Macroamylasaemia in association with the acquired immunodeficiency syndrome

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Summary: A patient with macroamylasaemia in association with the acquired immunodeficiency syndrome is described. Patients with the acquired immunodeficiency syndrome commonly have gastrointestinal symptoms that often prompt serum amylase determination. Macroamylasaemia has been found to occur in a variety of diseases including various autoimmune disorders. The marked immunological abnormalities and increased circulating immunoglobulins associated with the acquired immunodeficiency syndrome may have predisposed this patient to macroamylase formation. Macroamylasaemia is a benign condition that requires no treatment and must be excluded in the patient with unexplained hyperamylasaemia to avoid unnecessary diagnostic tests and treatment.

Introduction

Infection with human immunodeficiency virus (HIV) results in profound dysfunction of both cell-mediated and humoral immunity predisposing patients to severe opportunistic infection and Kaposi's sarcoma. Patients with the acquired immunodeficiency syndrome often develop multi-system organ damage including widespread involvement of the gastro-intestinal tract. The development of abdominal symptoms often prompts serum amylase determination.

Patients with unexplained hyperamylasaemia are often subjected to multiple diagnostic tests or even laparotomy. Macroamylasaemia is a frequently overlooked cause of hyperamylasaemia and must be excluded to avoid making erroneous diagnoses. We report the first case of macroamylasaemia in association with the acquired immunodeficiency syndrome.

Case report

A 23 year old promiscuous heterosexual male was hospitalised after two months of fever, dyspnoea, and chest pain. Seven months previously oral candidiasis was noted and four months before admission a routine blood count revealed a leucocyte count of $1.9 \times 10^9/l$ and platelet count of $1.17 \times 10^9/l$. For two months before admission he experienced fever, chills, night sweats, non-productive cough and dyspnoea on exer-

tion. Physical examination was remarkable for mucocutaneous candidiasis, small non-tender bilateral cervical and axillary lymph nodes and a palpable spleen tip. Serum immunoglobulin determination by radial immunodiffusion revealed an IgM of 840 mg/dl (normal 56–352) an IgA of 900 mg/dl (normal 70–312), and an IgG of 2100 mg/dl (normal 639–1349). The T4/T8 lymphocyte ratio was 0.17 (normal 1.2–3.8), and HIV antibody was detected by Western blot testing. Flexible fiberoptic bronchoscopy with trans bronchial biopsy and bronchoalveolar lavage revealed abundant *Pneumocystis carinii* on Gomori's methenamine silver stain. Therapy was instituted with pentamidine isethionate 250 mg administered intravenously over one hour daily.

On the tenth hospital day he experienced multiple episodes of bilious vomiting, but denied any abdominal pain or distension. Serum amylase was 3480 IU (normal 60–160); creatinine was 159 mmol/l, SGOT-68 U/l and SGPT, alkaline phosphatase and bilirubin were normal. Repeat serum amylases were 2990 IU and 3180 IU with quantitative urine amylases of 21 units/hour and 9 units/hour (normal 50–400 U/h). The vomiting and mild renal insufficiency were attributed to pentamidine and subsided 48 hours after therapy was changed to trimethoprim sulphamethoxazole. Computerized tomographic examination of the pancreas was normal. Polyethyleneglycol 6000 precipitated 82% of the patient's serum amylase consistent with macroamylasaemia. In addition, determination of amylase isoenzymes by cellulose acetate electrophoresis revealed a diffuse and wide-

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Accepted: 18 February 1987

spread band midway between the pancreatic and salivary peaks confirming macroamylasaemia. Six months after resolution of the *Pneumocystis carinii* pneumonia serum amylases continue to remain at approximately 3000 IU/l.

Discussion

Macroamylasaemia occurs when normal circulating serum amylase binds to another serum protein forming a high molecular weight complex that is too large to be excreted in the urine. The macroamylase is usually a complex of S type amylase bound to an immunoglobulin or occasionally a polysaccharide.¹ It occurs in 1.0% of the general population, 2.5% of patients with hyperamylasemia, and 29% of patients with chronic unexplained hyperamylasaemia.^{2,3} It is an acquired condition of uncertain significance that may represent a nonspecific dysproteinemic response to disease.¹

Macroamylasaemia has been found to occur in association with a variety of diseases including diabetes mellitus, cancer, alcoholism, systemic lupus erythematosus, and liver disease and occurs with greater frequency in patients with disturbed humoral immunity and autoimmune diseases. In the latter setting, macroamylasaemia may reflect an aberrant state of immunoglobulin production.¹ It has also been described in malabsorption syndromes and other inflammatory diseases of the gut suggesting increased absorption of luminal antigen from altered gut permeability.⁴ The significance of macroamylasaemia in apparently healthy persons is unknown and it remains unclear whether this represents an early marker of disease. However, the correlation in some patients between macroamylase level and fluctuations in activity of underlying disease suggests a direct relationship between the two conditions.⁵

The acquired immunodeficiency syndrome (AIDS) is characterized by a profound alteration in both the

cellular and humoral arms of the immune system.⁶ The polyclonal B cell activation, increased spontaneous immunoglobulin secretion, and elevated levels of serum immunoglobulins and circulating immune complexes in AIDS may predispose these patients to macroamylase formation. In addition, the enteropathy of AIDS may result in the presentation of an increased antigenic load through the diseased mucosa to the enteric immune system similar to that described in patients with other malabsorption syndromes and macroamylasaemia.⁷

This patient has type I macroamylasaemia characterized by an increased serum amylase and a low urinary amylase. An abnormally low ratio of amylase to creatinine clearance is a useful screening test for type I macroamylasaemia. However, a low ratio is not specific for macroamylasaemia and would not exclude type II macroamylasaemia which is associated with hyperamylasaemia and a normal $C_{am}:C_{cr}$ ratio or type III which is associated with normal levels of serum and urine amylase. If available, a serum lipase assay is useful to exclude pancreatic disease as a cause of hyperamylasaemia. The selective precipitation of at least 73% of macroamylase by polyethylene glycol (PEG) 6000 provides a simple assay to detect its presence.⁸ PEG 6000 precipitated 82% of this patient's amylase and cellulose acetate electrophoresis revealed the typical broad band intermediate between salivary and pancreatic isoamylase peaks confirming macroamylasaemia.⁹ Although we cannot exclude pre-existing macroamylasaemia we believe the marked immunological abnormalities as reflected by a reduced T4/T8 lymphocyte ratio and increased circulating immunoglobulins may have predisposed this patient to macroamylase formation.

Macroamylasaemia is a benign condition that requires no special treatment. Gastrointestinal symptoms commonly occur in AIDS and often prompt serum amylase determination. Macroamylasaemia should be excluded in patients with AIDS and hyperamylasaemia to avoid an invasive and prolonged workup.

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