Clin. Lab. 2026;72:XXX-XXX

CASE REPORT

Detection of Macroamylasemia Using Polyethylene Glycol Precipitation

Minggang Lu [1], Ying Wang [2]

[1] *Clinical Laboratory, Shaoxing People's Hospital, Shaoxing, P.R. China*
[2] *Hemodialysis Room, Shaoxing People's Hospital, Shaoxing, P.R. China*

SUMMARY

Background: **There are many factors that can cause elevated serum amylase levels, including pancreatic causes such as acute pancreatitis and chronic pancreatitis. Additionally, non-pancreatic causes, such as acute abdomen and acute parotitis, can also lead to increased serum amylase. These factors generally explain the consistency between elevated serum amylase and clinical symptoms. However, there are some special cases where patients exhibit atypical clinical symptoms but have persistently elevated serum amylase levels. Among these, macroamylasemia is an important differential diagnosis.**
Methods: **This is a report on a case of persistent serum amylase elevation (ranging from 217.0 to 452.1 U/L over five years) without clinical symptoms. The patient exhibited normal renal function, serum lipase levels, and tumor markers. Serial abdominal CT scans, magnetic resonance cholangiopancreatography (MRCP), and chest CT examinations revealed no significant abnormalities. The polyethylene glycol precipitation method (PEG precipitation) was employed as an adjunctive screening tool for macroamylasemia.**
Results: **The most recent serum amylase test result was 295.8 U/L. Using the polyethylene glycol precipitation method (PEG), the polyethylene glycol precipitation activity (%PPA) was 85.46% (%PPA > 60%), indicating interference from macromolecular proteins during the detection of serum amylase in this patient. This preliminary finding suggests the possibility of macroamylasemia. Further confirmation can be performed with gel filtration chromatography or immunofixation electrophoresis if laboratory conditions permit.**
Conclusions: **Macroamylasemia is often detected in serological tests due to its atypical clinical symptoms and lack of awareness, leading to common misdiagnosis, unnecessary investigations, and heightened patient anxiety during medical consultations. The polyethylene glycol precipitation method (PEG) serves as a screening tool, and definitive diagnosis can prevent unnecessary healthcare resource utilization.**
(Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250568)

Correspondence:
Ying Wang
Hemodialysis Room
Shaoxing People's Hospital
No. 568 North Zhongxing Road
Shaoxing City, Zhejiang Province
China
Phone: +86 13735290913
Email: lmgwy128626@163.com

Case Report accepted June 9, 2025

KEYWORDS

serum amylase, macroamylasemia, polyethylene glycol precipitation (PEG)

CASE PRESENTATION

A 67-year-old female patient was admitted five years ago with complaints of "pharyngalgia accompanied by epigastric discomfort for half a month and worsening abdominal pain for 2 - 3 days. During hospitalization, imaging and endoscopic evaluations, including abdominal ultrasound, contrast-enhanced CT of the upper and

lower abdomen/pelvis, gastroduodenoscopy, colonoscopy, and non-contrast chest CT, showed no significant abnormalities. However, ultrasound of the parotid glands and surrounding lymph nodes revealed left parotid enlargement with adjacent lymphadenopathy. Laboratory findings demonstrated markedly elevated serum amylase (622.8 U/L) and urinary amylase (996.5 U/L), while renal function and tumor markers were normal. She was diagnosed with "left sialadenitis" and treated accordingly. At discharge, serum amylase had decreased to 378.3 U/L (still above the upper reference limit), and urinary amylase normalized to 55.3 U/L. Due to persistent hyperamylasemia, she was advised to undergo regular serum amylase monitoring. Over the subsequent five years, the patient remained asymptomatic but underwent repeated serum amylase testing during routine follow-ups in emergency internal medicine, gastroenterology, general surgery, and respiratory medicine clinics. Results consistently ranged between 2 - 3 times the upper reference limit (refer to Figure 1). Serum lipase levels remained normal, and multiple follow-up abdominal CT scans, magnetic resonance cholangiopancreatography (MRCP), and chest CT scans showed no abnormalities.

Serum amylase was assayed using Beckman Coulter AU5800/AU680 analyzers with Beckman Coulter reagents via the PNP-G7 method. Macroamylasemia was screened by PEG precipitation.

Multiple factors can lead to elevated serum amylase levels, with common pancreatic causes including acute pancreatitis, chronic pancreatitis, and pancreatic cancer. Non-pancreatic causes, such as acute abdomen, intestinal obstruction, peptic ulcer disease, acute parotitis, and renal insufficiency, may also result in increased serum amylase levels [1,2]. This patient underwent regular serum amylase monitoring not due to any subjective symptoms or abnormal findings from other tests, but because her repeated measurements consistently showed elevated levels, fluctuating around 330 U/L. This raised concerns for potential underlying pathology in both the patient and her physicians, yet no definitive cause was identified, prompting continued periodic testing.

During the review of this patient's report, I noticed the prolonged historical trend of her serum amylase levels, which drew my attention. Upon reviewing her medical history, I found that she had persistently elevated amylase levels without any clinical symptoms, leading me to strongly suspect the possible presence of macroamylasemia. Macroamylasemia refers to the presence in the serum of abnormally large molecular weight amylase complexes, typically formed by the combination of amylase with immunoglobulin A (IgA), resulting in a molecular weight exceeding 150,000 Da. These complexes retain amylase enzymatic activity but cannot be filtered through the renal glomeruli, thereby manifesting as persistent hyperamylasemia [3].

Macroamylasemia is generally not considered an independent disease but rather a group of conditions caused by multiple factors. This condition is clinically rare, with an estimated incidence of 0.4%, and shows no gender predilection. Notably, macroamylasemia can also be detected in healthy individuals, typically without clinical manifestations or requiring treatment. Polyethylene glycol (PEG) precipitation is a commonly used protein precipitation technique. It involves adding PEG solution to induce protein precipitation and utilizes the interaction forces between PEG and proteins to achieve protein separation and purification. The PEG sedimentation activity (%PPA) is calculated as: %PPA = 100 x (1 - PEG group activity/control group activity). A %PPA > 60% indicates interference from large molecular proteins [4-6].

The patient's most recent serum amylase measurement was 295.8 U/L. A PEG6000 precipitation test was performed, yielding a PEG precipitation activity of 85.46%, which preliminarily suggests the possibility of macroamylasemia in this patient. Further confirmation can be achieved through gel filtration chromatography or immunofixation electrophoresis if experimental conditions permit [7].

DISCUSSION

Diagnostic Criteria for Macroamylasemia Based on Literature Review: 1) Presence of hyperamylasemia with normal or decreased urinary amylase levels and atypical clinical symptoms; 2) Diagnosis via amylase-creatinine clearance ratio (ACCR): Formula: ACCR = [urine amylase (U/L) x serum creatinine (mg/dL)]/[serum amylase (U/L) x urine creatinine (mg/dL)] x 100. Under normal renal function conditions, decreased amylase clearance is observed, with 24-hour CAmY/CCr < 1% [8]. 3) Measurement via PEG precipitation method, generally %PPA > 60%. Reviewing the patient's serum amylase levels measured at the same time before discharge revealed elevated results, while urine amylase levels remained within normal limits. Over the past five years, serum amylase levels have consistently remained elevated despite the absence of significant clinical symptoms and normal findings across all other examinations, which is consistent with the diagnostic criteria for macroamylasemia.

Although this patient exhibited persistently abnormal serum amylase levels, the degree of elevation was relatively mild and lacked significant clinical symptoms. Given the numerous potential causes of elevated serum amylase, such cases are easily overlooked during outpatient consultations. The exclusion of this condition is not technically challenging, but requires adequate clinical knowledge. In routine laboratory practice, systematic internal case sharing regarding rare or frequently misdiagnosed laboratory findings (such as macroamylasemia) can significantly enhance staff's ability to recognize abnormal results and improve diagnostic efficiency. For clinicians, accurate identification of this condition can reduce diagnostic errors and optimize healthcare resource utilization.

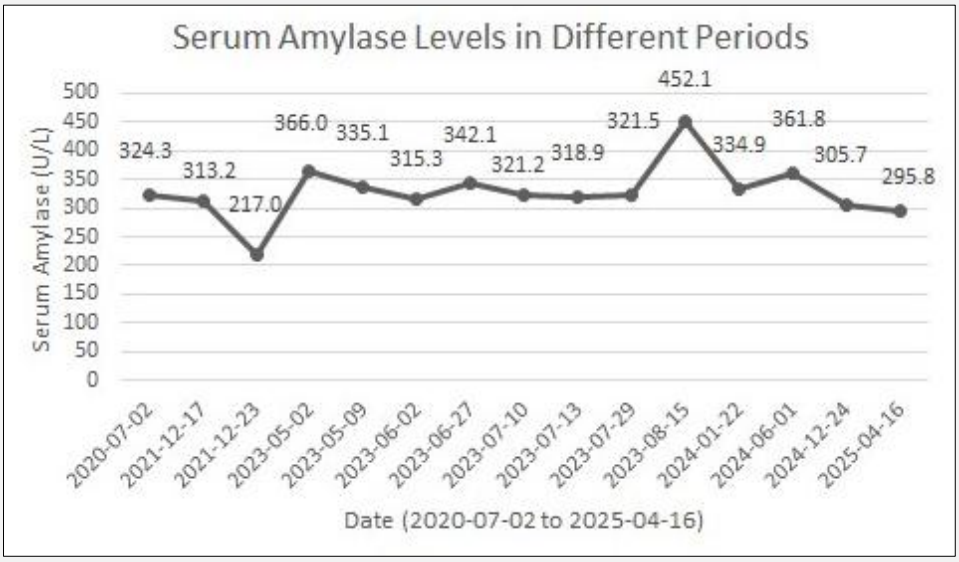

Figure 1. Record of changes in serum amylase levels at different time points.

The reference range for serum amylase is 40 - 132 U/L.

When laboratory results are inconsistent with clinical manifestations, the standardized workflow of 'Technical Verification → Clinical Correlation → Dynamic Validation' should be followed to prevent premature conclusions. The core principles include prioritizing the exclusion of technical errors, comprehensive clinical logical analysis, and multidisciplinary collaborative closed-loop management. Through systematic approaches, discordant results can be transformed into breakthrough points for precise diagnosis and treatment.

Declaration of Interest:

All authors declare that they have no competing interests.

References:

1. Azzopardi E, Lloyd C, Teixeira SR, Conlan RS, Whitaker IS. Clinical applications of amylase: Novel perspectives. Surgery 2016 Jul;160(1):26-37. (PMID: 27117578)

2. Lam R, Muniraj T. Hyperamylasemia. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing 2025 Jan. (PMID: 32644699)

3. Hu J, Chen J, Xu G. Hyperamylasemia of Abnormally Elevated Serum Amylase: Macroamylasemia in a Healthy Individual. Clin Lab 2021 Apr 1;67(4). (PMID: 33865250)

4. Burki C, Volleberg M, Blomgren L, Froese S, Hersberger M. Reference ranges for the polyethylene glycol (PEG) precipitation activity (%PPA) of eight routine enzyme activities. Pract Lab Med 2022 Dec 17;33:e00304. (PMID: 36582817)

5. Casenska J, Franekova J, Jabor A. Macrocomplexes: An establishing critical limits of post-PEG serum enzymes and proteins in adults and children. Clin Chim Acta 2025 Jun 15;574:120326. (PMID: 40268214)

6. Dedeene L, Stockman M, Steels S, Vermeersch P, Frans G. Detection of macroenzymes: establishing upper reference limits for eight enzymes after polyethylene glycol precipitation. Biochem Med (Zagreb) 2023 Feb 15;33(1):010705. (PMID: 36627975)

7. Casenska J, Franekova J, Macinga P, Jabor A. Significant Elevations of serum amylase caused by macroamylase: Case reports and detection possibilities. J Clin Lab Anal 2023 Mar;37(5): e24859. (PMID: 36916750)

8. Al-Johani WM. Macroamylasemia as a Rare Cause of Hyperamylasemia: A Case Report. Korean J Fam Med 2023 Nov;44(6):347-9. (PMID: 37989276)