

## Case Report

# Macroamylasemia in a patient with elevated serum amylase: case report

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**Abstract:** Macroamylasemia is characterized by an elevated serum amylase activity. It results from the circulation of a macromolecular complex consisting of amylase molecule and a serum component, often an immunoglobulin. The present study presents marked elevation of serum amylase level in a 43-year-old male, who had been admitted to our hospital for slight abdomen ache for 4 months. After treatment following pancreatitis, the symptom did not improve. Abdominal CT did not find any typical malignancy. The amylase clearance : creatinine clearance ( $C_{AM}:C_{CR}$ ) ratio is 0.001. Polyethylene glycol (PEG) precipitation assay shows that the PEG-precipitated amylase activity for this patient is 77%, whereas all six healthy controls are below 52%. Therefore, in this case, the elevated amylase levels may be a result of macroamylasemia.

**Keywords:** Macroamylasemia, PEG, abdomen pain

### Introduction

Elevated serum amylase activity is clinically used for the diagnosis of acute pancreatitis in patients with abdominal pain. Here, we report a case that a patient with recurrent abdominal pain has abnormally high serum amylase concentration, which peaks at more than 50 times of ULN (upper normal limit) However, both lipase and urine amylase activities of this patient are normal. The imaging examinations further support the view that no obvious salivary gland diseases or pancreatic diseases are present. Although hyperamylasaemia is most commonly due to pancreatic diseases, the case reported here highlights the needs for investigating non-pancreatic causes.

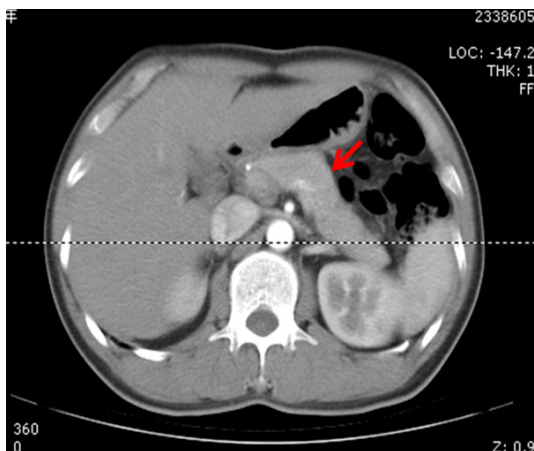
### Case report

On 15th October 2014, a 43-year-old male was admitted to the Tongji Hospital (Wuhan, China) presenting with slight abdomen ache for 4 months and marked elevation of the serum amylase level. On 22th June 2014, the patient was directed to the Xinhua hospital of Beijing and diagnosed with gastritis. Treating gastritis

with medicine had no effect on the patient. Subsequently, on 22th July 2014, the patient was admitted to Taihe Hopspital of Hubei, where he was found to have chronic superficial gastritis and Duodenal bulb inflammation by endoscopy examination. After the patient was treated with medicine, he felt better than before. On 15th September 2014, he was discovered to have a high serum amylase activity at 912 U/L (normal range, 20-119 U/L) in Taiihe Hospital of Hubei, but his urine amylase activity (115.2 U/L) was found to be normal (normal range, 10-490 U/L). He still had slight abdomen and back pain without fever, headache, bosom frowsty, flustered, giddy, keck. Then he was diagnosed with acute pancreatitis and treated with related medicine. After treatment for 10 days, the serum amylase level remained high at 849 U/L (20-119 U/L). On October 15th 2014, he was directed to the internal medicine of Tongji hospital of Wuhan for more precise diagnosis.

The patient was a peasant of non-smoking, non-drinking, had a history of appendix resection twenty years ago. The physical examination showed light pressure under xiphoid and peri-

## Elevated amylase in macroamylasemia



**Figure 1.** Abdomen CT scanning on admission showed no specific abnormalities identified. The red arrow indicated the pancreas, there is no morphology change.

umbilical without rebound tenderness and the laboratory examination revealed that the serum amylase level increased to 916 U/L (normal range, 28-100 U/L), the serum lipase level was 49.8 IU/L (normal range, 13-60 U/L), the urine amylase was 346 U/L (normal range, 16-491 U/L), serum creatinine was 63  $\mu\text{mol/L}$  (normal range, 59-104  $\mu\text{mol/L}$ ), and urine creatinine was 16774  $\mu\text{mol/L}$  (normal range, 3560-25600  $\mu\text{mol/L}$ ), and the amylase clearance : creatinine clearance ( $C_{AM}:C_{CR}$ ) ratio was 0.0014. The tumor markers (CEA, NSE, CYFRA21-1, SCC, AFP, CA125, CA15-3, CA72-4, CA199) and immunoglobulins (IgA, IgG, IgM, IgE, IgG4) were all in the normal range. Results of examinations for blood routine, liver function, electrolyte, urine routine and stool routine were all normal. Sialoceles Emission Computed Tomography (ECT) showed normal to exclude parotid diseases. To exclude the possibility of an underlying abnormal malignant lesion, upper and lower gastrointestinal endoscopy, abdominal ultrasonography, abdominal computed tomography (CT), were performed with no specific abnormalities identified (**Figure 1**).

PEG molecules can bind to macroamylase proteins. As a confirmatory measure, we carried out PEG precipitation to pull down macroamylase proteins as described by Isham [1], and then determined macroamylase activity in the precipitates as described by Letitt and Ellis [2]. Briefly, the blood serum from this patient and other 6 control people without pancreatitis and

mumps were collected. To precipitate macroamylase proteins in the serum, 0.2 ml of a 240 g/L solution of PEG6000 was added to one 0.2 ml aliquot of serum, whereas a control sample was prepared by adding 0.2 ml of 0.9% saline to the other 0.2 ml aliquot of serum [1]. Both aliquots were incubated at 37°C for 10 min, then centrifuged (5000 g, 10 min). The supernatants were collected and analyzed for amylase activity. So serum amylase activity minus supernatant amylase activity equals to precipitated amylase activity. If 73% or more of the amylase activity was precipitated by PEG, macroamylasemia was considered to be present. In contrast, PEG precipitation of <52% of amylase activity was expected with amylase of normal molecular mass [1-3]. The results in **Table 1** demonstrate that the ratio of PEG-precipitated amylase activity in all 6 control people is <52% and in the patient is 77%.

The patient was treated with stomach protecting medicine, and the remission of his abdomen ache was observed. However, the serum amylase remained high at 667 U/L. On 21th December, the patient's serum amylase level was still abnormally high at 631 U/L, but the levels for serum lipase (29.8 U/L), the urine amylase (140 U/L), serum creatinine (67  $\mu\text{mol/L}$ ), and urine creatinine (13793  $\mu\text{mol/L}$ ) as well as the amylase clearance : creatinine clearance ( $C_{AM}:C_{CR}$ ) ratio (=0.001) were all in normal range. But the abdomen pain had been relieved. Taken together, it seems that the marked elevation of serum amylase level in this patient is not due to pancreatitis, but macroamylasemia.

### Discussion

Hyperamylasaemia is commonly used for diagnosing acute pancreatitis. However, the diagnosis accuracy using hyperamylasaemia for pancreatic diseases can be as low as 61% depending on the patient population studied. In this respect, elevated amylase levels may be due to other non-pancreatic causes including intra-abdominal and salivary gland pathologies [4]. Macroamylasemia is generally a benign condition caused by circulating macroamylase complex, in which pancreatic or salivary amylase binds to plasma proteins such as immunoglobulins. The physical properties of the macroamylase are heterogeneous; however, the

## Elevated amylase in macroamylasemia

**Table 1.** The Ratio of Macroamylase

	Serum Amylase	supernatant Amylase	Macroamylase	Ratio of Macroamylase	Activity (U/L)
Control	1	28	22	6	21%
	2	38	29	9	23%
	3	19	16	3	16%
	4	17	15	2	12%
	5	29	20	9	31%
	6	25	17	8	32%
Patient		343	80	263	77%

The ratio of PEG-precipitated amylase activity in all 6 control people is <52% and in the patient is 77%. Macroamylase activity (PEG precipitated) equals to serum amylase minus supernatant amylase, the ratio of macroamylase is the activity of precipitated to serum.

large size of this protein complex impairs its clearance by the renal glomeruli. Macroamylasemia may be associated with a variety of disorders, such as IgA deficiency, celiac disease, lymphoma, carcinoma, systemic lupus erythematosus, rheumatoid arthritis, liver disease and various autoimmune diseases [5-7]. It has been shown that macroamylasemia occurs in 2.5 percent of hyperamylasemic patients and 1 percent of apparently healthy subjects with normal amylase levels, respectively [8]. In this case report, the patient had several important biochemical markers for the diagnosis of macroamylasemia including elevated serum amylase, low 24-hour urine amylase, low serum lipase, and reduced ratio of amylase clearance/creatinine clearance ( $C_{AM}:C_{CR}$  ratio of less than 1 percent). In addition, macroamylasemia in this patient was confirmed by a PEG precipitation assay, which can easily and quickly purify macroamylase molecules from serum [9]. We demonstrated that the patient had much higher PEG-precipitated amylase activity compared to that in the control group. Therefore, the hyperamylasemia in this case is due to non-pancreatic macroamylasemia. The case reported here also suggests that it is imperative to investigate the pathogenic mechanisms for macroamylasemia.

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### Disclosure of conflict of interest

None.

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