Case report

Acute pancreatitis due to hypercalcemia related to bone metastasis from breast cancer

Y.-G. CHEN¹, T.-Y. HUANG², T.-Y. HSIEH² and P.-J. CHEN²

From the ¹Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei and ²Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan

Address correspondence to Dr P.-J. Chen, Division of Gastroenterology, Department of Internal Medicine, Tri-Service General Hospital, No. 325, Section 2, Cheng-Gong Road, Neihu 114, Taipei, ROC.
email: endoscopy@ndmctsgh.edu.tw

Case presentation

A 48-year-old woman had infiltrating ductal cell carcinoma of left breast status post modified radical mastectomy 7 years ago. About 2 years ago, prior to this presentation, she had severe lower back pain, particularly at night. Breast cancer with sacrum and lumbar spinal metastases was found from the examination of Tc-99m whole-body bone scan. Radiotherapy and chemotherapy with adriamycin and cyclophosphamide were prescribed. One month before admission, new-onset tenderness over the left forearm and multiple bone pain progressed, and the repeat Tc-99m whole-body bone scan disclosed increased uptake found in the left humeral head, left tibia tuberosity, L2 spine, lower half of right femoral shaft and left hip joint. However, she had not received any chemotherapy during this month.

One month later, she presented to our emergency department with severe epigastric pain, poor appetite and persistent vomiting. Upon arrival, physical examinations showed oral temperature of 38.4°C, pulse rate of 112/min, respiratory rate of 26/min and tenderness of epigastric area with rebounding pain. Laboratory tests showed a white blood cell count of 17.4 x 10³/µl, with 82% neutrophils, C-reactive protein of 16.34 mg/dl (normal range: <0.5 mg/dl), serum amylase of 2084 U/l (normal range: 28–100 U/l), serum lipase of 3000 U/l (normal range: 13–60 U/l) and impairment of renal function with an increase in blood urea nitrogen and serum creatinine of 3.1 mg/dl. Hypercalcemia was confirmed with increased serum calcium concentration of 13.6 mg/dl (albumin-modified serum calcium concentration 14.2 mg/dl). The free (ionized) calcium concentration was 7.1 mg/dl (normal range: 3.5–4.5 mg/dl). Further laboratory investigation of the hypercalcemia revealed decreased serum phosphorus levels at 1.3 mg/dl, and normal levels of serum free T4 (FT4) and thyroid-stimulating hormone (TSH). The serum intact parathyroid hormone (iPTH) was 15.2 pg/ml (normal range: 10.0–69.0 pg/ml). Parathyroid-related peptide (PTHrP) levels were measured by radioimmunoassay within normal limit. The serum antinuclear antibody (ANA) and rheumatoid factor (RF) could not be detected.

Computed tomography of the abdomen revealed diffuse swelling with surrounding fat stranding and accumulating peripancreatic fluid (Figure 1). The area of necrosis was also found, but there was no evidence of gallstones or obstructed bile duct. Exudative pancreatitis was diagnosed. The endoscopic retrograde cholangiopancreatography (ERCP) demonstrated no evidence of the choledolithiasis. Without evidence of alcohol abuse, hypertriglyceridemia, biliary calculi or acute hypercalcemic pancreatitis was diagnosed. Ultrasound of the parathyroid glands showed no abnormalities, which was compatible with the secondary hypercalcemia caused by...
Table 1 Theses cases reported the malignancy-associated hypercalcemia complicated with acute pancreatitis between 1990 and 2011

<table>
<thead>
<tr>
<th></th>
<th>Age/Sex</th>
<th>Cancer type</th>
<th>Mechanism of hypercalcemia</th>
<th>Treatment</th>
<th>Patient outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63/F</td>
<td>Metastatic neuroendocrine tumor</td>
<td>Local osteolytic hypercalcemia</td>
<td>Fluid resuscitation, Intravenous furosemide</td>
<td>Expired</td>
<td>Dhar et al.¹</td>
</tr>
<tr>
<td>2</td>
<td>50/M</td>
<td>Renal cell carcinoma</td>
<td>Humoral hypercalcemia of malignancy (PTHrP mechanism)</td>
<td>Fluid resuscitation, Intravenous furosemide</td>
<td>Expired</td>
<td>Nabi et al.²</td>
</tr>
<tr>
<td>3</td>
<td>57/M</td>
<td>Multiple myeloma</td>
<td>Local osteolytic hypercalcemia</td>
<td>Fluid resuscitation, Calcitonin, Steroid (Prednisolone), Hemodialysis</td>
<td>Expired</td>
<td>Celik et al.³</td>
</tr>
<tr>
<td>4</td>
<td>44/F</td>
<td>ATL</td>
<td>Humoral hypercalcemia of malignancy (PTHrP mechanism)</td>
<td>Fluid resuscitation, Calcitonin</td>
<td>Expired</td>
<td>Ono et al.⁴</td>
</tr>
<tr>
<td>5</td>
<td>58/F</td>
<td>Multiple myeloma</td>
<td>Local osteolytic hypercalcemia</td>
<td>Fluid resuscitation, Calcitonin, Chemotherapy (VAD)</td>
<td>Expired</td>
<td>Ito et al.⁵</td>
</tr>
<tr>
<td>6</td>
<td>39/M</td>
<td>ATL</td>
<td>Humoral hypercalcemia of malignancy</td>
<td>Fluid resuscitation, Calcitonin, Steroid (Prednisolone)</td>
<td>Expired</td>
<td>Dazai et al.⁶</td>
</tr>
<tr>
<td>7</td>
<td>38/F</td>
<td>ATL</td>
<td>Humoral hypercalcemia of malignancy</td>
<td>No mention in this article</td>
<td>Expired</td>
<td>Dazai et al.⁶</td>
</tr>
<tr>
<td>Our patient</td>
<td>49/F</td>
<td>Metastatic breast cancer</td>
<td>Local osteolytic hypercalcemia</td>
<td>Fluid resuscitation, Intravenous Biphosphate, Hemodialysis</td>
<td>Expired</td>
<td></td>
</tr>
</tbody>
</table>

VAD refers to vincristine, doxorubicin and dexamethasone. ATL, adult T-cell leukemia.
osteolytic bone metastasis of infiltrating ductal carcinoma.

The patient received fluid replacement with saline and bisphosphonates. After therapy, the serum calcium concentration decreased and the acute pancreatitis subsided. One week later, another episode of hypercalcemia was found even with aggressive medical control. The bone marrow aspiration revealed diffuse infiltration of the atypical cells. For persistent hypercalcemia and oliguria, she underwent emergent hemodialysis on the 25th days after admission. After dialysis, the serum value returned to the normal limit. A line chart during the whole admission period about the relationship between serum amylase and free (ionized) calcium is summarized in Figure 2. However, the patient died of septic shock with multiple organ failure despite aggressive management.

**Discussion**

Acute pancreatitis induced by cancer-related hypercalcemia has been rarely reported. Reviewing related references between 1990 and 2011, most cases resulted from hematological malignancies such as T-cell leukemia or multiple myeloma-associated humoral hypercalcemia. We summarize the associated clinical features and management in Table 1.1–6

The pathophysiology of acute pancreatitis induced by hypercalcemia remains unclear. In recent studies, aberrant intra-acinar calcium signals are critical to the transduction of acinar cell injury.7 To treat acute pancreatitis caused by hypercalcemia, rapidly lowering the serum level of calcium plays an important role in the initial management. The general therapeutic principle is adequate fluid resuscitation with intravenous saline. Combining diuretic agents such as loop diuretics could be prescribed together to enhance the renal clearance of the calcium. Intravenous bisphosphonates such as zoledronate or pamidronate could serve as the first line of therapy to treat malignancy-related hypercalcemia, while calcitonin is an alternative choice. However, recent studies suggest that therapy with furosemide to manage hypercalcemia is not effective. The vigorous fluid resuscitation with normal saline and the immediate institution of bisphosphonate therapy have been considered to be the new standard for management of hypercalcemia.8 If the patient's status does not allow for adequate fluid resuscitation or progressive worsening of the renal function, dialysis is an alternative method.9

**Acknowledgements**

Many thanks to Shih-Hua Lin, Professor of Internal Medicine, Tri-Service General Hospital, National Defense Medical Center, Taipei, Taiwan, for reading and offering valuable advice.

**Conflict of interest**: None declared.

**References**