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AUTOIMMUNE PANCREATITIS

[1]Dr Hafiz Rashid Mahmood,[2]Dr Yumna Ameer,[3]Dr Muhammad Shaheryar
[1]MBBS,Quaid e Azam Medical College,Bahawalpur., [2]MBBS,Rashid Latif Medical College,Lahore., [3]MBBS,Rawal Institute of Health Sciences,Islamabad.

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Abstract:
An autoimmune pancreatitis is a form of chronic fibro-inflammatory pancreatitis. It was introduced in 1995 and till now multiple pieces of research have been made to aid in its diagnosis and treatment. As technology has gained advancement so ultrasonography, magnetic resonance imaging, and computed tomography is no longer complex for the diagnosis of autoimmune pancreatitis. It is diagnosed by a combination of imaging studies like pancreatography, CT scan, laboratory analysis like autoantibodies and lgG4, and histopathological evaluations. Multiple conservative therapies are available for this disease, but many points are still unclear. These gaps have created widespread interest for pathologists, endoscopists, prevalent research, and gastroenterologists in this particular disease. This article aims to provide a better understanding of the diagnosis and treatment of autoimmune pancreatitis.

Corresponding author:
Dr. Hafiz Rashid Mahmood,
MBBS,Quaid e Azam Medical College,Bahawalpur.

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INTRODUCTION:

In 1995, autoimmune pancreatitis was described by Yoshida, a scientist. [1] He introduced this disease by elaborating its association with autoimmune manifestations. Recent research has revealed that this disease is not just linked with the pancreas, but also with several other organs like bile duct, lymph nodes, and the retroperitoneum. Autoimmune pancreatitis (AIP) is also known with other names like idiopathic duct destructive pancreatitis, primary inflammatory pancreatitis, tumefactive pancreatitis, and non-alcoholic duct destructive chronic pancreatitis and much more, all depending upon the predominant symptoms and tissue changes found on biopsy.[2,3]

Despite various technological advancements, the diagnosis of AIP at an early stage and the differential diagnosis between small pancreatitis cancers and the pancreatitis are not as easy as it seems to be, as some patients might present with issues concerning their other body parts.

DIAGNOSIS:

The chances of AIP occurrence are twice in men as in women. The usual stage of this disease development is 50- 60, but it can also occur in the 30s or late in life.

Moreover, it also varies from patient to patient that either the AIP is present alone or in association with other autoimmune disorders like primary biliary cirrhosis, sclerosing cholangitis, rheumatoid arthritis, inflammatory bowel disease, sarcoidosis, and Sjogren's syndrome. Besides, AIP has also been found to be in association with lung nodules and retroperitoneal fibrosis in some patients. [6,7]

Jaundice, weight loss, and mild abdominal pain are the most common symptoms of AIP. Severe abdominal pain is an unusual symptom. [4] However, as AIP is associated with multiple other diseases, so symptoms can vary with the relapsing-abrogating type of disease, and they may alternate with periods of remission. [8]

- **Diagnostic interpretation of Autoimmune Pancreatitis**

Agreed diagnostic criteria and nomenclature reveals that typical immunological abnormalities in AIP include the presence of autoantibodies and high levels of serum gammaglobulin, IgG or IgG4. The histopathological evidence reveals that the presence of IgG4 positive plasmacytes and storiform fibrosis with infiltration of lymphocytes are also the indicators of AIP. T regulatory cells are also found involved in the development of various autoimmune diseases and the shift of B-cell towards IgG4 that produces plasmacytes. To further expand the search and fill the empty gaps created by the complications of this disease, doctors and researchers took many important immune regulatory cells into account.

By studying the immunohistochemistry and IL-10 producing cells by flow cytometry in the peripheral blood lymphocytes in 35 plus patients with autoimmune pancreatitis, many points were highlighted. CD4 + CD 25 high Tregs, which produces IL-10 were analyzed from the peripheral blood flow. No significant differences were found among CD3+, CD4+, or CD79+ cells between the controlled sections and autoimmune pancreatitis hit sections. On the other hand, high levels of Foxp3+ and CD4+ were found in the pancreas with AIP as compared to the low level in controlled areas. When AIP is left untreated, CD4+ CD25+ high Tregs are positively interlinked. This means that these IL- 10 producing immune regulatory cells have the ability to influence IgG4 production in AIP. [9]

However, a study encapsulating patients with ileal, colonic, duodenal, or gastric biopsies revealed that IgG4+ plasma cells are numerous in controls and comparatively less in the digestive mucosa of AIP patients. Plasma and IgG4+ cell infiltration are more abundant in the colon of inflammatory bowel diseased patients than in patients with autoimmune pancreatitis. Therefore, it was concluded that immunostaining of the digestive mucosa IgG4 isn't very helpful in AIP diagnosis because these markers are detectable in other tissues of the patient as well, besides the pancreas.[10]

To effectively diagnose AIP, many criteria are reported. A detailed examination and survey showed that patients simultaneously presenting elevated autoantibodies, autoimmune disease, pancreatic disease, or disease response to steroids, were diagnosed with "autoimmune pancreatitis". Presence of elevated IgG4, high level of autoantibodies, pancreatic disease, and other autoimmune diseases are indicators of "Probable AIP" and "Possible AIP".

- **Histopathological Evaluation**

Histological evaluation of AIP show lymphocytic and plasmacytic infiltration accompanied by lymphoid follicles around the pancreatic duct. The intralobular septate and fibrosis along with obliterans phlebitis also thickens. In such conditions, it is possible that extrapancreatic lesions may develop just like primary sclerosant cholangitis. But in the AIP case, the situation can be diagnosed by the detection of IgG4+ plasma cell infiltration and their appropriate response

to corticosteroid therapy. The overall prognosis is not yet well defined, but an endoscopy might help. It can reveal the focal infiltration of plasma cells in the GIT. CT scans aids in the detection of multiple things like pancreatic enlargement, mild lymphadenopathy, or an increase in pancreatic mass. The absence of diffuse pancreatic duct stenosis reveals that it is not a carcinoma.

A combination of radiologic, laboratory and histopathological findings can lead to an accurate diagnosis of AIP. Even in the absence of serological and histopathological findings, doctors still prefer to administer short-course corticosteroid treatment for typical autoimmune pancreatitis. Due to its association with various other autoimmune disorders, AIP is sometimes introduced as a systemic disease.

Differential Diagnosis:

Some diseases come up with symptoms similar to other diseases. The diagnosis of such conditions is usually perplexing and quite challenging, as a slight misinterpretation can lead to wrong treatment and increased complications.

The most common condition, which must be differentiated from autoimmune pancreatitis is pancreatic cancer. Dual-phase CT scan has demonstrated that differentiation can be done based on enhancement characteristics of normal and carcinoma pancreas. It is observed that patients with AIP have low-value CT attenuation of the pancreatic parenchyma, as compared to normal people with normal pancreas. In the hepatic phase, the value of CT attenuation of the mass in autoimmune pancreatitis is significantly higher than that of carcinoma, but no significant difference was found in the mean value of CT attenuation of AIP and carcinoma.

DISCUSSION:

Images have revealed that the size of the pancreas increases, a halo of plasma cells and lymphocytes surrounds it. Initial examination of 33 CP- SjS cases with computed tomography or ultrasonography has shown that 90% of the patients have enlarged the pancreas upon the first presentation. [11] Granulomas may surround the pancreatic ducts and a mass can obstruct those ducts in some cases. A cross-sectional diagnosis revealed a long attenuated segment of the pancreatic duct and diffuse enlarge glands. When corticosteroids were administrated, a favorable response was observed, which also differentiated AIP from alcohol-induced pancreatitis. This is because, in AIP, a mass obstructs the biliary ducts which aren't present in cases of pancreatic cancer.

So, autoimmune pancreatitis can be diagnosed and assessed based on the following points:

1. Localized or diffused, enlarged pancreatic glands and narrowing of the pancreatic duct owing to the presence of granulomas or irregularity revealed in imaging modalities
2. Presence of high levels of autoantibodies like rheumatoid factor and antinuclear antibody, and high IgG4 serum levels
3. Local lymph node enlargement, plasma cell concentration, intralobular fibrosis and lymphocytic infiltration around the pancreatic ducts

When any of the above-mentioned conditions are present, individually or in combination with one another, then it depicts the presence of autoimmune pancreatitis.[12]

Treatment:

The autoimmune disorder not necessarily requires surgery, it can be treated with steroids. The critical point here is the differentiation between malignancy and autoimmune pancreatitis because the failure to do so can lead to abnormalities and unnecessary pancreatic resection. Past clinical trials have shown that many patients who underwent suspected pancreatic malignancy were having lymphoplasmacytic infiltrate of AIP. In such conditions, steroid therapy helps a lot, as it prevents a Whipple process or pancreatectomy for benign disease, and is effectively responsive to medical therapy.

Improvement in clinical symptoms and signs indicates either the therapy is effective for the patient or not.

The following indicators can be observed:

1. Reduce back pain, jaundice, and abdominal pain
2. Decreased pancreatic size on imaging, or stop in size enlargement
3. Recovery of normal blood insulin and glucose levels
4. Reduced levels of hepatobiliary enzymes, pancreatic enzymes, and total bilirubin

CONCLUSION:

Autoimmune pancreatitis is a disease which is gaining clinical recognition more than before. With the help of various methods, significant progress has been observed in understanding the AIP profile, but its pathogenesis is still uncertain. Despite multiple factors like increased serum IgG4 and IgG4+ levels in the bile duct are considered related to AIP, but

these diagnostic criteria still do not throw complete light upon this disease's spectrum. It is found that AIP is a steroid-responsive disease, and it can be effectively treated with it but maintaining remission is quite a challenge.

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