


# Macroamylasemia at the Hospital Víctor Lazarte Echegaray in Trujillo (Peru): Case report

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## Abstract

Macroamylasemia should be suspected in any patient with a persistent catalytic increase of plasma  $\alpha$ -amylase but no other clinical signs of abdominal pain after ruling out other causes of pancreatic and extra-pancreatic disease. The binding of  $\alpha$ -amylase complexes with immunoglobulin, most commonly immunoglobulin A, characterizes this condition. Macroamylasemia is classified into three kinds. To prevent unnecessary procedures, it is critical to make a differential diagnosis of other conditions that can cause amylase increase. The present article reports the case of a 53-year-old female patient who was admitted to the emergency room with abdominal pain and hyperamylasemia, who was initially diagnosed with acute pancreatitis.

## Keywords

Macroamylasemia; Hyperamylasemia; Acute pancreatitis.

## INTRODUCTION

Macroamylasemia diagnosis is challenging when it is associated with abdominal pain, as it can lead to a false diagnosis of acute pancreatitis. Acute pancreatitis is characterized by pancreatitis-like abdominal pain, imaging findings of pancreatitis, and a three-fold increase in the plasma upper normal limit of the catalytic concentration of  $\alpha$ -amylase and lipase enzymes (1-4).

However, said increase may also be related to pancreatic and extrapancreatic metabolic diseases and pancreatic duct anomalies (5). Non-pancreatic hyperamylasemia is mainly caused by salivary gland diseases (mumps, lithiasis), intestinal diseases (bowel infarction, celiac disease, ulcerative colitis and peritonitis), chronic liver diseases, neoplasms, diabetic ketoacidosis, renal failure, ectopic pregnancy, polycystic ovary syndrome, head injury, and macroamylasemia

(6-8). The existence of macroamylase was first described by Wilding in 1964 (6). The term was proposed by Berk in 1967 and published in several case reports (9).

Macroamylasemia is a rare benign condition characterized by the presence of hyperamylasemia or elevated serum  $\alpha$ -amylase levels without elevation of  $\alpha$ -amylase levels in urine, provided that kidney function is preserved (10). Macroamylasemia occurs in 0.1%-1.5% of the general population (nonalcoholic); amylase isoforms are encoded in chromosome 1p21 (11). It occurs more frequently in males, but the reasons of this predominance are unknown. Macroamylasemia is a condition in which serum amylase protein binds to other serum proteins such as immunoglobulins A (IgA) (up to 92%) and G (IgG) (<30%), among others (<5%), forming large macromolecule complexes that exceed 400 KDa (amylase in its active cytoplasmic form contains 496 amino acids with a molecular weight of 54 KDa) (11-13).

Macroamylasemia can be diagnosed indirectly by measuring amylase activity in urine; specifically, the amylase to creatinine clearance ratio (ACCR) can contribute to differentiating hyperamylasemia. This ratio is calculated using the following equation:

$$\text{ACCR} = (\text{amylase [urine]} \times \text{creatinine [serum]}) / (\text{amylase [serum]} \times \text{creatinine [urine]}) \times 100.$$

An ACCR >5% is suggestive of acute pancreatitis.

An increased ACCR may also occur in diabetic ketoacidosis, surgery, and renal disease. An ACCR <1% is suggestive of macroamylasemia (11). Chromatography and polyethylene glycol (PEG) precipitation are the methods of choice for detecting macromolecules that contain macroamylase (6, 11).

## CLINICAL CASE PRESENTATION

This is the case of a 53-year-old woman with a history of high blood pressure (treated with losartan 50 mg every 12 hours) and cholecystectomy who was admitted due acute pancreatic abdominal pain. Epigastric pain on palpation was evidenced on physical examination. The following laboratory and imaging studies were performed: amylase: 1407 U/L; ultrasound: normal pancreas, 7.4 mm common bile duct, and mild left hydronephrosis. The patient was diagnosed with mild acute pancreatitis, for which she was hospitalized. Five days after hospital admission, a control amylase test was performed (1419 U/L; associated with absence of pain). She was then discharged and referred to the outpatient department to conduct further tests aimed at determining the causes of hyperamylasemia. **Table 1**

summarizes the results of these tests on hospital admission and at 5 days, 3 months, 8 months, 10 months and 1 year in the outpatient service.

During the patient's follow-up, laboratory tests were performed to rule out associated diseases that could cause hyperamylasemia (**Table 1**). She also underwent an endoscopy in which a duodenal biopsy was performed, which in turn showed glandular architecture associated with chronic nonspecific infiltrate, intraepithelial lymphocyte count <40/100 epithelial cells, without atrophy. Besides, during colonoscopy diverticula were observed in the sigmoid colon. Regarding imaging studies, no lymphadenopathies were evidenced on a CT of the neck (soft tissue), and evidence of cancer was observed in the CT scan of the chest, abdomen and pelvis (**Figure 1**); likewise, a normal biliary tract and no signs of choledocholithiasis were evidenced during magnetic resonance cholangiopancreatography (**Figure 2**). Further tests included ACCR (0.02%) and a confirmation test for macroamylasemia, which was positive (**Table 2**). The patient was asymptomatic during her evaluation at the outpatient department.

## DISCUSSION

It should be noted that our patient was a woman, as it has been described macroamylasemia occurs more frequently in males (11). In this case, the patient's abdominal pain on admission was associated with hyperamylasemia, which led to a wrong diagnosis of acute pancreatitis; 6% to 9.6% cases of hyperamylasemia are caused by macroamylasemia (14, 15). The highlight of our case is that no abdominal pain was experienced by the patient during the course of hyperamylasemia, so further testing was required to rule



**Figure 1.** CT scan of the chest, abdomen and pelvis.

**Table 1.** Evolution of laboratory test results.

	On hospital admission	At 5 days	At 3 months	At 8 months	At 10 months	At 1 year
Amylase $\alpha$ (IU/L)	1407	1419	2445	2454	2495	1174
Lipase (IU/L)		32		---		
Creatinine (mg/dL)	0.48	---	0.54	---	---	---
Urea (mg/dL)	23	---	22	---	---	---
Creatinine clearance (mL/min)	120	---	107	---	---	---
Glucose (mg/dL)	106	---	88	90	---	---
AST/GOT (IU/L)	17	---	18	22	---	---
ALT/GPT (IU/L)	13	---	10	27	---	---
Albumin (g/dL)	4.50	---	4.54	4.43	---	---
Total protein (g/dL)	7.32	---	7.30	7.45	---	---
Globulin (g/dL)	2.82	---	2.76	3.02	---	---
Alkaline phosphatase	200	---	205	244	---	---
Gamma-glutamyl transpeptidase	40	---		14	---	---
Total bilirubin (mg/dL)	0.8	---	0.57	0.53	---	---
Triglycerides	156	---		66	---	---
Hemoglobin (g/dL)	12.8	---		12.9	---	---
Platelets mL/mm <sup>3</sup>	350.000	---		380.000	---	---
TSH (mIU/dL)	---	---	---	3.1	---	---
Free T4 (ng/dL)	---	---	---	1.83	---	---
ANA	---	---	---	---	Negative	---
VRDL	---	---	---	---	Negative	---
Rheumatoid factor	---	---	---	---	28.18	---
Total hepatitis B core antibody	---	---	---	---	Non-reactive	---
Hepatitis B, Australia antigen	---	---	---	---	Non-reactive	---
Hepatitis C Virus	---	---	---	---	Non-reactive	---
Elisa for HIV	---	---	---	---	Non-reactive	---
AMA	---	---	---	Negative		---

Source: Sistema de Atención Historia Clínica Hospital Lazarte Echegaray - Essalud (Medical Record Health Care System Hospital Lazarte Echegaray - Essalud). GOT: glutamic-oxalacetic transaminase (NV: 0-35 IU); GPT: glutamic-pyruvic transaminase (NV: 0-35 IU); TB: total bilirubin (NV: 0.3-1.2 mg/dL); DB: direct bilirubin (NV: 0-0.3 mg/dL); TP: total proteins (NV: 6-8 g/dL); ALB: albumin (NV: 3.5-5.5 g/dL); ALP: alkaline phosphatase (36-129 IU); GGT: gamma-glutamyl transpeptidase (NV: 8-78 IU); serum amylase (NV: 0-100IU/L); T4 (NV: 0.8 to 1.9 ng/dL); TSH (NV: 0.5-4.5 mIU/dL); platelets (NV: 150-450 ml/mm<sup>3</sup>); hemoglobin (NV: 12-14 g/dL); serum creatinine (NV: 0.4 to 1.4 mg/dL); VRDL: The Viral and Rickettsial Disease Laboratory; NV: normal values.

out other pancreatic and extrapancreatic causes, as well as associations with other diseases. Celiac disease is the condition most frequently associated with macroamylase-mia development; in this regard, Rabsztyń et al. (16), in a case-control study, concluded that a significant proportion of patients recently diagnosed with celiac disease have

macroamylase-mia; therefore, if a patient has macroamylase-mia, celiac disease must be also considered. In our case, 6 biopsy samples were taken by means of an endoscopy, and in which a MARSH 0 score was reported, without criteria to carry out more tests to confirm or rule out the presence of celiac disease. Other macroamylase-mia-

**Table 2.** Macroamylasemia study

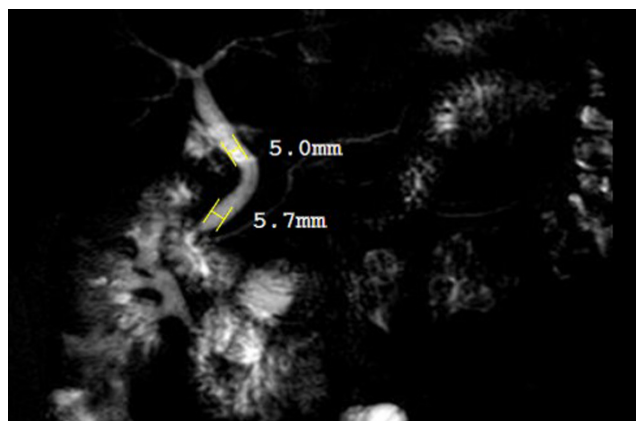
	Result
Amylase clearance	0.02
Amylase in urine	19 IU/L
Serum amylase	1174 IU/L
Creatinine	0.5 mg/dL
Urine creatinine (24-hour urine collection)	43.9 mg/dL
Macroamylasemia*	Positive

\*Chromatography; precipitation with polyethylene glycol (PEG). Source: Sistema de Atención Historia Clínica Hospital Lazarte Echegaray - Essalud (Medical Record Health Care System Hospital Lazarte Echegaray - Essalud). Amylase clearance (NV: <5); amylase in urine (NV: <460 U/L); serum amylase (NV: 0-100 U/L); serum creatinine (NV: 0.4-1.4 mg/dL).

associated diseases include chronic liver diseases (17), diabetes *mellitus* (18), rheumatoid arthritis (19), systemic lupus erythematosus (20), T-cell lymphoma (21), inflammatory bowel disease (22), asymptomatic HIV (23) and renal cell and thyroid carcinoma (16). All these conditions were ruled out in our patient.

Levitt et al. proposed the existence of two forms of macroamylasemia (24): the first one was characterized by the presence of malabsorption with an 11 S serum amylase resulting from the binding of normal-sized amylase by IgA immunoglobulin. In the second type, patients did not suffer from malabsorption, the sedimentation coefficient was 7 S and the complex was not the result of amylase binding to an immunoglobulin. Currently, 3 types of macroamylasemia have been described (Table 3) (25).

A very low ACCR (0.02%) and a short time to the positive result were observed in our patient; based on these findings, type 1 macroamylasemia was suspected, which was confirmed by means of chromatography and PEG precipitation. Thus, it can be concluded that this is a case of a type 1 macroamylasemia. Macroamylasemia must be considered in cases of persistent hyperamylasemia, even if



**Figure 2.** Magnetic resonance cholangiopancreatography.

**Table 3.** Types of macroamylasemia

Typo	1	2	3
Serum amylase	Persistently elevated amylase levels	Increased	Normal
Amylase in urine	Decreased or Normal	Decreased or Normal	Normal
ACCR	Very decreased	Disminuido	Decreased
Macroamylase concentration	Relatively high	Lower than type 1	Low
Time to result	Short	Long	Long

Source: taken from (25).

the initial manifestation is abdominal pain, also ruling out other etiologies and associated diseases of importance.

### Conflict of interest

None declared by the author.

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