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Review and case report

# Acute pancreatitis with normal serum lipase and amylase: case report

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**Abstract.** Pancreatitis represents one of the main causes of hospitalization for acute abdominal pain. In addition to clinical presentation, serum lipase is used to confirm the diagnosis. Although diagnosis is based mainly on clinical and laboratory findings, isolated cases with normal lipase and amylase have been reported in literature, hence further investigations are necessary where clinical suspicion persists. We present the case of a patient admitted for acute epigastric abdominal pain suggestive for acute pancreatitis, with normal serum enzyme levels and imaging consistent for this diagnosis. The patient was treated conservatively with partial resolution of symptoms, but was discharged against medical advice, as a result a conclusive etiology could not be established.

**Key Words:** pancreatitis, lipase, amylase



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## Introduction

Acute pancreatitis is one of the most common causes of hospital admission with a significant overall mortality of about 5%, that increases with age and in the presence of organ failures (Ismail et al 2017). Although in most cases the etiology accounts for pancreatic tract obstruction by gallstones and alcohol consumption, other causes like endoscopic retrograde cholangiopancreatography (ERCP), infections, hypercalcemia, hypertriglyceridemia, medication, tumors or trauma are often responsible for this disease (Ismail et al 2017; Lankisch et al 2015).

As recommended by the Revised Atlanta Classification, the diagnosis of acute pancreatitis requires the presence of at least 2 of the 3 criteria defined by the consortium: clinical presentation, laboratory changes and typical findings on imaging (Banks et al 2013). Abdominal pain in the epigastric region, often irradiating in the back, with an acute onset and progressive worsening represents the most common presentation (Foster et al 2016; Ismail et al 2017). Serum lipase and amylase levels are generally used to confirm this diagnosis. An elevation higher than 3 folds the normal value is used as a threshold to increase the specificity of the diagnosis (Banks et al 2013). In addition to this, abdominal ultrasound, contrast-enhanced computed tomography (Sureka et al 2016) or magnetic resonance imaging (Sun et al 2019) can provide an accurate confirmation of the disease and may aid in ruling out other etiologies or revealing local complications of pancreatitis (Foster et al 2016).

Serum lipase has a better sensitivity and specificity for the diagnosis of acute pancreatitis when compared to serum amylase and a negative predictive value of 94-100% (Sharma et al 2017; Jasdanwala et al 2015). Lipase levels increase at 4 to 8 hours after the onset of symptoms, peaks at 24 hours and persists for up to 2 weeks, therefore providing a large diagnostic window (Nadhem et al 2017; Ismail et al 2017). Albeit the combination of lipase and amylase is frequently used in clinical practice, current guidelines do not recommend testing these enzymes simultaneously because it does not improve the diagnostic accuracy, but the costs, having similar efficacy (Jasdanwala et al 2015; Batra et al 2015). Based on these data, for atypical presentations with abdominal pain and negative laboratory tests, if the suspicion for acute pancreatitis persists, abdominal imaging remains the cornerstone in detecting this disease (Nadhem et al 2017).

We report a case with suggestive clinical presentation, contrast-enhanced computed tomography (CE-CT) imaging proven alterations and normal serum lipase and amylase, representative for acute pancreatitis.

## Case Presentation

A 51 year old male presented in the Emergency Department of our hospital for intense, persistent epigastric abdominal pain, radiating to the back, 9/10 in intensity at presentation, associated with abdominal distension and nausea, symptoms that had started approximately 3 days before, consecutive to a fatty-enriched large meal, with progressive worsening in the last

hours. The patient was previously healthy and denied having similar episodes before.

Medical history was significant for grade 2 obesity and hypertension. The patient denied alcohol intake, smoking or illicit drugs use. His current treatment included Ramipril, Indapamide and Nebivolol.

Physical examination revealed an alert and oriented middle aged obese man, with an altered status, epigastric tenderness, abdominal distension and decreased bowel sounds. His vital signs included a blood pressure of 148/76 mmHg, heart rate of 61 beats per minute, respiratory rate of 20 breaths per minute, with an oxygen saturation of 95% on ambient air, with no recent episodes of fever or chills reported.

On presentation, laboratory studies revealed a normal blood count, an elevated C reactive protein of 31.7 mg/l (upper normal limit – UNL= 10 mg/l), alanine aminotransferase of 36 U/l (UNL= 35 U/l) and no cholestasis. Lipase and amylase were within normal range.

Abdominal ultrasound revealed no pathological findings, but was limited by the important abdominal distension. Subsequently a CE-CT of the abdomen and pelvis was performed, that showed decreased attenuation of the uncinate process, peripancreatic and periduodenal inflammatory changes, with thickening of the adjacent duodenal wall, cumulating a modified computed tomography severity index (MCTSI) score of 2, consistent with mild acute pancreatitis (Figure 1). Other changes visible on CT were significant for diffuse fatty liver infiltration, pancreatic steatosis, gaseous distension of the intestine and lithiasis of the right renal calyces, with preservation of renal function.

Considering the presence of acute pancreatitis, further investigations were performed for the assessment of etiology. Lipidic profile showed a mildly elevated LDL cholesterol with normal total cholesterol and triglycerides. Calcium was within normal range. The patient denied taking any new medication, except for his chronic treatment. He was not a heavy drinker and denied alcohol consumption before the symptoms onset. He accepted having eating a high caloric lunch, rich in lipids, a few hours before the onset of pain. Abdominal ultrasound did not find any gall stones and CE-CT scan did not describe any dilations of the bile ducts or morphologic alterations (i.e. pancreas divisum). On follow-up, repeated values for C reactive protein showed a marked increase of the inflammatory syndrome on day 3 of hospitalization, reaching values of 253 mg/l, with normal procalcitonin, while lipase and amylase remained within normal limits throughout the hospitalization.

Patient management was supportive, with bowel rest, intravenous fluids, analgesics and antiemetics. His symptoms improved and the patient was discharged on personal request, against medical advice on day 4, with partial resolution of symptoms, in a stable condition.

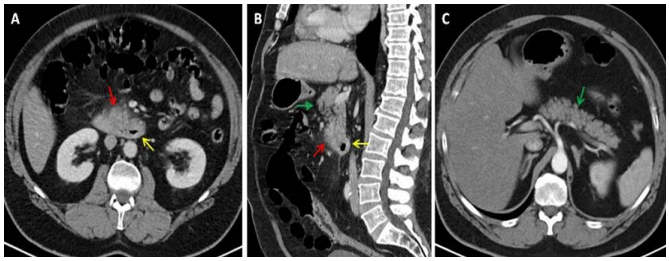


Figure 1. Contrast enhanced abdominal CT: Axial (A, C) and sagittal (B) images show acute inflammation with focal enlargement of the uncinate process of the pancreas and surrounding fat stranding (red arrows); there is adjacent duodenal wall thickening (yellow arrows). The rest of the pancreatic parenchyma and its surrounding fat (green arrows) appears normal.

## Discussion

Acute pancreatitis remains one of the main causes of hospital admission for acute abdominal pain, with a significant mortality rate, depending on the severity of the pathology (Ismail et al 2017). Clinical presentation consists of acute, sharp epigastric abdominal pain, often irradiating in the back, but other symptoms like nausea or vomiting may be associated (Ismail et al 2017). Currently, in clinical practice, the diagnosis is based mostly on symptoms and lipase and amylase levels, elevated higher than 3 times the normal value, with a tendency to exclude acute pancreatitis in case of normal serum levels of these enzymes (Foster et al 2016; Banks et al 2013; Sureka et al 2016).

Despite the fact that this combination provides the correct diagnosis in most of the cases, atypical presentations can occur (Banks et al 2013). A review of the literature returned an approximate number of 34 cases of acute pancreatitis with normal serum enzyme levels, a small fraction in contrast with the high incidence of this disease, thus highlighting the importance of elevated serum lipase for diagnosis and its high negative predictive value (Sharma et al 2017; Jasdanwala et al 2015; Batra et al 2015; Hofmeyr et al 2014).

As this case report emphasizes, although biological markers can be found within normal limits, additional investigations must be carried out to secure a complete evaluation when the suspicion of acute pancreatitis remains high (Agrawal et al 2016). The most reliable radiological investigation is represented by contrast enhanced computed tomography, frequently performed after 48-72 hours to assess for local complications and severity of pancreatitis, but it can also be used as an initial examination to confirm acute pancreatitis or deliver an alternative diagnosis, in cases with atypical presentation and diagnostic uncertainty, similarly to the case we presented (Sureka et al 2016; Bollen et al 2016; Sahu et al 2017). In our case, CE-CT provided the diagnosis, but also assessed the severity of pancreatitis, as the presentation occurred late, at approximately 72 hours after the debut of symptoms.

Multiple factors responsible for this disease have been documented, with lithiasis and alcohol consumption consisting for almost 80% of the cases (Ismail et al 2017; Mathur et al 2016). Based on anamnesis and paraclinical investigations, causes such as gallstones, alcoholism, chronic pancreatitis, hypercalcemia, hypertriglyceridemia, surgery, ERCP, trauma, tumors or medication have been excluded. Due to the premature discharge from the hospital, other factors like infections or autoimmune diseases could not be further investigated.

The role of diet as a single bolus meal in the pathogenesis of acute pancreatitis has been suggested, but current data in literature regard diet as a cofactor, in addition to prolonged alcohol intake or lithiasis, rather than a single causative factor (Thomas et al 2012). Malnutrition, refeeding or a high intake of proteins and fats have been mentioned as possible triggers, but a direct causative role could not be assigned (Thomas et al 2012). However, obesity has been demonstrated as a likely

contributor to the rising incidence and severity of acute pancreatitis (Khatua et al 2017).

The central mechanism in the pathophysiology of acute pancreatitis is the premature activation of trypsin in acinar cells that initiates the autodigestive process (Singh et at 2016). An increase in the oxidative stress, impaired autophagy or mitochondrial dysfunction are events that contribute to the acinar cells injury, initially generating a local response, that can further propagate through the release of inflammatory cytokines in the blood stream and produce a systemic inflammatory response, leading to multiple organ failure, increasing the severity and mortality of this disease (Lankisch et al 2015; Singh et al 2016). Inflammation of the pancreas induces the release of lipase, mainly produced by acinar cells, as a result it rapidly increases the blood levels at 4-8 hours, peaks at 24 hours and persists for up to 2 weeks (Agrawal et al 2016). Since lipase is mainly produced by the pancreatic cells, using a threshold for the diagnosis of acute pancreatitis significantly increases the specificity when compared to amylase alone (Hofmeyr et al 2014; Tadehara et al 2019). In spite of this, causes of non-pancreatic elevations are possible, but rare, and are seen in diseases like: renal or hepatic failure, diabetic ketoacidosis, inflammatory bowel disease, appendicitis, hypertriglyceridemia, fat embolism, trauma (Ismail et al 2017) or lipase secreting malignant tumors (Gardini et al 2016).

Unlike lipase, amylase has a lower diagnostic utility because, apart from the pancreatic origin, salivary glands are responsible for producing a significant amount of it and in smaller proportions other tissues like intestinal tract, adipose tissue, gonads or skeletal muscles (Ismail et al 2017). Another inconvenience when measuring amylase is the dosing of total serum amylase, widely used because of the reduced costs (Ismail et al 2017; Jasdanwala et al 2015; Akinfemiwa et al 2021).

Based on these data serum lipase is preferred over amylase for the diagnosis of acute pancreatitis (Aljomah et al 2019; Bhat et al 2018). Although in daily practice this combination is commonly used for diagnosis, most guidelines do not recommend it since there is a marginal increase in sensitivity (Ismail et al 2017; Hofmeyr et al 2014; Aljomah et al 2019; Bhat et al 2018). Neither of these enzymes is recommended for monitoring or predicting the severity of pancreatitis (Lankisch et al 2015), except for the cases with an early presentation, in the first 3-4 hours after the clinical onset of symptoms (Lankisch et al 2015; Agrawal et al 2016).

Normal serum levels of lipase or amylase are possible and can be detected in some cases, particularly when the hospital presentation occurs very early or late after the debut of symptoms, in hypertriglyceridemia or recurrent pancreatitis (Ismail et al 2017; Hofmeyr et al 2014; Argueta et al 2013; Konwe et al 2008), neither of these being highlighted in our case.

As mentioned in literature, the leading factors responsible for acute pancreatitis with normal serum lipase are represented by alcohol consumption (Nadhem et al 2017; Agrawal et al 2016; Konwe et al 2008; Shah et al 2010) and cholelithiasis (Shah et al 2019; Mukherjee et al 2020; Cartier et al 2006; Deschasse et al 2011), followed by hypertriglyceridemia (Kitagawa et al 2018; Kumar et al 2018; Limon et al 2016; Ko et al 2011), medication (Mathur et al 2016; Karkee et al 2016; Shafqet et al 2015) and end-stage kidney disease (Sharma et al 2017; Mathur et al 2016). Other possible factors associated with this disease, like Covid-19 infection (Sudarsanam et al 2021; Rao et al 2015), diabetic ketoacidosis (Argueta et al 2013), inflammatory bowel disease (Tauseef et al 2021) or sphincter of Oddi dysfunction (Agrawal et al 2016) are possible, but rarely seen. In a number of cases the etiology could not be elucidated (Mogrovejo et al 2015; Zafar et al 2016; Alam et al 2014), as was in our case, because of the premature discharge from hospital.

## Conclusion

In conclusion, acute pancreatitis with normal serum enzymes levels may be responsible for acute episodes of abdominal pain. In daily clinical practice clinicians oftentimes rely only on clinical presentation and amylase or lipase serum levels. However, considering the cases with normal levels of pancreatic enzymes, as this case confirms, in a clinical context highly suggestive for acute pancreatitis, the diagnosis workout should continue with specific imaging in order to confirm or exclude an acute pancreatitis.

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