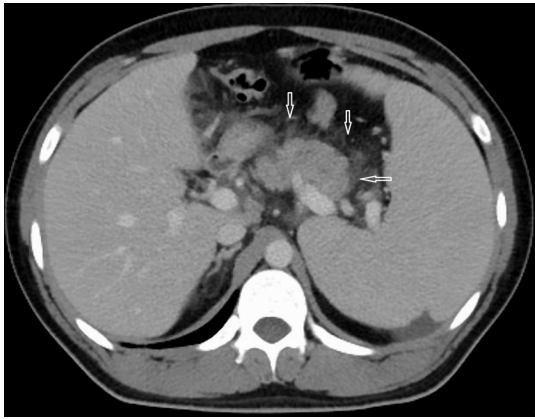


Figure 1. Axial enhanced abdominal CT showing minimal diffuse enlargement and peripancreatic heterogeneity (arrows).

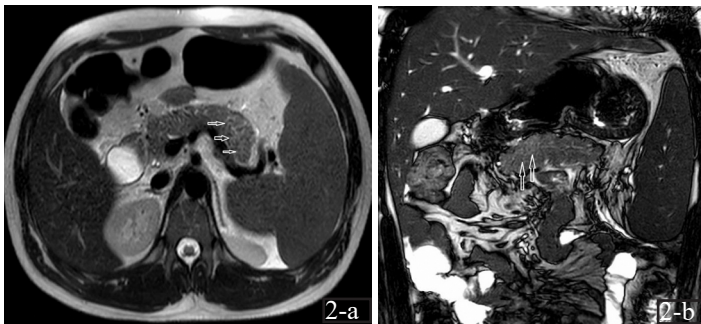


Figure 2. In axial (a) and coronal (b) T2-weighted abdomen MRI, the affected areas were mild hyperintense in the tail and body of the pancreas (arrow).

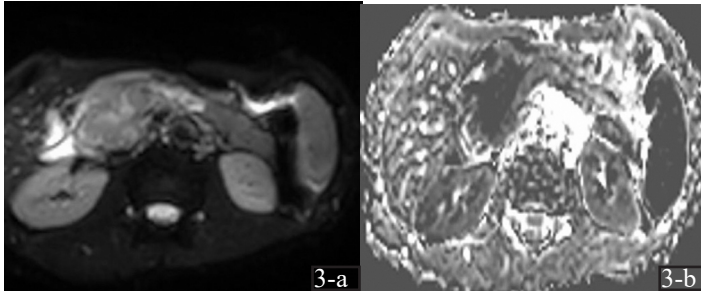


Figure 3. Diffusion MRI showed mild diffusion restriction in the head and body of the pancreas (a), ADC map (b).

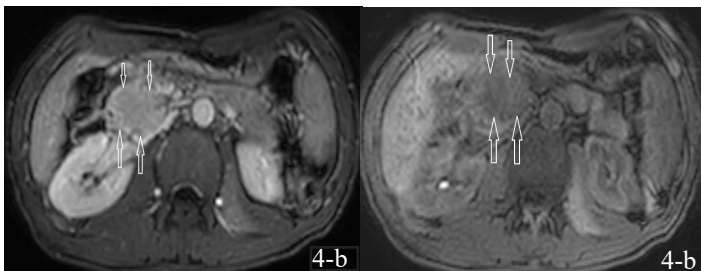


Figure 4. Dynamic abdomen MRI shows progressive enhancement in the late venous phase in the head of pancreas. Unenhanced axial T1A (a) and in the late venous phase (b) (arrows)

Discussion

Autoimmune pancreatitis can involve all or part of the pancreas. Focal involvement is most common at the head of the pancreas.

There is plasma cell infiltration that shows IgG4 positivity in the periductal and interlobular areas histologically. Inflammation causes fibrosis, irregular ductal stenosis, and acinar atrophy. When there is a slight involvement in the pancreas, only the pancreatic ducts are affected. In severe involvement, inflammation and fibrosis are seen in the acinar parenchyma in addition to the ducts. There may be enlargements in the peripancreatic and peribiliary lymph nodes [7-9].

Diffuse enlargement in the pancreas is a common finding in CT. Focal enlargement is most common in the head, less body, and tail of the pancreas. Rarely, pancreatic size may be normal. Atrophy is not usually seen. The normal lobular contour of the pancreas disappears in the affected area. In autoimmune pancreatitis, minimal peripancreatic heterogeneity may be observed, similar to acute edematous pancreatitis. Capsule-shaped hypodense rim around the pancreas (halo sign) is defined in 15-80% of patients. In the late phase, this rim can be contrasted. The fibrosis and inflammation in the bile duct and gallbladder wall thickening with contrast enhancement are defined in CT [3, 8-11].

In MRI, affected areas are hypointense in the contrast-enhanced arterial phase. Progressive enhancement is seen due to the fibrosis in the portal venous and late phase. Pancreatic adenocarcinoma may also show a similar enhancement pattern. Because of this, focal autoimmune pancreatitis should be included in the differential diagnosis [5,8,9,12]. Also, diffusion restriction appears in the diffusion-weighted MRI sequence [10]. In pancreatic cancer, there is a sudden interruption in the pancreatic duct and dilatation proximally. In autoimmune pancreatitis, there is a smooth and narrow contraction in the pancreatic duct. This feature has high specificity in differentiating focal autoimmune pancreatitis from ductal adenocarcinoma (13,14). Also significant factors differentiating focal autoimmune pancreatitis from pancreatic cancer included: homogeneous delayed enhancement on contrast-enhanced CT, and ERCP findings of long-segment stenosis of the main pancreatic duct, and a lesser degree of main duct dilatation proximal to stricture [8]. In this study, our radiological findings were compatible with the literature.

In type 1 autoimmune pancreatitis, the organs frequently accompanied are salivary glands, kidneys, lacrimal glands, and retroperitoneum. Other extrapancreatic pathologies associated with IgG4 are thyroiditis, interstitial pneumonia, cervical and mediastinal lymphadenopathy, cholangitis and cholecystitis [2,8,15,16]. In our study, the patients were accompanied by retroperitoneal fibrosis, thyroiditis, cholangitis and cholecystitis. Kawa and Hamano reported that the sensitivity of IgG was 70.5 % and that of IgG4 was 90.9 % in the diagnosis of IgG4 related autoimmune pancreatitis [17]. In another study, the limit value of 135 mg/dl for IgG4 was 95 % specific and 97 % sensitive in the differential diagnosis of pancreatic cancer and IgG4 related autoimmune pancreatitis. In addition, there was a correlation between IgG4 levels and the activity of the disease [8,9,18]. Increased IgG4 was measured in 65 % in our study.

Steroid treatment provides a complete and generally permanent clinical and radiological remission. With this treatment, it was

shown that serology returned to normal, stenosis in the ducts disappeared, the gland regained its exocrine and endocrine functions. In patients with pancreatic mass who have been given steroid treatment should be taken in terms of malignancy when near-resolution cannot be achieved within 2-4 weeks by imaging methods. Some studies have shown that recurrent pancreatitis, strictures, or non-pancreatic disease developed with steroid therapy [8,15,16,18].

Conclusion

In conclusion, igG4 related autoimmune pancreatitis is rare that occurs with autoimmune mechanisms. It can be confused clinically with pancreatic cancer. Other extrapancreatic pathologies associated with acute pancreatitis. IgG4 is helpful in diagnosis. Also clinical and radiological findings have an important role in the diagnosis of the disease.

Conflict of interests

The authors declare that they have no conflict of interest and any financial disclosures.

Financial Disclosure

All authors declare no financial support.

Ethical approval

Ethics committee approval received from the Institutional Ethics Committee of University

References

1. Tanaka A, Takikawa H. Geoepidemiology of primary sclerosing cholangitis: a critical review. *J Autoimmun.* 2013;46:35-40.
2. Okazaki K, Tomiyama T, Mitsuyama T, Sumimoto K, Uchida K. Diagnosis and classification of autoimmune pancreatitis. *Autoimmun Rev.* 2014;13:451-8.
3. Kawamoto S, Siegelman SS, Hruban RH, Fishman EK. Lymphoplasmacytic sclerosing pancreatitis (autoimmun pancreatitis): Evaluation with multidetector CT. *Radiographics.* 2008;28:157-70.
4. Weber SM, Cubukcu-Dimopulo O, Palesty JA, et al. Lymphoplasmacytic sclerosing pancreatitis: inflammatory mimic of pancreatic carcinoma. *J Gastrointest Surg.* 2003;7:129-37.
5. Dede K, Salamon F, Taller A, Bursics A. Autoimmune pancreatitis mimicking pancreatic tumor. *Magy Seb.* 2014;67:18-23.
6. Hardacre JM, Iacobuzio-Donahue CA, Sohn TA, et al. Results of pancreaticoduodenectomy for lymphoplasmacytic sclerosing pancreatitis. *Ann Surg.* 2003;237:853-8.
7. Yamamoto M, Takahashi H, Sugai S, Imai K. Clinical and pathological characteristics of Mikulicz's disease (IgG4-related plasmacytic exocrinopathy. *Autoimmun Rev.* 2005;4:195-200.
8. Lee LK, Sahani DV. Autoimmune pancreatitis in the context of IgG4-related disease: review of imaging findings. *World J Gastroenterol.* 2014; 20:15177-89.
9. Tang CSW, Sivarasan N, Griffin N. Abdominal manifestations of IgG4-related disease: a pictorial review. *Insights Imaging.* 2018;9:437-48.
10. Hafezi-Nejad N, Singh VK, Fung C, et al. MR imaging of autoimmune pancreatitis. *Magn Reson Imaging Clin N Am.* 2018;26:463-78.
11. Kim JH, Byun JH, Lee SS, et al. Atypical manifestation of IgG4 related sclerosing disease of the abdomen: Imaging findings and pathologic correlation. *AJR.* 2013;200:102-12.
12. Bor R, Farkas K, Balint A, et al. Autoimmune pancreatitis in a patient with ulcerative colitis simulating a pancreatic tumor. *Orv Hetil.* 2014;155:1000-4.
13. Ichikawa T, Sou H, Araki T, et al. Duct-penetrating sign at MRCP: usefulness for differentiating inflammatory pancreatic mass from pancreatic carcinomas. *Radiology.* 2001;221:107-16.
14. Kim HJ, Kim YK, Jeong WK, et al. Pancretic duct "Icicle sign" on MRI for distinguishing autoimmun pancreatitis from pancreatic ductal adenocarcinoma in the proximal pancreas. *Eur Radiol.* 2015;25:1551-60.
15. Brito-Zeron P, Ramos-Casals M, Bosch X, et al. The clinical spectrum of IgG4-related disease. *Autoimmun Rev.* 2014;13:1203-10.
16. Islam AD, Selmi C, Datta-Mitra A, et al. The changing faces of IgG4-related disease: Clinical manifestations and pathogenesis. *Autoimmun Rev.* 2015;14:914-22.
17. Kawa S, Hamano H. Assessment of serological markers for the diagnosis of autoimmune pancreatitis. *J Jpn Pancreas Soc.* 2003; 17:607-10.
18. Sánchez-Castanon M, de las Heras-Castaño G, Lopez-Hoyos M. Autoimmune pancreatitis: an underdiagnosed autoimmune disease with clinical, imaging and serological features. *Autoimmun Rev.* 2010 9:237-40.