Autoimmune Pancreatitis

by Tianna E. Johnson, Kenneth M. Sigman

Autoimmune pancreatitis is an uncommon cause of recurrent and chronic pancreatitis. It may be characterized by clinical findings resembling pancreatic carcinoma posing a diagnostic challenge to practitioners. Misidentifying autoimmune pancreatitis as pancreatic carcinoma results in unnecessary surgeries for a condition that may be managed medically. Conversely, misdiagnosis of pancreatic carcinoma as autoimmune pancreatitis delays treatment of a potentially fatal malignancy. The pathogenesis, diagnosis and treatment of autoimmune pancreatitis are discussed in the context of a case presentation and literature review. This report summarizes the diagnostic criteria required to distinguish this disease from pancreatic carcinoma. In conclusion: 1) the diagnosis of autoimmune pancreatitis requires a multidisciplinary approach, 2) autoimmune pancreatitis should be strongly considered among the differential diagnosis in patients presenting with presumed pancreatic carcinoma and 3) thorough evaluation for this condition should be pursued to determine the most appropriate treatment and avoid unnecessary surgery.

INTRODUCTION

Autoimmune pancreatitis represents a small percentage of all forms of recurrent and chronic pancreatitis.[1] It occurs due to a primary pancreatic autoimmune process or as a secondary component of a systemic autoimmune disorder.[2] This condition accounts for approximately six percent of chronic pancreatitis cases in the United States.[1]

There are two subtypes of autoimmune pancreatitis.[3] Type 1 is typically found in elderly men and is associated with systemic disease affecting extra-pancreatic organs such as the bile duct, kidneys, lymph nodes, and salivary glands.[2,3,4] Elevated serum immunoglobulin four (IgG4) is a defining feature.[2,3] Type II autoimmune pancreatitis is typically seen one decade before type I.[2,3] It is not predominant to one gender, does not involve other organs with the exception of inflammatory bowel disease and is not linked with increased IgG4 levels.[2,3] Both subtypes demonstrate lymphoplasmacytic infiltrate upon histologic examination.

The diagnosis of autoimmune pancreatitis requires a high index of suspicion and a multidisciplinary approach involving serologic tests, radiologic imaging, endoscopic imaging with tissue sampling, and sometimes surgical biopsies.[1] The Mayo Clinic proposed the HISORt criteria to help better define and confirm the presence of this disease.

Autoimmune pancreatitis is treated with corticosteroids, typically beginning with 40 mg/d of prednisone daily for four weeks.[1,3,5] The patient's clinical status is thereafter reassessed and serologic and radiologic studies are repeated.[1] If the response is appropriate, the dose is tapered by 5 mg/week until completion.[1] Azathioprine or rituximab are used for patients who have contraindications to taking steroids or to treat recurrent relapses.[1]

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CASE REPORT

A 69-year old Caucasian man presented with a 10 day history of jaundice accompanied by two weeks of dark colored urine, acholic stool and pruritus. He further admitted to resolved lower abdominal pain that lasted for two weeks and 30 pounds of intentional weight loss achieved with diet and exercise. He denied fever, chills, nausea, vomiting, dyspnea, prior jaundice, joint pain, ankle edema, dysuria and hematuria. His past medical history was pertinent for anemia, gallbladder disease and hyperlipidemia for which he had been taking lovastatin for seven years until two weeks prior to his presentation. He had no other personal or family history of gastrointestinal or autoimmune disorders or diabetes. His surgical history was significant for a cholecystectomy and Nissen fundoplication for a hiatal hernia. Social history was remarkable for smoking approximately five pipefulls per day for 53 years and consuming four beers per year plus an occasional glass of wine. He denied history of illicit or intravenous drug use, tattoos, or transfusions. He had no known drug allergies

All vital signs were within normal limits upon presentation. Physical was otherwise remarkable for jaundice with no other abnormalities.

A complete blood count revealed a hemoglobin of 12.6 (14-17 gm/dL), hematocrit of 36.9 percent (42-52 percent) and normal white blood cell and platelet counts. A basic metabolic panel was remarkable only for a potassium of 2.8 mEq/L (3.5-5.1 mEq/L). A hepatic

Table 1. Autoimmune Pancreatitis: HISORt Diagnostic Criteria

Histology (Must Include 1 of the Below)	Imaging Findings	Serology	Involvement of Other Organs	Corticosteroid Therapy Responsiveness
• Periductal lymphoplasmacytic infiltrate with obliterative phlebitis and storiform fibrosis • Lymphoplasmacytic infiltrate with storiform fibrosis with numerous IgG4 cells (≥ 10 IgG4 cells/HPF)	**Typical** • Diffusely enlarged pancreas with a delayed "rim" enhancement • Diffusely irregular and attenuated main pancreatic duct **Atypical** • Localized pancreatic mass or focal enlargement • Focal pancreatic ductal stricture • Atrophy of the pancreas • Calcification • Pancreatitis	Elevated serum IgG4 level	• Hilar or intrahepatic biliary strictures • Distal biliary stricture • Parotid or lacrimal gland involvement • Mediastinal lymphadenopathy • Retroperitoneal fibrosis	Complete resolution or pronounced improvement of pancreatic and/ or extra-pancreatic findings

Adapted From: Gardner, TB., Levy, MJ., et. al. Misdiagnosis of Autoimmune Pancreatitis: A Caution to Clinicians American Journal of Gastroenterology. 2009 Jul;104(7):1620-23.

panel showed an alkaline phosphatase of 542 U/L (50-136 U/L), alanine aminotransferase of 133 U/L (12-78 U/L), aspartate aminotransferase of 117 U/L (15-37 U/L), and total bilirubin of 11.2 mg/dL (0.2-1 mg/dL). Repeat total and direct bilirubin were 16.6 mg/dL and 9.8 mg/dL, respectively, within the same week. His amylase and lipase were normal. His hepatitis panel was negative. His carbohydrate antigen 19-9 (CA 19-9) was 236 U/mL (normal less than 55 U/mL). Repeat CA 19-9 less than two weeks later was 709 U/mL.

Computed tomography (CT) of the abdomen and pelvis without contrast showed a prominent common bile duct and mild edematous changes in the area of the pancreatic head with a small amount of fluid in the cul-de-sac. Endoscopic retrograde cholangiopancreatography (ERCP) revealed a lengthy stricture in the pancreatic duct suggesting a neoplasm, a malignant appearing distal bile duct stricture and a dilated proximal bile duct. Pancreatic and bile duct brushings were obtained and were negative for malignancy. Endoscopic ultrasound (EUS) with fine needle aspiration (FNA) of the pancreatic head was subsequently performed.

The patient's serum IgG4 level was elevated based on hospital parameters at 138 mg/dL (2.4-121 mg/dL). The patient's FNA pathology report of his lymph node was benign. Two histologic specimens from the pancreatic head showed chronic active inflammation but no malignancy. One of two specimens was positive for an increased number of IgG4 cells consistent with autoimmune pancreatitis. The patient was treated with steroids and responded well to this. His CA 19-9 one month later was normal at 7 U/mL. Repeat liver enzymes were also all within normal limits after one month and remained normal six months after the patient's biliary stent removal.

DISCUSSION

Various guidelines have been established to distinguish autoimmune pancreatitis from pancreatic carcinoma. The Mayo Clinic HISORt, Japanese Pancreas Society and Kim (Korean) criteria have emerged as leading diagnostic tools.[2] Each share histology, imaging and serology as key diagnostic components; however, the Mayo Clinic model places more emphasis on core biopsy and response to steroid therapy.[2] The Japanese strategy is more dependent upon imaging; steroid therapy is considered optionally inclusive.[1] The efficacies of these criteria are reliant on the clinicians' expertise.[1] Both have similar trends of algorithmic progression to surgical intervention for suspected malignancy, with the Mayo Clinic and Japanese models having resection rates of 16.7% and 16.2%, respectively.[1]

Autoimmune pancreatitis presents diversely. Painless obstructive jaundice is noted in approximately 70% of patients.[6] A third of individuals report abdominal pain and weight loss.[6] Others are asymptomatic and are incidentally found to have laboratory derangements.[6] Extreme cachexia, anorexia, and severe pain necessitating narcotics for relief are less suggestive of autoimmune pancreatitis.[2] A lack of alcohol abuse or family history of pancreatitis further support the diagnosis of autoimmune pancreatitis.[7,8]

Increased serum IgG4 is the best serologic diagnostic marker for autoimmune pancreatitis; however, one study reports that only 44% of patients initially presenting with this disease had elevated levels.[2,3] Serum IgG4 can also be elevated in pancreatic cancer.[2] Guidelines therefore endorse a level above two times the upper limit of normal as being highly suggestive of autoimmune pancreatitis.[2,3] Additionally, CA 19-9, often elevated in pancreatic cancer, may also be increased in autoimmune pancreatitis, but tends to decline with steroid treatment.[2] An escalating CA 19-9 suggests malignancy rather than autoimmune pancreatitis.[2]

Core biopsy is considered the best mode of obtaining specimens to assess for autoimmune pancreatitis while fine needle aspiration is preferred for evaluating for pancreatic carcinoma.[6] In the absence of malignant histology, biopsy samples demonstrating lymphocytic and plasma cell infiltrates along with fibrosis support the diagnosis of autoimmune pancreatitis especially when plasma cells are positive for abundant IgG4.[1]

Multiple imaging modalities have been used for the evaluation of autoimmune pancreatitis and preferences vary geographically.[2] CT, ERCP, MRCP (magnetic resonance cholangiopancreatography) and EUS are commonly utilized.[1,6,7] Classic findings for autoimmune pancreatitis on CT and MRCP include a pancreas that is diffusely enlarged with a rimmed capsule coupled with diffusely attenuated pancreatic duct; however, this disease can be represented by a wide radiographic spectrum.[4,7] Pancreatic cancer is more likely to have a low attenuation mass and pancreatic ductal dilatation.[2]

Two to five percent of patients undergoing surgical resection for presumed malignancy are later discovered to have autoimmune pancreatitis.[2,3] Some researchers propose that patients in this category have increased

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likelihood of postoperative complications such as diabetes and are at higher risk of needing additional invasive interventions later.[6,8] Some of the major causes for the misdiagnosis of this condition are a lack of awareness of the disease or a widely accepted consensus of diagnostic criteria.[6]

CONCLUSION

Autoimmune pancreatitis is an under-recognized form of recurrent and chronic pancreatitis that can be medically managed. Though less prevalent than pancreatic carcinoma, it must be considered among the differential diagnoses for patients with questionable malignancy as early recognition may prevent unnecessary surgeries for presumed cancer. Distinguishing autoimmune pancreatitis from pancreatic carcinoma and other causes of pancreatitis remains a diagnostic challenge that requires a high index of suspicion along with a multidisciplinary approach. New diagnostic criteria with increased sensitivity and specificity are needed to more definitively distinguish autoimmune pancreatitis from pancreatic carcinoma and to reduce morbidity and mortality. ■

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Answers to this month's crossword puzzle:

1 S	I	2 G	M	3 O	I	4 D	O	5 S	C	6 O	P	7 Y		8 N
E		E		L		R		I		C		9 E	10 T	A
11 R	A	N	D	O	M			12 P	13 A	R	E	S	I	S
A		O		G			14 A		G				15 D	C
		16 M	17 A	Y	O	18 S	C	O	R	E		19 B	E	E
20 D	21 A	I	S			22 I	A		E			I		N
23 U	L	C	E	24 R	A	T	I	V	E		25 C	O	A	T
C				U		U				26 A		C		
27 T	U	28 B	U	L	U	S		29 H	Y	D	R	A	T	30 E
		U		E				E		V		T		G
31 B	I	L	E		32 P	33 O	L	Y	M	E	34 R	A	35 S	E
U		I		36 A		X				37 R	I	L	E	S
38 R	E	M	I	S	S	I	O	39 N		40 S	O	Y		T
S		I		H		D		41 U	S	E		S		E
42 A	T	A	X	Y		43 E	B	B			44 S	T	U	D