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Case Report

Markedly Elevated Lipase as The First Manifestation of Celiac Disease: A Case Report

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Abstract

Lipase is a hydrolytic enzyme and commonly used for the diagnosis of pancreatitis with amylase. Except for pancreatitis, lipase is elevated in many clinical conditions such as hepatobiliary disorders, bowel diseases, malignancies, renal impairment. Celiac disease (CD) should be considered as one of the causes. In patients with CD, the frequency of pancreatic hyperenzymemia and possible pathophysiological mechanisms are not well studied. To date, several mechanisms explaining pancreatic hyperenzymemia in CD are reported. Malnutrition, disease bowel induced pancreatic dysfunction, autoimmune pancreatic inflammation, and macroenzymemia are the main ones. Herein, we report a patient with newly diagnosed CD, representing markedly elevated serum lipase level with normal amylase.

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Introduction

Lipase is an enzyme that catalyzes the breakdown of triglycerides into glycerol and free fatty acids. It is produced by various cells in many organs such as the pancreas, liver, bowel, tongue, and stomach. Lipase is mostly found in the pancreas and crucial test for the diagnosis of pancreatitis. Except pancreatitis, serum lipase levels may also increase in a wide range of conditions, including renal impairment, hepatobiliary disorders, gastroduodenal perforations and ulcers, bowel necrosis and obstruction, certain neoplasms, critical illness, and other diseases such as diabetic ketoacidosis and celiac disease (CD).[1]

Celiac disease is a small bowel disorder characterized by mucosal inflammation, villus atrophy, and crypt hyperplasia dependent on gluten ingestion. The mainstay of the treatment is a gluten-free diet, which concerns most of the

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patients' social life. Therefore, diet adjustment is commonly problematic—gluten tolerability changes from person to person.[2] Although the time to the beginning of patients' treatment response is different, clinical improvement is observed in two weeks for 70%.[3] Trace elements, vitamin levels, and serological markers are used for patient follow-up.[4] The level of anti-tissue transglutaminase IgA antibody reaches optimum for 75% of patients having a gluten-free diet in almost one year.[5] The other indicator for an appropriate gluten-free diet is intestinal fatty acid-binding peptide, which was of working response to treatment quicker than any serological marker.[6]

Although the digestive tract is the main target organ, CD may present with extraintestinal manifestations and atypical laboratory findings such as pancreatic hyperenzymemia.[7,8] The frequency of pancreatic hyperenzymemia (PH) in CD is not well-known, but CD is suggested to be on the checklist of differential diagnosis in case of unexplained hyperenzymemia.[8,9] Isolated elevation of lipase is a rare manifestation in celiac disease.[8] Herein, we report a CD representing markedly elevated serum lipase levels.

Case Report

A 45-year-old female patient was admitted to the state hospital with abdominal pain. Laboratory evaluation revealed hyperlipasemia, but serum amylase level was within the normal range. In computed tomography (CT) imaging of the pancreas, enlargement of the pancreas was observed, and there were no inflammatory changes, peripancreatic fluid collections, or necrosis. She was diagnosed with acute pancreatitis and treated for 20 days. Notwithstanding treatment, the level of serum lipase remained high. Therefore, he was referred to the gastroenterology department of Bursa Uludag University.

The patient complained of fatigue and slight abdominal pain persisting for six months while taking her detailed history. She did not smoke, get any medications, or use alcohol. Likewise, she did not report nausea, vomiting, or diarrhea. Physical examination showed neither rebound nor tenderness. Laboratory examination revealed markedly elevated serum lipase, normal amylase (upper limit of normal range), minimal elevation of liver enzymes, and slight anemia consistent with iron deficiency *(Table 1)*. The levels of serum glucose, creatinine, triglyceride, calcium, total bilirubin, and C-reactive protein were all in normal range (92 mg/dL, 0.79 mg/dL, 148 mg/dL, 9.4 mg/dL, and 0.33 mg/dL, respectively). The amylasetocreatinine clearance ratio was 1.5.

Further laboratory studies revealed normal serum levels of tumor markers (CEA, AFP, CA125, CA15-3, CA19-9) and immunoglobulins (IgA, IgG, IgM, IgG4). Hepatitis B, C, and HIV were negative. Magnetic resonance cholangiopancreatography and CT imaging

Table 1. Laboratory findings at diagnosis and after one year of the gluten-free diet

	At the time of diagnosis	After one-year gluten-free diet	Normal range
AST	33	18	11-25 IU/L
ALT	32	15	7-28 IU/L
Amylase	124	85	25-125 IU/L
Lipase	**943**	39	8-78 IU/L
Hemoglobin	**11.9**	13.3	12.20-18.0 g/dL
ESR	**57**	40	0-32 mm/h
Ferritin	**14.5**	44	4.63-204 ng/mL
IgA-anti-tG	**266**	8	<20 EU/mL

ESR: erythrocyte sedimentation rate, **IgA-anti-tG**: anti-tissue transglutaminase A

of the abdomen were performed to exclude pancreatic disease, hepatobiliary disorders, and malignancy. Imaging studies revealed no pathological findings. Endoscopic examination revealed that duodenal mucosa appeared atrophic with loss of fold and had a nodular appearance. Then, anti-tissue transglutaminase A and G were studied and found positive at high titer *(Table 1)*. Human leukocyte antigen (HLA) typing was positive for HLA-DQ2. On histopathological examination of duodenal biopsy, increased intraepithelial lymphocytes, mucosal atrophy was observed, immunohistochemical C3 and C8 staining revealed intraepithelial lymphocytosis *(Figure 1)*.

The patient was diagnosed with CD and started on a gluten-free diet (GFD). After a strict one-year GFD, serum lipase level decreased into the normal range *(Table 1)*.

Discussion

Increased serum lipase level is commonly an expression of pancreatic disease. Nevertheless, a wide range of clinical conditions, including CD was reported in previous publications.[1,9] To our knowledge, we present the first case that had more than ten-fold isolated lipase elevation as the first manifestation of CD.

To date, there are a few conflicting reports on the frequency of PH in CD. Carrocio et al.[8] reported that 40 of 202 newly diagnosed CD patients had elevated pancreatic enzymes, and in 14 of them (6.9%), the isolated elevation of lipase

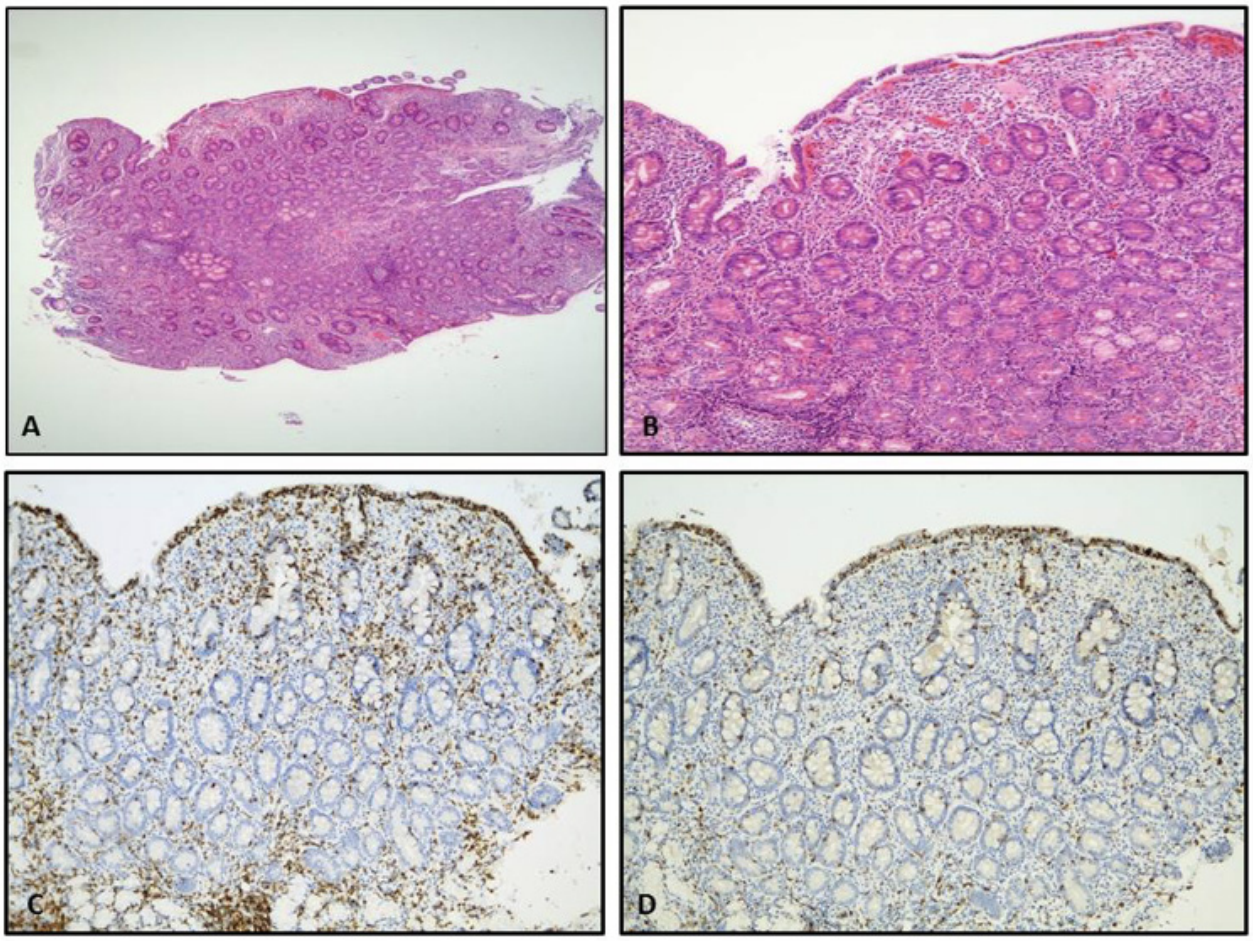

Figure 1A. Duodenal biopsy shows a flat lesion with villous atrophy (hematoxylin-eosin staining, x40). **Figure 1B.** The hematoxylin-eosin staining section shows increased intraepithelial lymphocytes (x100). **Figure 1C**. The immunohistochemical CD3 staining section demonstrates the intraepithelial lymphocytosis in the flat lesion (x100). **Figure 1D.** Increased intraepithelial lymphocytosis is also present in the section of CD8 immunohistochemical staining (x100).

was observed. In contrast, Migliori et al.[10] reported that the search for CD in their 65 subjects with benign pancreatic hyperenzymemia was negative.

The pathophysiological mechanisms explaining PH in patients with CD is not well studied. Several mechanisms underlying PH in CD were reported. Malnutrition-induced low-grade pancreatic inflammation was published as one of the mechanisms.[11,12] Malabsorption of critical nutrients causes reduced production of pancreatic enzyme precursors and protein malnutrition, altering the pancreatic structure. Another mechanism is diseased bowel induced pancreatic dysfunction. Chronic inflammation in the small bowel in CD results in alterations in neuroendocrine cells, and it causes the impaired secretion of the pancreas stimulating hormones. Also, chronic inflammation may cause mechanical obstruction by papillary scaring. Subclinical autoimmune pancreatic damage was speculated to be one of the reasons for hyperenzymemia.[12,13] Many autoimmune disorders such as autoimmune hepatitis, primary biliary cirrhosis, diabetes mellitus, autoimmune thyroid disease, rheumatoid arthritis, psoriasis, pancreatitis accompany CD. Th1-associated cytokines (interferon-gamma and interleukin-18) are increased in both CD and autoimmune pancreatitis. Therefore, autoimmune pancreatic inflammation may be observed in patients with CD. The formation of macroenzymes (macroamylasemia and macrolipasemia) is another mechanism to explain hyperenzymemia in CD.[14,15] Serum amylase and lipase are bound to other macromolecules like immunoglobulins and escape glomerular filtration, resulting in decreased renal clearance and elevated serum levels.

Among asymptomatic celiac patients, pancreatic hyperenzymemia was reported.[16] Since clinical manifestations are limited for these 'silent' patients, serum pancreatic enzyme levels may help to monitor an appropriate gluten-free diet.[16] Considering the underlying possible physiopathological mechanisms, normalization of pancreatic enzyme level with diet might have prognostic value due to the demonstration of intestinal and pancreatic inflammation.

In conclusion, multiple factors can cause isolated hyperlipasemia, and CD should be considered in the differential diagnosis. To understand the relation between CD and pancreatic hyperenzymemia, mainly the frequency and pathophysiological mechanisms, further studies with a high number of patients can be helpful.

Conflict of Interests

Authors declare that there are none.

Authors' Contribution

Study Conception: ABS, MG; Study Design: ABS, MG; Supervision: ABS, MG, NU; Funding: ABS, NU; Materials: ABS, NU, FCH; Data Collection and/or Processing: ABS, NU; Statistical Analysis and/or Data Interpretation: ABS, FCH; Literature Review: ABS, FCH; Manuscript Preparation: ABS, FCH; and Critical Review: MG, NU.

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