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Short Communication

Differential Diagnosis of Uncommon to Rare Causes of Pancreatitis

Perry Hookman*

Consultant Gastroenterologist in Private Practice, USA

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***Corresponding author:** Dr. Perry Hookman, MD, FACG, AGAF, Consultant Gastroenterologist in Private Practice, USA, E-mail: hookman@hookman.com; g278298@gmail.com

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Abstract

There is an emergence of more uncommon to rare cases of pancreatitis. This review aims to increase clinicians' awareness of pancreatitis's less common and rare causes, thereby facilitating differential diagnosis, especially in patients labelled Idiopathic Pancreatitis.

Introduction

Most clinicians are aware of the common causes of pancreatitis, which include

- Gallstones are the most common cause of acute pancreatitis. Gallstones can block the common bile duct, leading to a backup of pancreatic enzymes and subsequent inflammation.
- Alcohol Consumption can lead to the premature activation of pancreatic enzymes and increase the permeability of the pancreatic duct.
- Elevated triglyceride levels, particularly above 1000 mg/dL, can precipitate pancreatitis.it is believed that free fatty acids released from triglycerides causes pancreatic injury.
- Hypercalcemia leads to the activation of pancreatic enzymes, causing inflammation.
- Medications: Certain medications, including some diuretics, antibiotics, and immunosuppressants, can induce pancreatitis.
- Genetic Factors: Mutations in genes such as PRSS1, SPINK1, CFTR, and CTRC are associated with hereditary pancreatitis. These mutations can lead to abnormal enzyme activity or ductal obstruction.
- Infections: Viral infections such as mumps, coxsackievirus, and cytomegalovirus can cause pancreatitis.

Less common causes of pancreatitis are:

- Idiopathic Causes: In some cases, the cause of pancreatitis remains unknown, termed idiopathic pancreatitis.
- Obesity: Obesity is associated with an increased risk of pancreatitis, possibly due to its association with gallstones, metabolic syndrome, and Fatty pancreatitis.
- Abdominal Trauma, whether from surgery, accidents, or endoscopic procedures, [ERCP], can lead to pancreatitis.

Rare cases of trauma causing pancreatitis:

- Duodenal ulcer bleeding associated with a pancreatic soft tissue mass, underscores a critical diagnostic challenge. Severe UGIB can produce imaging findings that closely resemble pancreatic pathology [1].

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- Autoimmune pancreatitis

Autoimmune pancreatitis is also called AIP. Two subtypes of AIP are now recognized, type 1 and type 2.

1. Type 1 AIP is called IgG4-related disease (IgG4-RD). This type often affects multiple organs, including the pancreas, bile ducts in the liver, salivary glands, kidneys, and lymph nodes. Type 1 AIP can be mistakenly diagnosed as pancreatic cancer. The two conditions share overlapping symptoms, but have very different treatments, so it is crucial to distinguish one from the other. About 80% of people with type 1 AIP have painless jaundice caused by blocked bile ducts. The most common sign of type 1 AIP is painless jaundice. People with type 2 AIP can have repeat episodes of acute pancreatitis. Pain in the upper abdomen, a common symptom of pancreatic cancer, is often absent in autoimmune pancreatitis.

2. Type 2 AIP seems to affect only the pancreas, although about one-third of people with type 2 AIP have associated inflammatory bowel disease.

Differences between type 1 and type 2 AIP are:

- In type 1 AIP, the disease may affect other organs in addition to the pancreas. Type 2 AIP affects only the pancreas. Type 2 disease also is associated with another autoimmune condition called inflammatory bowel disease.

- Type 1 AIP mostly affects men in the sixth to seventh decade of life. The most common sign of type 1 AIP is painless jaundice. People with type 2 AIP can have repeat episodes of acute pancreatitis. Pain in the upper abdomen, a common symptom of pancreatic cancer, is often absent in autoimmune pancreatitis.Type 1 AIP is more likely to relapse after treatment is discontinued.

- Type 2 AIP affects both men and women equally and has a younger age of onset compared with type 1 AIP.

Risk factors

The two types of AIP happen with different frequencies in different parts of the world.

- In the United States, about 80% of people with autoimmune pancreatitis, also called AIP, have type 1. People with type 1 AIP often Are over age 60. Are male.

- People with type 2 AIP Are often one or two decades younger than those with type 1. Are as likely to be female as male. They are more likely to have inflammatory bowel disease, such as ulcerative colitis.

- The diagnosis of autoimmune pancreatitis (AIP) involves a combination of clinical, serological, imaging, and histopathological criteria.

1. Imaging:

- Pancreatic Parenchyma and Duct: Imaging studies such as CT or MRI may show diffuse or focal enlargement of the pancreas, often described as a "sausage-like" appearance. MRCP or ERCP may reveal narrowing of the pancreatic duct.

2. Serology:

- Elevated serum IgG4 levels are a common finding in type 1 AIP and can support the diagnosis. However, normal IgG4 levels do not exclude the diagnosis.

3. Other organ involvement:

- IgG4-Related Disease: AIP can be associated with other IgG4-related diseases, such as sclerosing cholangitis, retroperitoneal fibrosis, or salivary gland involvement.

4. Pancreatic histology:

- Histopathological Features: A biopsy may show lymphoplasmacytic sclerosing pancreatitis, characterized by dense lymphoplasmacytic infiltrate, storiform fibrosis, and obliterative phlebitis. IgG4-positive plasma cells are often present.

5. Response to steroid therapy:

- Therapeutic Trial: A positive response to corticosteroid therapy can support the diagnosis, especially when other criteria are inconclusive.

Diagnostic criteria

- The ICDC and other national criteria (such as the Japanese and HISORt criteria) use combinations of these features to establish a diagnosis. The criteria emphasize the importance of differentiating AIP from pancreatic cancer and other forms of pancreatitis.

Complications

Autoimmune pancreatitis can cause a variety of complications.

1. Pancreatic exocrine insufficiency. Symptoms include diarrhea, weight loss, metabolic bone disease, and vitamin or mineral deficiency.

2. Diabetes.

3. Pancreatic and bile duct stricture.

4. Pancreatic calcifications or stones.

Summary

- Type 1 AIP is called IgG4-related disease (IgG4-RD). This type often affects multiple organs, including the pancreas, bile ducts in the liver, salivary glands, kidneys, and lymph nodes, and can be mistakenly diagnosed as pancreatic cancer.

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- Type 2 AIP seems to affect only the pancreas, although about one-third of people with type 2 AIP have associated inflammatory bowel disease.

- The recent emergence of autoimmune pancreatitis (AIP) and IgG4-related sclerosing cholangitis (IgG4-SC) should be added to the list of differential diagnosis of pancreatitis.

Camilla Gallo, et al. [2] report that Autoimmune Pancreatitis (AIP) is an autoimmune subtype of chronic pancreatitis resulting from the aberrant immune response against the pancreas, leading to inflammation and fibrosis. Although AIP is rare, its incidence is increasing and is often misdiagnosed as other pancreatic diseases. AIP is commonly classified into two types. Type 1 AIP (AIP-1) is typically associated with elevated serum immunoglobulin G4 (IgG4) levels and systemic manifestations, while type 2 AIP is typically a more localized form of the disease and may coexist with other autoimmune disorders, especially inflammatory bowel diseases. Additionally, there is emerging recognition of a third type (type 3 AIP), which refers to immunotherapy-triggered AIP, although this classification is still gaining acceptance in medical literature. The clinical manifestations of AIP mainly include painless jaundice and weight loss. Elevated serum IgG4 levels are particularly characteristic of AIP-1. Diagnosis relies on a combination of clinical, laboratory, radiological, and histological findings, given the similarity of AIP symptoms to other pancreatic disorders. The mainstay of treatment for AIP is steroid therapy, which is effective in most cases. Severe cases might require additional immunosuppressive agents. This review aims to summarize the current knowledge of AIP, encompassing its epidemiology, etiology, clinical presentation, diagnosis, and treatment options. We also address the challenges and controversies in diagnosing and treating AIP, such as distinguishing it from pancreatic cancer and managing long-term treatment, highlighting the need for increased awareness and knowledge of this complex disease [2].

Rare causes of pancreatitis

Cystic fibrosis [CF] is associated with pancreatitis [3-7].

In one study, the authors present a case of a pancreatic mucinous cystic neoplasm in a patient with CF, recognized as a premalignant lesion for pancreatic adenocarcinoma [8].

Pediatric pancreatitis

Pediatric pancreatitis is a condition that causes the pancreas to become inflamed in children. Acute refers to conditions that occur suddenly and have a short course. Symptoms of acute pediatric pancreatitis may include stomach pain, persistent vomiting, and fever.

Acute pediatric pancreatitis may also be associated with systemic disease (e.g., hemolytic uremic syndrome). If left untreated acute pancreatitis can progress to the chronic form which is more persistent and involves inflammation and scarring of the pancreas.

Symptoms

Children with acute pancreatitis may experience stomach pain, persistent vomiting, and fever. Their abdomen may be distended and tender. The pain increases in intensity for 24 to 48 hours, during which time vomiting may increase and the child may require hospitalization for dehydration.

Severe acute pancreatitis is rare in children. This form of pancreatitis can become life-threatening. In addition to the symptoms listed above, these children may have ascites, jaundice, hypocalcemia, shock, and pleural effusions. A bluish discoloration may be seen around the umbilicus [9-13].

Rare conditions causing pancreatitis

Fishbone-induced pancreatitis is a rare cause of pancreatitis.

Ingestion and migration: The ingestion of a fishbone can lead to its migration through the gastrointestinal tract. The fishbone can sometimes penetrate the stomach or intestinal wall and migrate into the pancreas, causing direct injury and inflammation.

Perforation and inflammation: The sharp nature of fish bones allows them to perforate the gastrointestinal wall, potentially leading to localized inflammation, abscess formation, and pancreatitis if the pancreas is involved [14-17].

Clinical presentation

Symptoms: Patients may present with abdominal pain, often localized to the epigastric region. The pain can be severe and may be accompanied by signs of peritoneal irritation.

Laboratory findings: Elevated pancreatic enzymes, such as amylase and lipase, are typically observed, indicating pancreatic inflammation.

Diagnosis

Imaging: Diagnosis often involves imaging studies. A CT scan can reveal a high-density foreign object, such as a fishbone, near or within the pancreas. Endoscopic ultrasound may also be used to identify and locate the foreign body [18,19].

Endoscopy: In some cases, endoscopic procedures may be necessary to visualize and potentially retrieve the fishbone.

Management

Endoscopic removal: If the fishbone is accessible, endoscopic removal is often the preferred approach to prevent further injury and resolve the inflammation.

Surgical intervention: In cases where endoscopic removal is not feasible, surgical intervention may be required to remove the fishbone and address any complications, such as abscesses or perforations.

Prognosis

Outcome: With appropriate intervention, the prognosis is generally good. However, delays in diagnosis and treatment

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can lead to complications such as abscess formation or chronic pancreatitis.

Fishbone-induced pancreatitis highlights the importance of considering foreign body ingestion as a potential cause of abdominal pain and pancreatitis, especially in regions where fish consumption is high. Prompt diagnosis and management are crucial to prevent complications.

Acute pancreatitis as a result of hemobilia

Hemobilia refers to extravasated blood in the biliary tract. The most common causes of hemobilia are iatrogenic, traumatogenic, and neoplastic. Although hemobilia remains an uncommon cause of gastrointestinal bleeding, its incidence has gradually increased due to widespread hepatopancreatobiliary procedures. Hemobilia classically presents with the triad of jaundice, right upper quadrant (RUQ) pain, and upper gastrointestinal bleeding (UGIB); however, presentation often depends on the etiology. Nevertheless, diagnosing hemobilia can be clinically challenging, and the ideal treatment approach may not be immediately clear or readily accessible.

Acute pancreatitis as a result of hemobilia after laparoscopic cholecystectomy is a rare vascular complication with a challenging clinical diagnosis. The authors report the fourth case of acute pancreatitis after laparoscopic cholecystectomy caused by hemobilia secondary to a right hepatic artery pseudoaneurysm [20-23].

Hui Guo, Qian Guo, Zhiqiang Li et al. report that from the first quarter of 2005 to the third quarter of 2023, there were 6,751 reports describing acute pancreatitis associated with GLP-1 RAs in the FAERS database. They state that a notable reporting signal for acute pancreatitis exists across all GLP-1 RAs in the FAERS database, particularly associated with exenatide and liraglutide. Clinicians must be vigilant and monitor this potentially serious adverse event. Moreover, the authors anticipate further pharmacovigilance studies, cohort analyses, and clinical trials in the future to develop evidence-based treatment strategies for patients experiencing GLP-1 RA-induced AP [24].

Patel et al. state that though recent evidence suggests no increased risk of acute pancreatitis (AP) with subcutaneous semaglutide use, some studies report an increase in pancreatic inflammation with GLP-1 RAs. They present a case of AP in a patient recently started on subcutaneous semaglutide for type 2 diabetes. They emphasize that as GLP-1 RA use increases, clinicians should be aware of their potential to cause acute pancreatitis [25].

Katie Hughes et al. state that semaglutide is a glucagon-like peptide-1 receptor agonist (GLP-1RA) that has recently gained popularity in its effective management of type 2 diabetes mellitus (T2DM) and obesity. Minimal evidence has reported the link between semaglutide use and acute pancreatitis. In this case report, they discuss the case of a 36-year-old female presenting to the Emergency Department with sudden-onset epigastric pain, subsequently diagnosed with acute pancreatitis. Moreover, she had recently started subcutaneous semaglutide injections for weight loss, which she had procured from one of her acquaintances without seeking medical advice. Semaglutide was thus stopped, and her lipase levels normalized with significant improvement of her symptoms, making semaglutide the likely causative factor for her acute pancreatitis. Given the increased use of GLP-1RA, the authors aim to increase awareness among patients taking this medication, whether prescribed or not, and increase clinician awareness when prescribing this medication [26].

Sodhi et al. highlighted the risk of gastrointestinal adverse events associated with GLP-1 RAs for weight loss, which may include acute pancreatitis [27].

Kezouh and Etminan also documented a case of acute pancreatitis in a patient taking semaglutide, further adding to the growing body of case-based literature on this complication [28].

Conclusion

This paper is not about hunting for Zebras. This paper attempts to alert the clinician to uncommon and rare but increasing entities for an important differential diagnosis, especially in those cases of pancreatitis termed idiopathic.

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