Chapter 5
Steroid-Responsive Chronic Pancreatitides: Autoimmune Pancreatitis and Idiopathic Duct-Centric Chronic Pancreatitis

Nicolo' de Pretis, Yan Bi, Saurabh Mukewar, and Suresh Chari

What Is Autoimmune Pancreatitis?

Autoimmune pancreatitis (AIP) is a peculiar form of chronic pancreatitis characterized by dramatic response to steroids. Currently, there are two isoforms that are called type 1 and type 2 AIP. However, these two isoforms have distinct pathological, epidemiological, serological and clinical features, although both show a dramatic response to steroid therapy. While type 1 AIP is commonly seen in elderly patients, and is characterized by other organ involvement and elevated serum IgG4 levels, type 2 AIP is more common in young patients, is pancreas-specific and lacks of serum IgG4 elevation. Over the last few years, AIP type 1 has been considered as the pancreatic manifestation of a multiorgan disease called immunoglobulin G4 (IgG4)-related disease (IgG4-RD) that may virtually involve any organ.

Due to the distinct difference between these two subtypes and the confusion in general practitioners regarding IgG4 and Type 2 AIP, it has recently been suggested that

N. de Pretis • Y. Bi • S. Mukewar • S. Chari (✉)
Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN 55905, USA
e-mail: Chari.Suresh@mayo.edu

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the term AIP to be used solely for type 1 AIP and the term idiopathic duct-centric chronic pancreatitis (IDCP), the characteristic histopathological changes of Type 2 AIP be used for type 2 AIP. Thus, based on this new terminology, which we follow in this review, steroid-responsive chronic pancreatitis includes two diseases: AIP and IDCP. The main clinical and epidemiological features in AIP and IDCP are summarized in Table 5.1.

How Is AIP Treated?

As mentioned earlier, both AIP and IDCP are characterized by a dramatic response to steroids and the rate of response is close to 100 %. Many different steroid protocols have been proposed. The most frequently reported approach is 40 mg prednisone by mouth daily for 4 weeks, followed by tapering the dose by 5 mg per week. After 4 weeks, and at the end of the treatment, a reassessment of lab work and/or imaging should be performed to confirm response to treatment.

The rate of recurrence of different subtypes of AIP is different. In IDCP, recurrences of the disease after steroid treatment are very uncommon, while the recurrence rate in AIP is between 30 and 50 %.

Multiple strategies to treat recurrent disease have been proposed: (1) Repeat similar protocol of prednisone regimen, followed by a slower taper; (2) Start with the com-

Table 5.1 Main clinical and epidemiological features in AIP and IDCP

Type	Mean age (decade)	Gender (male) (%)	Serum IgG4 elevation (%)	OOI (%)	IBD (%)	Steroids response (%)	Relapse (%) after steroids
AIP	Sixth	75	70	20–45	5	100	30–50
IDCP	Fourth	50	15	0	20	100	0–5

OOI other organs involvement, *IBD* inflammatory bowel disease (Crohn's disease and ulcerative colitis)

bination of Prednisone and immunosuppressive drugs (IS) such as azathioprine, mycophenolate mofetil, cyclosporine or methotrexate and then taper down steroid. The IS should be continued after the steroid tapering. (3) The biological agent CD20 inhibitor Rituximab has been reported to be effective in both inducing and maintaining remission, but the experience is currently limited.

Is AIP Associated with Malignancy?

Although AIP patients may suffer from complications of chronic pancreatitis including diabetes and mal-digestion, it has not been associated with shortened life span compared to age-matched controls. Chronic pancreatitis is a well-established risk factor for pancreatic cancer. Although some case reports have been published about the occurrence of cancers, especially pancreatic cancer in AIP, however, due to the rarity of this disease, the true association remains unclear.

Other complications are typically related to AIP in the setting of a diffuse IgG4-related disease that may involve many other organs. The most relevant complications are related to the involvement of the bile ducts and of the urinary tract and are normally well responsive to steroids.

Brief Review of the Literature

AIP

AIP is a rare type of steroid-responsive chronic pancreatitis. It is presumed to be of autoimmune etiology because of its frequent association with elevated gamma globulins and autoantibodies and the dramatic response to steroid therapy. The term of AIP was first coined by Yoshida in 1995 [1] and its association with elevated IgG4 levels was first reported in 2001 by Hamano [2].

Introduction

AIP is the pancreatic manifestation of the multiorgan IgG4-Related Disease (IgG4-RD) which may virtually involve any organ in the body. IgG4-RD is defined as a fibroinflammatory condition characterized by tumefactive lesions in multiple organs, a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells, storiform fibrosis and often, but not always, elevated serum IgG4 concentrations [3].

AIP, despite being the most frequent manifestation of IgG4-RD, is considered a rare disease. The estimated prevalence of AIP in Japan is 2.2/1,00,000 [4, 5]. This disease still remains highly underdiagnosed and the real prevalence may be significantly higher. In Europe [6] and America [7], AIP is 3–4 times more common than IDCP while IDCP is rarely reported in Japan and other eastern countries.

As part of IgG4-RD, AIP is frequently characterized by the involvement of extra-pancreatic organs (Other Organ Involvement (OOI)). The presence of synchronous or metachronous OOI is reported in around two thirds of the cases. The most frequent organs involved are the biliary tree (intra- and extra-hepatic bile ducts), the kidneys, the retroperitoneum, and the salivary glands [3, 6, 7]. Different from AIP, IDCP is not part of IgG4-RD and OOI is rarely reported. However, IBD has been shown in 20–30 % IDCP patients.

Pathogenesis

The pathogens of AIP are incompletely understood. The pathogenesis and pathophysiology of AIP have been studied mainly from immunological approaches and focused for the most part on the role of IgG4.

Elevation of serum IgG4 and a massive infiltration of IgG4-expressing plasma cells in the pancreatic tissue are characteristic of AIP (and of IgG4-RD) [3, 8]. However, it is unclear if IgG4 plays a role in the pathogenesis of AIP or is simply an epiphenomenon of the disease.

Apart from elevated serum IgG4, many antibodies have been reported elevated in AIP suggesting possible autoimmune etiology. About 40 % of patients with AIP have elevated titers of anti-nuclear antibodies (ANA). Other studies have reported elevated serum autoantibodies, such as, those against lactoferrin (75 % of patients), carbonic anhydrase (55 % of patients), ubiquitin ligase, trypsin, and pancreatic secretory trypsin inhibitor [8].

Furthermore, circulating antibodies against antigens of *Helicobacter pylori* have been isolated in AIP patients, suggesting a role for infections in triggering the immunologic response [9].

Currently, none of these antibodies are used in clinical practice and IgG4 still remains the only serological marker clinically useful for diagnosis [10].

Some studies suggest that a genetic predisposition may play a role in the pathogenetic mechanism of AIP. HLA serotypes, such as DRB1*0405, DQB1*0401, are associated with a higher risk of developing AIP, while DQB1*0302 seems associated with a higher risk of relapses after steroid treatment [8]. The rarity of the disease, the limited data, and the costs of genetic analysis limit the validation of these studies and their use in clinical practice.

Clinical Presentation

AIP patients are predominantly male (62–83 %) with a mean age at diagnosis in the sixth and seventh decade of life [8]. AIP has protean clinical presentations. The most frequent symptom reported at the time of diagnosis is painless obstructive jaundice (~60 %), which may be difficult to distinguish from a malignant entity. The majority of AIP patient do not complain of any pain; in those who do the intensity of the pain is usually mild to moderate and not disabling. Other symptoms, less frequently reported, are fatigue, weight loss, hyperglycemia, steatorrhea, acute pancreatitis and symptoms related to the involvement of other

organs such as salivary gland, kidneys, retroperitoneum, and lungs. Abnormal imaging findings, such as pancreatic mass or focal/diffuse enlargement of the pancreas, are a more rare first presentation of the disease. Pancreatic atrophy, calcifications, ductal dilation and other features of advanced painless chronic pancreatitis are reported in patients with long-standing AIP.

Marked cachexia, inability to eat, and narcotic-requiring pain are more suggestive of malignant processes and are rarely seen in AIP [8, 11].

Diagnosis

The diagnosis of AIP is frequently challenging and the differential diagnosis with pancreatic cancer or other malignances is crucial. Multiple diagnostic strategies have been proposed with the most commonly used ones are HISORt, Asian Criteria, and the International Consensus Diagnostic Criteria (ICDC) developed in 2011 by the International Association of Pancreatology [10]. These criteria are focused on the diagnosis of AIP and IDCP in an early phase, while the diagnosis in very advanced stages is practically impossible. According to the ICDC, the diagnosis of AIP requires a combination of cardinal features that include:

H Histopathology of the pancreas
I Imaging features of pancreatic parenchyma and pancreatic duct
S Serology
O Other organ involvement
Rt Response to steroid therapy

Every feature is classified into level 1 and level 2, depending on the specificity of the findings. A definitive diagnosis may be reached only in presence of histopathological confirmation of AIP, whereas in the absence of a clear histopathological confirmation, various diagnostic combinations of the criteria should be used for the diagnosis [10].

Histopathology

Lymphoplasmacytic sclerosing pancreatitis (LPSP) is pathognomonic of AIP. LPSP is diagnosed when at least three of the following four histologic criteria are present on a pancreatic core biopsy or resection specimen: (a) peri-ductal lymphoplasmacytic infiltrate without granulocytic infiltration; (b) obliterative phlebitis; (c) storiform fibrosis; (d) abundant (>10 cells/HPF) IgG4-positive cells.

As reported by many authors, a diffuse IgG4 infiltration may be seen in the pancreatic tissue of these patients. However, both an elevation of serum IgG4 and a positive tissue immunostaining for IgG4 are by themselves insufficient for the diagnosis. Many other benign and malignant diseases, such as primary sclerosing cholangitis, cholangiocarcinoma and pancreatic cancer, may have an elevated serum IgG4 and positive IgG4 immunostaining. Furthermore, a European multicenter study on resected AIP showed that only 79.4 % of the patients with AIP have high tissue levels of IgG4+ plasma cells [12]. The IgG4 infiltration is highly suggestive of AIP only if the ratio IgG4/IgG is >40 % or if their frequency is >10 cells/HPF [10].

Because of the complexity of the histological finding and the frequent small size of the tissue biopsies obtained by endoscopic ultrasound-guided core biopsy, an expert pathologist is required for the interpretation of the pathological specimens. The final diagnosis of AIP is frequently difficult on preoperative biopsies and the differential diagnosis with malignant diseases may remain.

Imaging

Computed tomography (CT) and Magnetic resonance (MRI) are the most commonly used imaging techniques when pancreatic and biliary diseases are suspected. The ICDC divided the finding into parenchymal and ductal changes [10]. The pancreatic parenchyma is more easily assessed by CT and MRI, while the ductal changes are more precisely evaluated

by magnetic resonance cholangiopancreatography (MRCP) or by the more invasive endoscopic retrograde cholangiopancreatography (ERCP).

The most typical appearance of AIP is a diffuse enlargement of the pancreas, which is described in about 40 % of the patients. This particular finding is frequently highly suggestive of AIP. The diagnosis is more challenging if there is a focal enlargement with a mass-forming appearance of the pancreas, which is reported in 36 % of cases. Ruling out a malignancy may be extremely difficult in these cases. Around 30 % of patient with AIP have no enlargement of the pancreas [13].

Contrast CT scan is usually helpful in differentiating AIP from pancreatic malignancies. Most AIP patients show hypoattenuation during the arterial/pancreatic phase with a hyperattenuation during the venous/delayed phase. Pancreatic cancer usually shows hypoattenuation in the arterial phase but remains hypo-enhancing even in the venous phase. The presence of a capsule-like rim around the pancreas or around the affected area is described only in 35 % of the patients, but is reported to have a high specificity for AIP (see Fig. 5.1). The presence of a low density mass, main pancreatic duct dilation, or distal atrophy are more typical for pancreatic cancer.

On MRI, AIP appears as diffuse or focally enlarged pancreas which is hypointense on T1-weighted images, slightly hyperintense on T2-weighted images, and has heterogenously diminished enhancement in the late phase of contrast enhancement. Even on MRI a capsule-like rim may be identified; it usually appears as hypointense rim on both T1 and T2-weighted images [14].

The presence of ductal changes is frequently reported in AIP. The main techniques for investigating the ductal structures of the pancreas are MRCP and ERCP. ERCP has been reported as the technique with the highest sensitivity for visualizing the main pancreatic duct narrowing. The typical appearance of AIP on ERCP is the presence of single or multiple segmental strictures of the main pancreatic duct, without upstream dilation as seen in pancreatic cancers. The strictures are typically long unlike short strictures in pancreatic cancer.

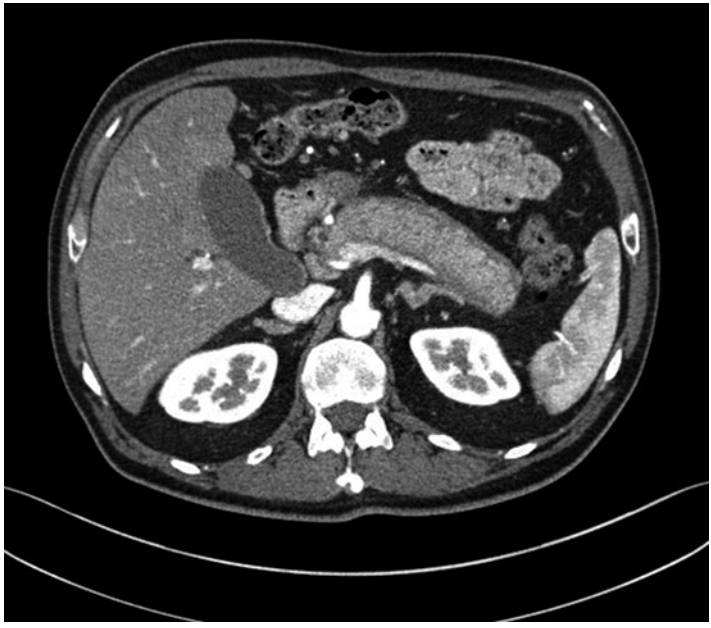

FIG. 5.1 Typical features of AIP type 1 at CT scan: diffuse enlargement of the pancreas with a peripheral capsule-like rim and dilation of the intra-hepatic bile duct

The use of secretin stimulation may be helpful in differentiating a stricture secondary to AIP because it frequently resolves after the secretin injection in AIP. While MRI is helpful in visualizing the pancreatic parenchyma and duct, MRCP should be interpreted with caution as ~25 % of normal subjects have non-visualization of portions of the pancreatic duct that could be mistaken for stricture without upstream dilation. MRCP is also useful for evaluating biliary involvement in the disease, especially the intrahepatic bile ducts [8, 14].

The role of endoscopic ultrasound (EUS) is particularly important for the diagnosis of AIP, especially in those cases in which serological and radiological criteria are not conclusive. It may be difficult to differentiate AIP from pancreatic

cancer using conventional EUS imaging alone. Some authors described particular features frequently detected in AIP and not in cancer, such as diffuse hypoechoic areas, diffuse enlargement of the gland, bile duct wall thickening, and peri-hypoechoic margins. Some studies showed that the accuracy of the technique may increase using contrast-enhanced harmonic EUS (CEH-EUS) and EUS-elastography. These additional techniques may provide additional information on the vascular patterns and the stiffness of the tissue, with a better differentiation among benign and malignant solid pancreatic masses [15]. The advantage of EUS is the ability to obtain histological samples by core biopsies for tissue diagnosis.

Serology

IgG4 is considered a serological marker of AIP and checking the levels of IgG4 in the serum is increasingly becoming a common practice. Like any other serologic markers, it is far from being optimal, and an unrestricted use may lead to diagnostic mistakes. Serum IgG4 elevation is not pathognomonic of AIP and many benign and malignant conditions (e.g., allergies, primary sclerosing cholangitis, pancreatic cancer, cholangiocarcinoma) may also have an elevation of serum IgG4. IgG4 is typically the least abundant of the IgG subclasses, making up <5 % of total serum IgG in healthy adults. It is a unique immunoglobulin with peculiar characteristics. The production of IgG4 is increased by repeated or prolonged exposure to allergens. IgG4 interacts poorly with the complement and is a weak activator of the complement pathways due to its half-antibody exchange reaction, also referred to as fragment antigen-binding (Fab)-arm exchange. Therefore, patients with AIP generally do not have decreased complement levels. In addition, IgG4 has rheumatoid-factor activity and can bind the Fc portion of other IgG antibodies, particularly other IgG4 molecules. Similar to the IgG rheumatoid factors, IgG4 can mediate a direct damage to cellular structures [3].

Clinical Use

AIP is strongly associated with an elevation of serum IgG4 and tissue infiltration with IgG4+ plasma cells, neither of which is specific to AIP. Hence, the measurement of serum IgG4 should be limited to patients with suspicion of AIP. The mean age of patients with AIP is around 60 years, and the presentation with pancreatitis is rare (see AIP clinical presentation). Therefore, in young patients with acute or recurrent pancreatitis, a routine check of IgG4 should be avoided. There is high variability in IgG4 levels between different subjects. Therefore, an acute or recurrent pancreatitis with isolated elevation in serum IgG4 levels may be inappropriately diagnosed as AIP. A pancreatitis with elevation of IgG4 should not be considered as AIP in the absence of other criteria confirming the diagnosis (see AIP clinical presentation). Furthermore, there are many other conditions and diseases, which may present with elevated serum IgG4 levels. The differential diagnosis between AIP and cancer is crucial, especially in those patients, in which the clinical presentation is jaundice, with a mass/enlargement of the pancreas head on imaging. Unfortunately, up to 10 % of the pancreatic cancers present with high IgG4 levels. Therefore, detecting an elevation in serum IgG4 levels, does not exclude a neoplastic disease.

Primary sclerosing cholangitis may also present with jaundice and elevated IgG4 levels and the differential diagnosis with AIP with biliary involvement may be very difficult. In fact, according to the ICDC serum IgG4 should be considered only as one of the criteria for the diagnosis.

The specificity of the IgG4 in differentiating AIP from other diseases, especially from cancer, is higher when serum IgG4 levels are >2× upper limit of normal. But even high IgG4 level is diagnostic as a sole criterion; a combination with the other criteria is needed for the diagnosis [10].

Treatment

As described above, both AIP and IDCP show a dramatic response to steroids. The remission of the disease under steroids is reported in close to 100 % of cases in AIP. There is no

complete consensus on the definition of remission, but at a minimum it should include resolution of inflammatory changes on imaging with normalization of the biochemical parameters (especially transaminase and cholestatic markers) and resolution of symptoms. The absence of response to steroids virtually excludes the diagnosis of AIP and requires more investigations to exclude other possible diseases, especially cancer. However, in advanced stages, the pancreas may be involved by severe fibrosis and atrophy, which are not reversible with the steroid treatment.

In a Japanese study [16], about 70 % of AIP patients improved spontaneously without any treatment. However, steroid therapy is strongly recommended for inducing the remission of the disease in symptomatic patients and in patients with extra-pancreatic lesions [17]. Furthermore, the response to steroids is useful for the confirmation of the diagnosis. However, the use of steroid trials for obtaining the diagnosis in patients with no collateral evidence of AIP should be limited to very select cases and should be considered only after a negative radiological and histological workup for malignancy. In patients with jaundice, some authors and the Japanese guidelines suggest endoscopic biliary drainage before starting steroid treatment. However, in AIP, a clinical and serological improvement of the jaundice is rapidly expected. Therefore, steroids alone without biliary drainage have been proposed in selected patients that not only avoid additional endoscopic procedures, but also facilitate the diagnosis using the fast improvement of the AIP-associated jaundice with steroid treatment.

Different strategies have been proposed for dosing steroids. The most accepted approach is a high-dosage of prednisone, 0.5–0.6 mg/kg/day or 40 mg/day for 2–4 weeks followed by tapering by 5 mg every 1–2 weeks over 3–4 months. The dose may be adjusted in old patients and in diabetics to reduce the steroid-related complications. After the first 4–6 weeks and at the end of the treatment, a clinical, radiological and biochemical reassessment should be performed to confirm response and complete remission of the

disease, respectively [8]. If biliary stent has been placed prior to onset of treatment, it should be removed at the 4–6 week assessment. Lack of response and/or persistence of biliary stricture needing replacement of biliary stent strongly suggest an alternate diagnosis.

Relapse

AIP is characterized by a high relapse rate, reported in the literature between 20 and 60 %. A slow and prolonged tapering of the steroids and continuing a low dose therapy for 1–3 years or more may decrease the relapse rate [17]. Considering the high rate of steroid-induced complications, there is no international consensus on the indiscriminate administration of a long-term steroid therapy to all patients suffering from AIP.

Some risk factors have been identified to be associated with a higher rate of relapse. The involvement of extra-pancreatic organs, particularly the proximal common bile duct (intrahepatic bile duct and /or the supra-pancreatic portion of the extrahepatic bile duct), is probably related to the highest relapse rate. Other risk factors include the presence of a diffuse enlargement of the pancreas at the initial presentation and high serum IgG4 levels, especially after steroids treatment. Certain genetic predisposition, such as the substitution of aspartic acid at position 57 of the *DQB1* gene may be a predicting factor for relapse.

AIP relapses have been classified into clinical relapse (recurrence of symptoms), radiologic relapse (recurrence of radiologic abnormalities in the pancreas or in extra-pancreatic organs), serologic relapse (elevation of serum IgG4), and biochemical relapse (elevation of liver enzymes). The presence of a clinical relapse should be confirmed by imaging evidence of radiological relapse, which is a clear indication for treatment. Presence of nonspecific symptoms without radiological or biochemical relapse is not an indication for treatment. Similarly, an isolated elevation of the serum IgG4 levels is not an indication for treatment, even if it may be

associated with a higher risk of future relapse. Marked (>2 fold) elevation of liver tests (transaminases, alkaline phosphatase), even without radiologic findings suggesting a relapse, is an indication for treatment, because it may represent an early relapse in the biliary three.

A relapse may occur during steroid taper or after withdrawal of steroids. If a relapse occurs while the patient is still on high dose (>20 mg/day) steroids, the diagnosis of AIP should be questioned. In relapses occur on low doses of steroid taper, increasing the dose of steroids and prolonging the taper is a reasonable approach; however, indefinitely exposing the patients to high-dose steroids should be avoided.

Many different strategies have been proposed for managing patients with disease relapse after a period of remission. The aim is to reinduce a complete remission and start a maintenance therapy to reduce the risk of relapses. These strategies include a second steroid treatment followed with slower steroids tapering, the combination use of steroids and immunosuppressive medications (ISs), or the use of biologic drugs (B-cell depletion therapy using monoclonal antibody) [8].

Typically, AIP relapse can be treated with the same regimen of high dose prednisone for 4 weeks followed by a prolonged taper. Some authors even keep the patient on a 2–3 years of low dose prednisone to reduce the relapse rate. A second strategy includes the combination use of steroids and ISs such as azathioprine, mycophenolate mofetil, and methotrexate as maintenance strategy. The patient should undergo a new cycle of steroids for reinducing remission. At the same time, the administration of ISs should be started and continued after steroid taper, since ISs have shown the ability to reduce the relapse rate. The third strategy is to use Rituximab (RTX), a monoclonal antibody that targeted against CD20 positive plasma cells which are mainly involved in the IgG4 production. It has been reported that RTX is able to induce and maintain remission in AIP and in other IgG4 related diseases [18]. Currently the use of RTX is limited only to patients in whom steroids therapy is contraindicated, who are intolerant to steroids or have side effects, or in those who

failed immunosuppressive therapy. As RTX is the only alternative to steroids in inducing the remission, in the near future it may become the first strategy in select patients.

Idiopathic Duct-Centric Chronic Pancreatitis (IDCP)

Introduction

AIP and IDCP are two different diseases despite many similarities in their clinical course. Both share the same presentation symptoms, including jaundice, abdominal pain, weight loss, imaging features (enlargement of the pancreas), and rapid response to steroids. However, significant differences exist between them. While, AIP is a male predominant disease with the mean age of presentation in the seventh decade of life (60 and 65), IDCP patients lack significant gender differences and the age on presentation is generally one to two decades younger than that of AIP (45 years). The prevalence of these two subtypes is quite different. IDCP appears to be relatively common in the USA and Europe but rare in East Asia; nevertheless, patients with AIP outnumber those with IDCP even in Western countries.

Pathogenesis

As a consequence of the rarity of the disease, very little is known about the pathogenesis of IDCP. It is likely an immune-related entity due to the frequent association with inflammatory bowel disease and the response to steroid treatment [8].

Clinical Presentation

IDCP may present with obstructive jaundice with diffuse pancreatic enlargement on imaging studies. While the majority of patients with AIP present with obstructive jaundice (75 %),

patients with IDCP more frequently present with abdominal pain (68 %) and pancreatitis (34 %) as well as obstructive jaundice (47 %). On imaging studies, 40 % of AIP have diffuse pancreas swelling compared to only 25 % of IDCP; majority of IDCP present with focal enlargement. The elevation of serum IgG4 is seen only in 20 % of these patients in contrast to 70 % of AIP; there is also an absence of extra-pancreatic involvement in IDCP and lack of IgG4 positive plasma cells in affected tissues. Inflammatory bowel disease (predominantly ulcerative colitis) is seen up to 20–30 % in IDCP, while it is a rare association with AIP. No clear differences are reported in the literature in the radiological presentation between AIP and IDCP.

Histological Characteristics

Periductal lymphoplasmacytic infiltrate and inflammatory stroma are present in both AIP and IDCP. Granulocytic epithelial lesions (GEL) are pathognomonic of IDCP and are often found in medium and small ducts. It is characterized by neutrophilic infiltration of pancreatic ductal epithelial, which in severe cases can resemble microabscess and lead to obliteration of ductal lumen. Pancreatic involvement may be patchy and multiple areas may show a high concentration of neutrophils. IgG4 positive plasma cells are, if present, small in number and never exceed 40 % of IgG plasma cells. Obliterative phlebitis and storiform fibrosis are less prominent than in AIP.

Diagnosis

The diagnosis of IDCP is challenging. International consensus guideline has been developed to facilitate diagnosis of IDCP [10]. Because the elevations of serum IgG4 levels and other organ involvement are typically absent in IDCP, definitive diagnosis can only be made through demonstration of GEL on histology. A diagnosis of probable IDCP can be made when idiopathic pancreatitis is associated with IBD.

Treatment

Similar to AIP patients, all patients with IDCP respond rapidly to corticosteroid therapy using a similar prednisone regimen. Unlike in AIP, disease relapses are rare in IDCP. Despite that, a clinical, biochemical and radiological reassessment is mandatory after 1 month and at the end of the steroid therapy, confirming a complete regression of the radiologic abnormalities. The absence of a radiological response or the recurrence of symptoms, especially pancreatitis, should strongly support a reevaluation of the patient and different diagnosis should be considered.

Future Directions

AIP and IDCP are rare but more frequently recognized causes of pancreatitis that require high levels of suspicion to make a diagnosis. As the field expands, we will learn more about the true incidence of the disease; understand further the disease pathogenesis using AIP animal models and explore more easily administered medical treatment that may lower the relapse rate of this disease. For IDCP, currently the diagnosis is based on pathology. With a better understanding of this disease, hopefully, noninvasive techniques can be used for this purpose.

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