Chronic Hyperamylasemia and Chronic Pelvic Inflammatory Disease

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A 54-year-old woman with chronic pelvic inflammatory disease and pyelonephritis developed persistent hyperamylasemia with transient increases in the amylase–creatinine clearance ratio. Even though chronic pancreatitis was suspected clinically, at postmortem examination the pancreas was found to be normal. We suggest that the hyperamylasemia resulted from entry into the circulation of amylase produced within sequestered endosalpingeal epithelial cysts, possibly amplified by impaired renal clearance. Thus, the potential of the serum amylase assay as a marker of serous ovarian tumors is further indicated.

Hyperamylasemia often indicates acute or exacerbated chronic pancreatic disease. However, many other pathological states can result in increased amylase (EC 3.2.1.1.) in serum (1–3). Although amylase production has been identified in female genital-tract tissues (4–8), only rarely have gynecologic abnormalities been associated with hyperamylasemia (2, 3, 5, 9–12). The production of amylase has been associated with ovarian carcinomas (13–16). It has recently been proposed that serum amylase may be a clinical marker for serous ovarian neoplasms (14–16).

This report describes a woman with chronic pelvic inflammatory disease and persistent hyperamylasemia but no evidence of pancreatic disease at postmortem examination.

Case Report

The body of a 54-year-old woman with a 22-year history of recurrent pelvic inflammatory disease and pyelonephritis was examined. The death was attributed to renal failure and uremic seizures.

A right tubo-ovarian abscess was diagnosed clinically 22 years before death, and a cul-de-sac multiloculated abscess was diagnosed surgically seven years later. Serum amylase values were noted to be slightly above normal 11 years before death. Five years before death, markedly supranormal serum amylase values were observed, associated with evidence of acute exacerbation of pelvic inflammatory disease. There was a sustained increase of greater than 800 U/L (normal reference interval 60–160 U/L) for a week, the maximum value observed being 1125 U/L. The ratio of amylase clearance to creatinine clearance was 0.06 early in her hospital course and later dropped to 0.037. Over the next five years, about 20 amylase determinations were made, and the results were always high, often >500 U/L, with a maximum value of 1110 U/L one year before death. This hyperamylasemia was attributed clinically to exacerbations of chronic alcohol-induced pancreatitis, although no hypercalcemia, hypomagnesemia, hyperglycemia, or conclusive radiographic evidence for pancreatitis were observed. The patient had persistent and progressive renal insufficiency during the last six years of life, clinically diagnosed as chronic pyelonephritis, which led to a uremic state requiring dialysis during the two weeks before death.

Findings at postmortem examination included chronic interstitial nephritis consistent with pyelonephritis, severe chronic pelvic inflammatory disease, and a grossly and microscopically normal pancreas. Both fallopian tubes and ovaries were surrounded by masses of fibrous tissue. Microscopic sections revealed numerous cystic structures adjacent to and within the residual identifiable fallopian tube tissue. Microscopically, these cystic structures were lined by predominantly cuboidal epithelium resembling salpingeal mucosal epithelium. We saw no acute inflammation.

Discussion

The pancreas is not the only body tissue that contains high concentrations of amylase. Therefore hyperamylasemia is not specific for pancreatic disease. Structures containing epithelium of müllerian and mesonephric duct origin—including salpingeal mucosa, fallopian tube cysts, and ovarian cysts—also produce amylase (4–8). As might be anticipated from these observations, certain diseases of the female genital tract are associated with hyperamylasemia. Ruptured ectopic tubal pregnancies can produce markedly increased values for serum amylase (5, 11, 12). Hyperamylasemia is also seen occasionally in acute salpingitis (3, 9). Ovarian carcinomas have been found to contain amylase, and increased serum amylase has been associated with them (3, 10, 13). This may be the result of functioning endosalpingeal-type epithelium within the neoplasm (14, 15). Immunohistochemical localization has identified amylase in normal endosalpingeal epithelium and in the epithelial cells of benign, borderline, and malignant serous ovarian tumors (16). Although high concentrations of amylase have been identified in cystic fallopian-type structures produced by chronic salpingitis (4), ours is the first reported case of chronic hyperamylasemia associated with chronic pelvic inflammatory disease.

The ratio of amylase clearance to creatinine clearance reportedly is a good discriminator between hyperamylasemia owing to acute pancreatitis and that of other causes (17). These investigators believed that amylase clearance increases relative to creatinine clearance only in acute pancreatitis. Thus a ratio exceeding the normal range of 0.01 to 0.04 was considered diagnostic of pancreatitis. It has been demonstrated that an increased clearance ratio reflects defective proximal tubular reabsorption of amylase, a situa-
tion that occurs in virtually all patients with uncomplicated acute pancreatitis (18). However, other conditions that may acutely impair tubular function, such as burns and diabetic acidosis, also may cause an increase in this ratio (18, 19). Hence the increased amylase clearance value we found in this case may be ascribable to the patient's pyelonephritis, which is known to cause proximal tubular damage. Macroamylasemia can be ruled out as the cause of her hyperamylasemia because it should cause a decrease in the clearance ratio, not an increase (18, 19).

Another potential cause for this patient's hyperamylasemia was the chronic renal insufficiency produced by pyelonephritis. However, one would expect serum amylase to be no greater than twofold normal as a result of renal insufficiency (2), while in this patient the values were repeatedly sixfold normal. Possibly there were two effects in this case: sequestered endosalpingal mucosa releasing more amylase into the circulation and impaired renal function delaying its clearance from the blood.

This anecdote certainly does not prove that hyperamylasemia can be produced by salpingal mucosa that has been altered by chronic disease. However, fallopian tube mucosa is known to produce amylase, and in the absence of lesions affecting any other tissues known to secrete amylase we believe salpingal mucosa altered by chronic disease is the most probable source of the chronic hyperamylasemia in this case. Furthermore, this report lends credence to the notion that the ectopic production of amylase by serous ovarian tumors may be a useful clinical sign of these neoplasms (14–16).

References