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Acute Pancreatitis in a Case of Multiple Myeloma with Hypercalcemia

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A patient with hypercalcemia and newly diagnosed multiple myeloma developed acute pancreatitis. Other etiologic factors for pancreatitis were excluded. Hypercalcemia secondary to hyperparathyroidism is associated with acute pancreatitis. In English literature, only one other case has been published where the hypercalcemia of multiple myeloma may have caused pancreatitis. Pancreatitis should be considered in patients with hypercalcemia and multiple myeloma who develop nausea/vomiting, and abdominal pain.

Key Words: *Hypercalcemia, Multiple Myeloma, Acute Pancreatitis*

INTRODUCTION

Although hypercalcemia of various etiologies is known to be associated with pancreatitis, most cases have been associated with hypercalcemia of primary hyperparathyroidism[1,3]. Few cases of pancreatitis have been reported to be secondary to the hypercalcemia of metastatic tumors or multiple myeloma[6,8]. We report a second case of acute pancreatitis occurring in a patient with multiple myeloma and discuss its clinical implication.

CASE REPORT

A 38-year-old male was hospitalized with a 3-week history of a painful sternal mass and low back pain. The patient also complained of generalized weakness, anorexia and occasional nausea. On physical examination, there was a 3 cm x 3 cm, ill defined, hard tender mass in the lower sternal area. No lymphadenopathy or hepatosplenomegaly was noted. The abdomen was soft with mild epigastric pain but no rebound tenderness. No mass was palpable. Initial laboratory studies in the emergency room the night before admission showed that the hemoglobin was 10.1 g/dl, the hematocrit 30.7% and the white blood cell count 11,200. The serum calcium was 12.7 mg/dl, serum phosphorus 4.2 mg/dl, total serum protein 11.7 g/dl, serum albumin 3.2 g/dl, serum urea nitrogen 15 mg/dl, and the serum creatinine was 1.4 mg/dl. The x-ray of the skull showed multiple lytic lesions. Serum protein electrophoresis showed an M-protein in the gamma region. There was a monoclonal IgG kappa component with decreased IgA and IgM on the serum immunoelectrophoresis. The diagnosis of multiple myeloma was confirmed by a bone marrow examination showing a hypercellular marrow with 40% plasma cells.

The day after admission, the patient developed nausea, vomiting and abdominal pain. The serum calcium level was 13.3 mg/dl and the patient was treated with IV hydration and IV furosemide 20 mg every 2 hours for 6 days. Despite the treatment, the calcium level remained elevated, and was 14.0 mg/dl on the fourth hospital day. Calcitonin 340 IU was given once intramuscularly.

Chemotherapy for multiple myeloma was begun on the fourth hospital day. The regimen included BCNU 80 mg and cytoxan 800 mg IV on the first day, melphalan 8 mg PO daily for 7 days, and prednisone

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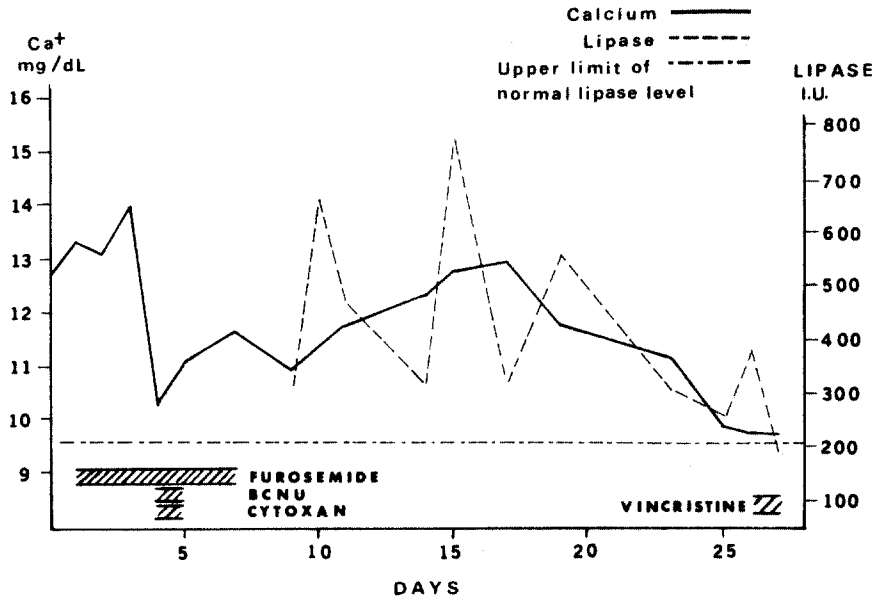

Fig. 1. *Calcium and lipase level during the hospital course.*

40 mg PO twice daily for 7 days then in tapering doses. Vincristine 2 mg intravenously was given on the 21st day. Due to severe emesis, the patient vomited the first doses of melphalan and prednisone. Subsequently, melphalan and prednisone were temporarily discontinued. The intravenous chemotherapeutic agents were given as scheduled. Further chemotherapy is shown in Fig. 1.

Because of persistent abdominal pain and Hemoccult positive emesis, nasogastric suction was started. An upper endoscopy was performed on the sixth hospital day, which showed multiple small erosions in the gastric antrum and a normal duodenum. The serum amylase was 120 u/ℓ (normal, 37-117), and the lipase was 311 u/ℓ (normal, 23-208). There was no history of abdominal trauma, pancreatitis or cholelithiasis. The patient denied any history of heavy alcohol use. There was no family history of pancreatitis. The lipase increased up to 661 u/ℓ on the subsequent day. Ultrasound examination of the abdomen showed no evidence of cholelithiasis or dilatation of the biliary ducts. The pancreas was not adequately visualized. The serum triglyceride level was 90 mg/dl (normal, 10-190). The serum PTH was also normal. A diagnosis of acute pancreatitis probably secondary to hypercalcemia was made. Subsequent serum lipase levels and calcium levels are shown in Fig. 1 along with the date when the therapeutic agents were administered. The patient was placed on parenteral hyperalimentation until he was asymptomatic and his serum amylase and lipase had returned to normal.

DISCUSSION

The association of acute pancreatitis with hypercalcemia of hyperparathyroidism is well described. The incidence of pancreatitis in cases of hyperparathyroidism ranges between 7% and 12%[1,3]. It is felt that the hypercalcemia of hyperparathyroidism favors the deposition of intraductal calculi in the pancreas, leading to ductal obstruction and pancreatitis[4]. Another possibility is that an increased concentration of calcium ions in pancreatic secretion and pancreatic tissue might promote activation of trypsinogen to trypsin[5].

Reports of pancreatitis secondary to the hypercalcemia of metastatic tumors or multiple myeloma are rare. In 1976 Grafter reported a case of acute pancreatitis in a patient with hypercalcemia due to metastatic breast carcinoma. In this case, the diagnosis of pancreatitis was made on the postmortem examination[6]. In another case, pancreatitis occurred in a patient with transitional cell and squamous cell carcinoma of the renal pelvis with metastasis to the bones. The patient had hypercalcemia and also an elevated serum parathyroid hormone level[8]. Meltzer et al described a patient

with multiple myeloma who had extensive bone disease with hypercalcemia and abdominal pain. A diagnosis of pancreatitis was made on the autopsy. There was pancreatic enlargement and fat necrosis with neutrophil infiltration. No antemortem serum pancreatic enzyme levels or parathyroid hormone levels were available[7].

In the present case, the possibility of coexistence of primary hyperparathyroidism is remote since the serum parathyroid hormone level was normal. Although the patient received intravenous furosemide, it is not likely the cause of pancreatitis since the symptoms of pancreatitis occurred before the beginning of furosemide therapy. Furosemide induced pancreatitis has been reported in patients on chronic oral therapy and the onset of the symptoms was 3-5 weeks after initiation of the therapy[8,10]. Alcohol intake, gallstones, trauma, peptic ulcer disease and hypertriglyceridemia have been ruled out as a cause of the pancreatitis by the history and appropriate tests. The chemotherapy reigmen for multiple myeloma included prednisone but the patient vomited the first dose and subsequently received no further steroids.

Although hypercalcemia was the suspected cause of pancreatitis, it is difficult to exclude direct involvemnt of the pancreas by multiple myeloma. Primary pancreatic carcinoma and tumors metastatic to the pancreas are known to be able to initiate acute pancreatitis[11]. In 1952 Hayes et al. reviewed 182 cases of extramedullary multiple myeloma. Seven cases had pancreatic involvement. Out of 38 consecutive autopsy cases, he found one with pancreatic involvement. It is not known whether the patient had the clinical manifestations of acute pancreatitis[12].

The rarity of reported cases of acute pancreatitis in patients with multiple myeloma seems surprising in view of a 30-60% incidence of hypercalcemia in multiple myeloma[13]. The pathogenetic association of hypercalcemia with pancreatitis may not be strong. The possibility of pancreatitis in a patient with multiple myeloma may be overlooked since the symptoms of acute pancreatitis, such as nausea, vomiting and abdominal pain, are easily attributable to hypercalcemia itself or the side effects of chemotherapeutic agents.

We believe this case represents a patient with pancreatitis secondary to hypercalcemia from multiple myeloma. Pancreatitis should be considered in patients with hypercalcemia and multiple myeloma who develop nausea and vomiting.

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