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Coeliac disease masquerading as macroamylasaemia

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SUMMARY

Macroamylasaemia (MA) is a biochemical disorder characterised by elevated serum amylase activity, resulting from the circulation of a macromolecular complex of amylase bound to a serum component, often an immunoglobulin. The increased molecular weight of this complex prevents the normal renal excretion of the enzyme. A few cases of adult patients with coeliac disease (CD) and MA have been reported, in which the biochemical disorder resolved after treatment with a gluten-free diet. However, in other cases, this resolution did not occur. Here, we report a case of CD masquerading as recurrent pancreatitis due to the presence of MA.

BACKGROUND

Macroamylasaemia (MA) is a biochemical disorder characterised by hyperamylasaemia without elevated urinary amylase and no associated signs or symptoms.[1] Serum amylase is primarily released from the pancreas (40%–45%) and salivary glands (55%–60%), with its clearance occurring through the kidneys (25%) and the reticuloendothelial system (75%).[2] MA results from circulating complexes of amylase bound to macromolecules, such as immunoglobulins and polysaccharides, forming macroamylase complexes that cannot be cleared by the renal glomeruli.[3] This condition may present as an isolated, benign phenomenon without pathological significance or may occur in association with inflammatory disorders, including coeliac disease (CD), inflammatory bowel diseases, rheumatoid arthritis, haematological malignancies and monoclonal gammopathy.[1] The prevalence of MA is approximately 2.5% among patients with hyperamylasaemia.[3 4] Some studies have observed the association between MA and CD as well as the disappearance of MA with a gluten-free diet (GFD).[5] Here, we describe a patient in whom persistent hyperamylasaemia was attributed to CD.

CASE PRESENTATION

A woman in her late 20s was admitted with a history of recurrent non-specific abdominal pain and persistent hyperamylasaemia. Her amylase level was 620 U (normal range: 35–120 U). She was referred to the gastroenterology service due to suspected acute pancreatitis. Her medical history was unremarkable, and she was not taking any medications. On admission, she reported intermittent heartburn and dyspepsia. She had postprandial, non-specific and recurrent epigastric pain, which was not typical of pancreatitis and was not associated to any specific food. She had no vomiting, dysphagia, bloating, diarrhoea or constipation. Additionally, she had no significant weight loss during the period of her ongoing symptoms. Her physical examination was unremarkable. Apart from hyperamylasaemia, all other laboratory results were normal, including serum lipase, triglyceride levels, C reactive protein, liver function tests, kidney functions tests and thyroid function tests. Serum immunoglobulins were also within normal limits. The patient showed no symptoms or signs of cholelithiasis, hepatitis, biliary cholangitis, systemic lupus erythematosus or rheumatoid arthritis. An ultrasound examination of the abdomen, including the liver and gallbladder, was normal. An abdominal CT with contrast yielded no pathological findings. Serology for CD was strongly positive, prompting an upper gastrointestinal tract endoscopy, which revealed normal examination till the second part of the duodenum (figure 1). Histological evaluation confirmed the diagnosis of CD, with findings consistent with Marsh type 3, Corazza: grade B1, showing hypertrophic crypts and partial to subtotal loss of villi (figures 2 and 3). The patient had MA, which can be the first presentation of autoimmune disease, such as CD. The patient had clinical, serological and intestinal histopathological features of CD. A GFD was initiated. Notably, despite the persistent and significant elevation of serum amylase, her serum lipase remained consistently normal throughout the follow-up period before starting the GFD.

DISCUSSION

CD is an immune-mediated response to ingested gluten, leading to varying degrees of villous atrophy and flattening of the small intestinal mucosa. Detection of CD-specific antibodies in the serum is valuable for the initial screening of suspected cases. An intestinal biopsy is required in most patients to confirm a diagnosis.[5] The diagnosis of MA in patients with isolated, elevated amylase levels can be established by determining the molecular weight of serum amylase using immunologic assays or the amylase-to-creatinine clearance ratio (ACCR). In patients with MA, the ACCR is reduced because of the poor filtration of large macroamylase complexes. In the absence of renal failure, a

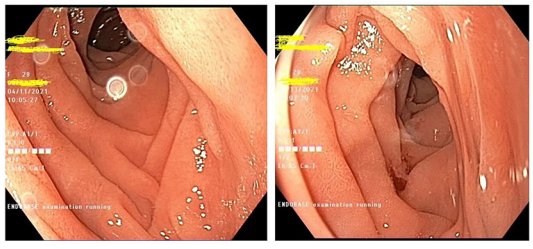

Figure 1 Endoscopic images of the duodenum.

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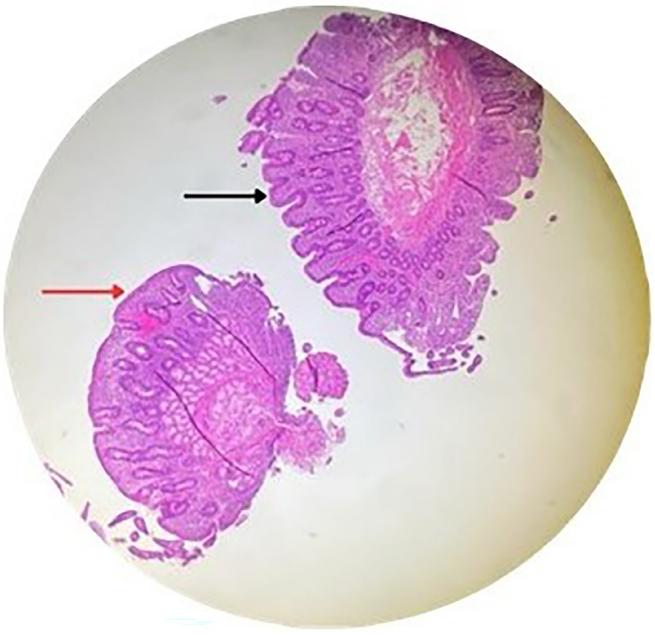

Figure 2 Low-power view of multiple duodenal biopsies showing an area of total villous atrophy (red arrow) and an area with significant villous shortening (black arrow).

low ACCR is indicative of MA.[6] The ratio is calculated using the following formula: ACCR=amylase(urine)×creatinine (serum)×100/amylase(serum)×creatinine (urine). A ratio of less than 1% in a 24-hour collection supports the diagnosis of MA, indicating poor clearance of amylase by the kidney (normal 3%–4%).[2] Patients with acute or recurrent pancreatitis were excluded. The patient had normal renal function and serum lipase levels, with an ACCR ratio of 0.16%.

MA was first called as such by Berk in 1967, who described it as 'a biochemical aberration in the search for a disease' due to time-consuming methods of analysis and a lack of obvious clinical implications.[7] MA is generally asymptomatic. In some cases, it may be detected incidentally during investigations of abdominal pain. Several hypotheses have been proposed to explain this association, including increased intestinal permeability.[8] Some authors have suggested that the abdominal pain may be attributed to the deposition of macroamylase molecules in the pancreas.[1] However, this observation does not confirm an association between the two. In patients with unexplained hyperamylasaemia without evidence of pancreatitis, MA should be assessed to avoid unnecessary diagnostic tests and treatment; if MA is present, the possibility of CD should be considered.[9] MA associated with CD has been described in adult patients.[3 7 9–13] A GFD may lead to significant improvement in MA.[8 10 12 13] However, Rabsztyn *et al*[9] found that MA levels remained elevated in some patients on a GFD. This is consistent with our case, as in 3-year follow-up, the serial serum amylase levels did not normalise despite a strict GFD, as evident by the normalisation of tissue transglutaminase (TTG) level.

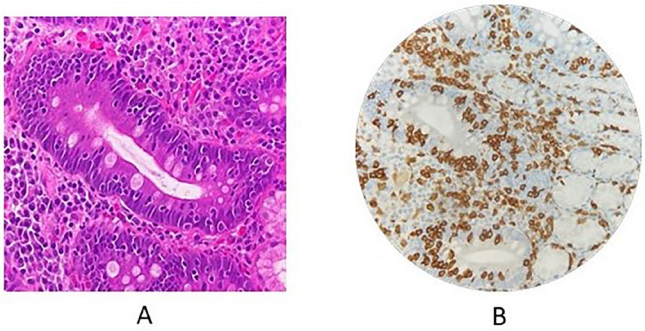

Figure 3 Heavy lymphocyte infiltration of the enterocytes, highlighted by H&E staining (A) and CD3 immunostaining (B).

The case described here demonstrates the association between CD and MA.

Several studies have described the link between MA and CD, showing differences in amylase levels in several patients. Studies have reported improvements in amylase levels in patients after switching to a GFD.[13] Bonetti *et al*[10] described a case of resolved MA. Liu *et al*[14] also explored cases of patients with CD, MA and combinations of other conditions such as hyperamylasaemia and immune abnormalities. Similar patient outcomes were reported by Depsames *et al*.[11] The study described a patient with CD and elevated serum amylase activity, but no classical gastrointestinal signs. MA eventually resolved after adopting a GFD, similar to observations in previous studies. A case report by La Villa *et al*[3] of a woman with unrecognised CD who exhibited various immune system abnormalities also revealed extraintestinal manifestations that improved or resolved entirely after transitioning to a GFD. The case report by Viswanath and Wynne[15] described that a woman with chronic malabsorption showed symptom improvement and disappearance of the macroamylase complex after switching to a GFD.

Notably, the population-based work by Rabsztyn *et al*[9] on MA reported rare cases of persistent MA in patients on a GFD. However, this study did not specify whether the patients strictly adhered to the GFD, which could be linked to the prevalence of MA in some patients on the GFD.

Contrary to most published findings, our current study on a patient in her late 20s with MA, who had clinical, serological and intestinal histopathological features of CD, showed transient improvement in amylase levels but never returned to normal levels after switching to a strict GFD, as demonstrated by the normalisation of serum TTG level.

Learning points

- Coeliac disease may be a cause of hyperamylasaemia.
- Consider macroamylasaemia as a cause of persistent hyperamylasaemia, particularly when serum lipase levels remain consistently normal, and the patient's clinical presentation is not typical of acute pancreatitis.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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