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Acute Pancreatitis: A Rare Manifestation of Hereditary Angioedema Due to C1 Inhibitor Deficiency – Case Report

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Case Report

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Abstract

Hereditary angioedema (HAE) is a rare genetic disorder inherited in an autosomal dominant pattern. It is characterized by recurrent episodes of subcutaneous or submucosal edema affecting several organs. Gastrointestinal involvement typically presents as bowel edema, accompanied by severe abdominal pain, nausea, vomiting, and/or diarrhea, with biliary tract involvement being uncommon. Here, we report an unusual case of acute pancreatitis as the clinical manifestation of a type I HAE attack in a female patient from Brazil. This highlights the importance of considering HAE as a differential diagnosis for acute abdominal pain in emergency settings, thereby preventing unnecessary surgical procedures.

INTRODUCTION

Hereditary angioedema (HAE) due to C1-inhibitor (C1-INH) deficiency is a rare genetic disease caused by a mutation in the SERPING1 gene, which codes for C1-INH, a serine protease inhibitor that blocks several complement and contact-system proteases and plasmin. The disease affects approximately 1 in 50,000 individuals globally, with type 1 HAE (HAE-1) accounting for 85% of HAE-C1-INH cases, characterized by low antigenic and functional levels of C1-INH.[1] Type 2 HAE (HAE-2) involves dysfunctional C1-INH protein, with normal or elevated amounts but low functional levels.[1] Both resulting in an overproduction of bradykinin that causes angioedema attacks by increasing vascular permeability. The edema episodes mainly affect the skin, abdomen, and upper respiratory tract, sometimes leading to life-threatening asphyxiation risk.[1] Other sites like the central nervous system are rarely affected, and the edema generally resolves spontaneously in 3–5 days.[2] Prodromal symptoms such as erythema marginatum can occur in 42–58% of cases, with triggering factors including emotional stress, trauma, infections, or medications (Table 1).[1,3]

Abdominal attacks occur in 93% of cases and are the second most affected site.[4] Bowel loops edema manifests as intense abdominal pain, sometimes accompanied by nausea, vomiting, diarrhea, and weakness, resulting from the overflow of peritoneal liquid and hypotension, with a risk of hypovolemic shock. Diagnosis is challenging, and the disease may remain undiagnosed for years, as abdominal pain can be the only manifestation for a long time. Misdiagnosis often leads to unnecessary surgeries, such as exploratory laparotomy in one-third of patients.[2,4] Clinical information such as a history of recurrent episodes of swelling or abdominal pain, positive family history, presence of triggers or prodromal symptoms, onset in childhood/adolescence, absence of wheals, no response to glucocorticoids, antihistamines, epinephrine, or omalizumab can help in diagnosing HAE.[1,3] Acute pancreatitis rarely occurs during abdominal attacks, probably due to duodenal edema obstructing the pancreatic duct or the ampulla of Vater. Differential diagnosis should be considered in idiopathic cases.[3] Here, we present an uncommon case of acute pancreatitis in a female patient previously diagnosed with HAE-1.

CASE REPORT

A 42-year-old female patient with HAE-1, a rare genetic disease characterized by recurrent abdominal attacks, was receiving long-term prophylaxis of 7.5mg/day of oxandrolone. She presented to the emergency room with a 24-hour history of intense epigastric pain, abdominal distention, and vomiting. Upon physical examination, she had significant abdominal distension, painful epigastric palpation, and a negative Blumberg sign. A computed tomography (CT) scan revealed diffuse intra-abdominal free fluid, including perihepatic and perisplenic spaces, parietocolic gutter, pelvis, and peripancreatic fat stranding, particularly in the head and uncinate process (Fig. 1). Laboratory test results were consistent with acute pancreatitis, and the patient was suspected of having HAE-related acute pancreatitis (Table 2).

The patient was hospitalized for pain control and received two units of fresh frozen plasma (FFP) as specific medications were not available. Three days later, she was asymptomatic, and magnetic resonance cholangiopancreatography (MRCP) and laboratory test results were normal (Table 2). The patient was subsequently discharged.

DISCUSSION

The diagnosis of acute pancreatitis is based on severe abdominal pain, elevated serum levels of amylase or lipase, and imaging findings.[3] The most common causes are gallstones and alcohol abuse, but autoimmune or medication-induced pancreatitis should also be considered when these are ruled out.[4–6] Danazol, an attenuated androgen used for hereditary angioedema (HAE) prophylaxis, has been associated with acute pancreatitis cases, but a recent literature review found no causative association between danazol and HAE-related acute pancreatitis.[4,7] Our patient was using oxandrolone for prophylaxis, another attenuated androgen that increases liver production of C1-inhibitor, reducing HAE attacks' risk.

Although HAE-related acute pancreatitis is uncommon, it is also underdiagnosed because serum levels of amylase and lipase are not routinely measured. Despite angioedema attacks are self-limited, lasting 2 to 5 days, abdominal and head and neck attacks must be immediately treated considering the risk of critical complications including death. In this case, the patient received two units of fresh frozen plasma (FFP), and three days later, she was discharged asymptomatic. FFP is not a first-line treatment for HAE attacks, but its use in Brazil is sometimes necessary due to limited access to licensed medications, such as plasma-derived C1-inhibitor concentrates or bradykinin-2 receptor antagonists.[1,3,4,6]

Efforts are necessary to increase access to on-demand treatment for HAE, as the use of FFP can lead to paradoxical exacerbation, and other medications are more effective and safer, approved for self-administration in Brazil. A detailed history can help emergency physicians, gastroenterologists, and surgeons in HAE suspicion. Warning signs such as family history, no response to antihistamines and corticosteroids, recurrent episodes of edema or abdominal pain, absence of wheals, and presence of triggers/prodrome symptoms are some important characteristics of HAE.[5–9]

Correct diagnosis and prompt treatment of HAE-related acute pancreatitis can reduce the economic burden, the impairment on patient quality of life, and avoid unnecessary interventions or fatal outcomes. Access to first-line medications for HAE attacks is still limited, especially in emerging countries like Brazil, and needs improvement to provide better options and the possibility of self-administration, reducing the duration and severity of symptoms.

Table 1
– HAE attack-triggering medications.

Estrogen	**Oral contraceptive agents,** **Estrogen hormone replacement therapy**
Antihypertensive agents	ACE* inhibitors, Angiotensin II receptor blockers
Antidiabetic agents	DPP-4** inhibitors (Gliptins)
*Angiotensin-converting enzyme	
**Dipeptidyl peptidase IV	

Table 2
– Laboratory test results

WBC	**Admission**	**Discharge**	**Reference**
	11430/µl	**6500/µl**	**3600–11000/ µl**
Amylase	130 U/L	33 U/L	30–118 U/L
Lipase	824 U/L	74 U/L	12–53 U/L
CRP	0,22 mg/dL	0,4 mg/dL	< 1,0 mg/dL

Declarations

Ethics and consent to participate

This case report was approved by the Research Ethics Committee (CEP) of the Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro (UFRJ).

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor in Chief of this journal.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying clinical information.

Availability of data and materials

The data supporting the findings of this case report are not publicly available due to patient privacy and confidentiality concerns. Further information may be available from the corresponding author upon reasonable request, subject to appropriate ethical and privacy considerations.

Competing interests

The authors declare that they have no conflicts of interest regarding this study.

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Authors' contributions

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Approval of the final version of the manuscript, intellectual participation in the conduct propaedeutic and/or therapeutic of studied case, critical review of the literature, manuscript, effective participation in research guidance.

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Figures

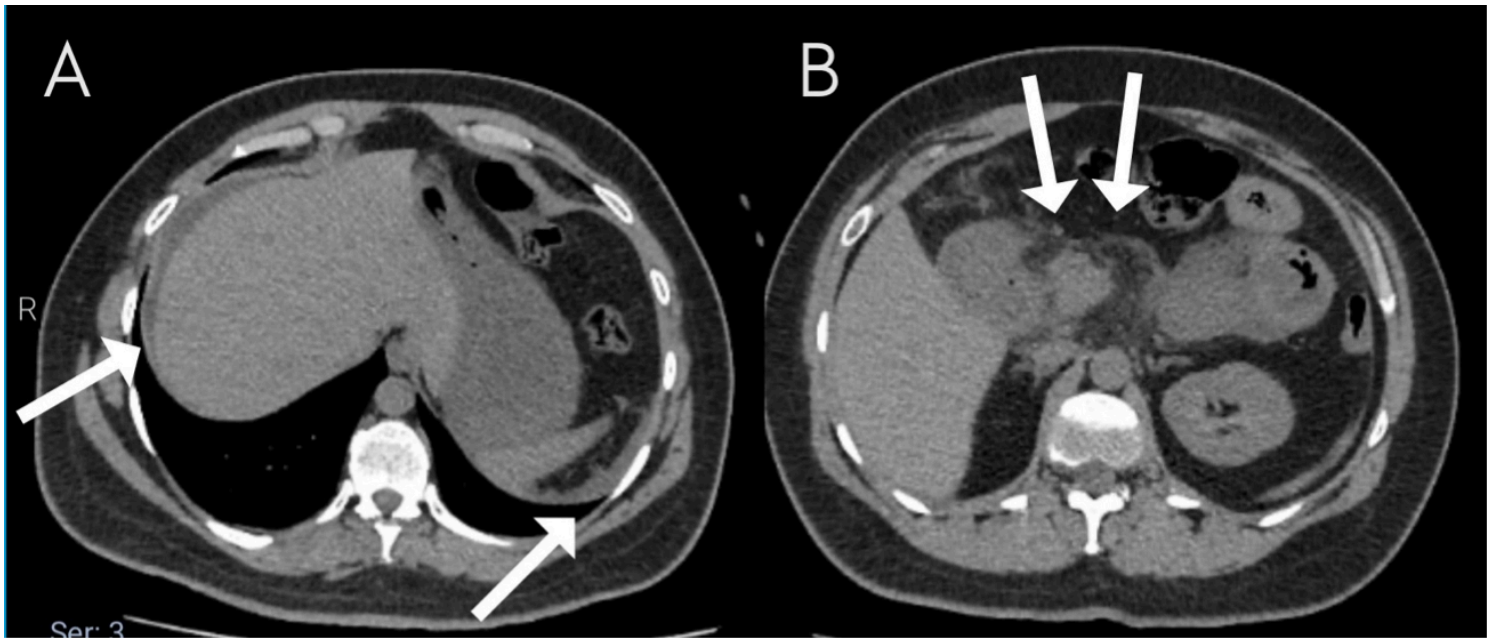


Figure 1

CT scan

A Free fluid in perihepatic and perisplenic spaces.

B Peripancreatic fat stranding in the head and uncinate process.