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CASE REPORT

Case report: macroamylasemia in a 13-year-old adolescent

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Abstract

Macroamylasemia is a biochemical abnormality caused by pancreatic or salivary amylase linked to another serum component, more usually immunoglobulins. Generally, this heavily aggregated component will not be excreted by the kidney causing hyperamylasemia. Macroamylasemia has been reported as a benign condition but could be a confusion factor in children presenting hyperamylasemia, leading to unnecessary investigation and treatment. This paper aimed to report the case of a 13-year-old adolescent presenting chronic abdominal pain and hyperamylasemia but serum lipase between the normal range and after diagnostic approach concluded as abdominal migraine and macroamylasemia.

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INTRODUCTION

The gastrointestinal tract has the primary function of digestion and absorption of nutrients from the diet. For the digestive process to take place, different secretions are produced and released into the gastrointestinal tract. Amylase is an enzyme secreted by the pancreas and salivary glands that participates in the digestion of dietary starch. The determination of serum amylase levels may be useful in the differential diagnosis of acute and chronic abdominal pain[1]. Elevated levels of serum amylase (hyperamylasemia) are found in a variety of diseases of the pancreas and other organs, such as chronic viral liver disease, inflammatory bowel disease, inflammatory lesions of the salivary glands, and diabetic ketoacidosis[1,2].

Among the causes of hyperamylasemia, there is macroamylasemia, a biochemical abnormality that affects up to 1% of the general population, but with rare scientific publications in children[3,4]. Macroamylasemia is characterized by an elevation in serum amylase, resulting from the binding of normal serum amylase (commonly the salivary isoenzyme) with another normal serum component, usually immunoglobulins (IgG and IgA), producing a large and heavy heterogeneous molecular complex that is difficult to excrete, thus resulting in in serum hyperamylasemia[3,5].

Although macroamylasemia is a biochemical abnormality, which usually has a benign course, it can be confused with acute pancreatitis or other causes of hyperamylasemia, leading to excessive diagnostic investigation or even unnecessary treatment[1,6,7].

CASE DESCRIPTION

A 13-year-old Caucasian adolescent with a two-year history of abdominal pain. She complained of abdominal pain every 2 or 3 months, lasting 1-3 days, requiring medical attention in the emergency room during crises. Pain occurred in the entire abdomen, in crisis, associated with nausea, vomiting and skin pallor; improved only after intravenous analgesia. She had no worsening factors, nocturnal awakenings, and fever during bouts of abdominal pain. She also had no weight loss or change in bowel habits during this period. Personal and family history: menarche at 11 years of age, continuous use of methylphenidate and imipramine for the treatment of attention deficit and hyperactivity disorder. Her father had migraine. Upon physical examination, she was in good general condition, with no evident changes in the abdominal physical examination and other segments.

A diagnostic investigation was performed revealing persistent elevation of serum amylase levels on different occasions (Table 1). There was no increase in serum lipase levels and no changes upon ultrasound scan. She was referred to the Pediatric Gastroenterology Service to investigate her hyperamylasemia. In addition to the amylase dosage, other laboratory tests were also requested (Table 1), as well as imaging exams.

Laboratory investigations were also carried out on her family members, with serum amylase and lipase levels from her parents and siblings. The family members tested were asymptomatic and had laboratory results within the normal range (Table 2).

The patient remains under outpatient follow-up with monitoring of serum amylase levels, which remained high (305 U/L and 264 U/L in the last measurements) but the patient has not had new episodes of abdominal pain in the last year.

DISCUSSION

Macroamylasemia Investigation is important in patients with persistent hyperamylasemia. [3,6,8] The main clinical interest lies in the need to distinguish macroamylasemia from other conditions that involve an increase in serum amylase and require specific treatment, such as diseases of the pancreas, parotid diseases, autoimmune diseases, neoplasms, malabsorption , alcoholism, liver disease and celiac disease[1,4,9,10].

Clinically, there is no typical sign or symptom of macroamylasemia, and it should be suspected in patients with serum hyperamylasemia, with normal or low amylasuria and normal kidney function[7,11].

The diagnosis of macroamylasemia is made by having the amylase complex with another serum component, using different methods, such as electrophoresis and filtration chromatography, as well as ultracentrifugation techniques or isoelectric focus[3,5].

Chromatography can be performed by separating immune complexes with the addition of polyethylene glycol (PEG), in equal proportion, to the patient's frozen serum. This procedure causes the enzyme-immunoglobulin complexes to precipitate, leaving the supernatant of amylase molecules not complexed with the immunoglobulins, evaluating their percentage value. Currently, values below 27% of the final supernatant are considered to indicate macroamylasemia, meaning that most of the amylase in the sample has precipitated with immunoglobulins. This test is a simple method that was used in the diagnosis of the case described, having good sensitivity and specificity and can be used as a screening test, since the occurrence of false negatives is minimal[5].

Another technique used for diagnosis is through the measurement of kidney amylase/creatinine clearance. In the case of macroamylasemia, there is a significant increase in serum amylase and low urinary amylase levels due to the size of the complex formed, with clearance lower than 1%. The patient must have normal kidney function for the technique to be reliable[3].

Scientific publications on macroamylasemia are rare in pediatrics[4,6-13], and its real prevalence is not known for sure. In adults, it is estimated that macroamylasemia affects 1 to 2% of the general population[3].

D'Avanzo et al. (1992)[13] described the case of a 5-year-old girl who presented with recurrent abdominal pain, vomiting, and fever. She was investigated and initially diagnosed with chronic

Table 1. Patient's lab exams.

LAB EXAMS	RESULTS	REFERENCE VALUES
Serum amylase	398U/L (1º)	VR: 25-125U/L
	430U/L (2º)	
	133U/L (3º)	
	264U/L (4º)	
Lipase	11U/L (1º)	VR: 11-46U/L
	14U/L (2º)	
TGO	18U/L	VR: 10-37U/L
TGP	10U/L	VR: 10-37U/L
GAMA-GT	8U/L	VR: 8-42U/L
Alkaline phosphatase	279U/L	VR: 75-390U/L
HB*	13.4g/dL	VR: 13.5 g/dL
HT**	39.8%	VR: 40%
Fasting glucose	86mg/dL	<110mg/dL
CEA***	1.4ng/mL	VR<3ng/mL
Creatinine	0.4mg/dL	VR: 0.4-0.9mg/dL
Urea	32mg/dL	VR: 11-38mg/dL
Cr Clearance	161mL/min/1.73m2	VR>70-140mL/min/1.73m2
Urinary amylase	133U/L	VR: 42-321U/L
Anti-SSA (RO)	<7U/mL	<7U/mL: non-reactant
Anti-SM	<7U/mL	<7U/mL: non-reactant
Anti-DNA	Negative	Negative
Anti-SSB-LA	<7U/mL	<7U/mL: non-reactant
Feces parasite test	Negative	Negative
Macroamylase (PEG)	5.41%	Positive if <27%
TTG-IgA**	Non-reactant	Non-reactant
Serum IgA	133mg/dL	VR: 58-359mg/dL
Antiendomisial antibody - IgG	Non-reactant	Non-reactant
Antiendomisial antibody - IgA	Non-reactant	Non-reactant
Abdomen CT scan	No changes	

*Hemoglobin; **Hematocrit; *** Carcinoembryonic antigen; **** Anti-transglutaminase antibody.

Table 2. Laboratory tests of the patient's family members

FAMILY MEMBERS	AMYLASE RESULTS	REFERENCE VALUES	LIPASE VALUES	REFERENCE VALUES
FATHER	56 U/L	VR:25-125 U/L	18 U/L	VR<67 U/L
MOTHER	51 U/L	VR:25-125 U/L	23 U/L	VR<67 U/L
SISTER 1	58 U/L	VR: 25-125 U/L	30 U/L	VR<67 U/L
SISTER 2	69 U/L	VR:25-125 U/L	13 U/L	VR= 7-39 U/L

pancreatitis as she had serum hyperamylasemia of 150 U/L. Due to the persistence of the abdominal pain, she was hospitalized and further investigated, reaching the diagnosis of macroamylasemia. After diagnosis, during follow-up, the patient no longer had abdominal pain but maintained serum hyperamylasemia.

Ko e Lee (2009)[7] reported the case of a 4-year-old child with a history of subacute abdominal pain and low-grade fever. The patient was hospitalized and investigated and hyperamylasemia was identified (687 U/L) but with normal serum lipase (31 U/L). The patient was fasted and total parenteral nutrition was started. On the second day of hospitalization, she was asymptomatic (complaining only of hunger) but maintained high serum amylase levels (700 U/L). Abdomen ultrasonography and CT scans were normal. Thus, the possibility of macroamylasemia was suspected and amylase/creatinine clearance was performed with a rate of 0.48%, suggesting macroamylasemia. As in the case described above, the child remained asymptomatic during follow-up, maintaining high levels of serum amylase.

Although the association between macroamylasemia and abdominal pain is likely to be circumstantial, as children with abdominal pain are more likely to undergo investigation for serum amylasemia and macroamylasemia usually persists despite

resolution of abdominal pain[4,7,12,13], some autoimmune conditions have been associated with childhood macroamylasemia such as celiac disease[4] and Crohn's disease[10].

Another condition to be investigated is familial hyperamylasemia, in which at least three generations of the patient's family members have increased serum amylase levels[2]. Gullo's syndrome is also a benign pancreatic hyperenzymia but it involves an increase in other pancreatic enzymes, such as lipase, and it is not associated with the formation of macrocomplexes[14].

Similar to existing reports, we describe the case of an adolescent referred to the pediatric gastroenterology outpatient clinic with recurrent abdominal pain and serum hyperamylasemia. An investigation was carried out, with the diagnosis of macroamylasemia using the PEG precipitation method. Despite the benign nature of this condition, due to the possible association with pathological conditions, complementary exams and family investigation were performed. In the case described, no associated pathologies were found, and chronic abdominal pain was classified according to the Rome IV criteria[15] as abdominal migraine attacks; and despite the lack of specific treatment, the patient showed improvement in the episodes of abdominal pain, maintaining persistent hyperamylasemia.

Disseminating and discussing macroamylasemia in the context of chronic abdominal pain in children is important in order to provide a better diagnostic and therapeutic approach for children with serum hyperamylasemia.

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