

A Case of Lung Cancer with Hypercalcemia which was Incidentally Complicated with Primary Hyperparathyroidism due to Parathyroid Adenoma

Joe Matsumoto, MD,¹ Tetsufumi Kojima, MD,¹ Tetsuya Shimizu, MD,¹
Shuji Kitashiro, MD,¹ Kazuya Konishi, MD,¹ Yoshiyuki Matsumura, MD,¹
You Kawarada, MD,^{2,3} Hitoshi Ikeda, MD,³ and Takashi Yoshiki, MD, PhD³

In lung cancer patients, hypercalcemia is a fairly common metabolic problem associated with malignancy. However, the occurrence of hypercalcemia in lung cancer patients means an ominous prognostic sign. As hypercalcemia often causes early death, quick diagnosis and treatment for hypercalcemia are required. A 69-year-old woman was admitted to our hospital with anorexia caused by hypercalcemia. On admission, serum level of PTH was elevated and PTHrP was normal. From the results of CT findings and transbronchial lung biopsy, the cause of the hypercalcemia was determined as lung cancer incidentally complicated with primary hyperparathyroidism. First, serum calcium level was returned to normal through hydration with saline and bisphosphonates. Next, left hemithyroidectomy for primary hyperparathyroidism was performed. Histologically, the tumor was diagnosed as parathyroid adenoma. Fifteen days later, left lower lobectomy for primary lung cancer was performed under a video-assisted thoracoscopic approach. Histologically, the tumor was diagnosed as a moderately differentiated adenocarcinoma. Four years and three months after the operation, the patient is alive and well with no sign of recurrence. When a lung cancer patient is complicated with hypercalcemia, we need to consider that primary hyperparathyroidism is a possible cause of the hypercalcemia. (Ann Thorac Cardiovasc Surg 2002; 8: 151–3)

Key words: lung cancer, hypercalcemia, primary hyperparathyroidism, parathyroid adenoma

Introduction

In patients with lung cancer, hypercalcemia is a fairly common metabolic problem associated with malignancy. The occurrence of hypercalcemia in lung cancer patients means an ominous prognostic sign.¹⁻³ In fact, as hypercalcemia often leads to early death, quick diagnosis and treatment for hypercalcemia are required.

From the ¹Department of Surgery, Hakodate Central General Hospital, ²Surgical Oncology, Division of Cancer Medicine, Hokkaido University Graduate School of Medicine, and ³Department of Pathology/Pathophysiology, Division of Pathophysiological Science, Hokkaido University Graduate School of Medicine, Japan

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Address reprint requests to Joe Matsumoto, MD: Department of Surgery, Hakodate Central General Hospital, 33-2 Honchou, Hakodate 040-8585, Japan.

We present a case of lung cancer with hypercalcemia which is caused by incidental hyperparathyroidism.

Case Report

A 69-year-old woman was admitted to our hospital with anorexia. The serum calcium level was 12.8 mg/dl (normal 8.6 to 11.1), phosphorus level 1.8 mg/dl (normal 2.2 to 4.9), alkaline phosphatase level 474 U/l (normal 60 to 160), intact-parathyroid hormone (intact-PTH) level 520 pg/ml (normal 15 to 50) and C-parathyroid hormone related protein (C-PTHrP) level 19.3 pMol/l (normal 13.8 to 55.3). Serum levels of carcino-embryonic antigen and squamous cell carcinoma antigen were normal.

A chest radiograph showed a mass of 3 cm in diameter in the left lower lung field. Computed tomography (CT) of the chest revealed a tumor shadow of 3.2 cm in diameter between segment 8 and segment 9 of the left lung



Fig. 1. CT of the chest reveals a tumor shadow of 3.2 cm in diameter between segment 8 and segment 9 of the left lung (white arrow).

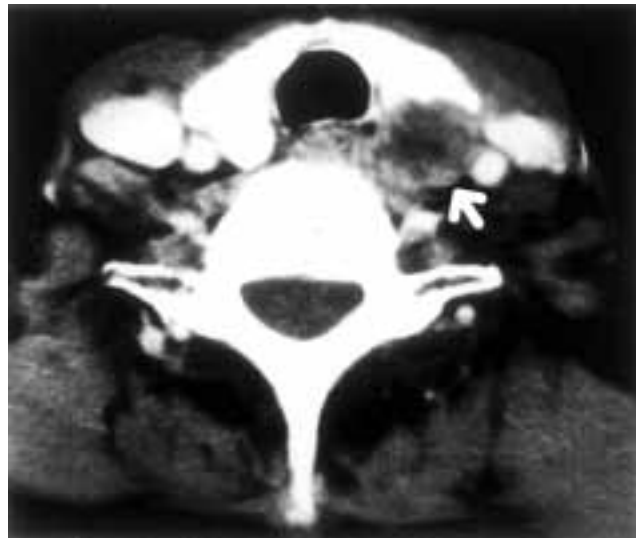


Fig. 2. CT of the neck demonstrates a well-demarcated and heterogeneous mass in accordance with the left lower parathyroid gland (white arrow).

(Fig. 1). CT of the neck demonstrated a well-demarcated and heterogeneous mass in accordance with the left lower parathyroid gland, and did not show any swelling of the other three parathyroid glands (Fig. 2). Transbronchial lung biopsy was performed and it was diagnosed as papillary adenocarcinoma histologically. Bone scintigraphy did not show abnormal findings. From the results of the above examinations, the cause of the hypercalcemia was determined as lung cancer incidentally complicated with primary hyperparathyroidism (cT2N0M0 Stage IB).

First of all, hydration with saline was indicated with loop diuretic drugs and bisphosphonates to treat hypercalcemia prior to surgery. After the serum calcium level was returned to normal, the operation for primary hyperparathyroidism was performed. Since the mass strongly adhered to the lower region of the left lobe of the thyroid, left hemi-thyroidectomy was performed. As the residual two parathyroid glands were not swollen, they were not resected. The mass measured 2.0×1.6×1.5 cm in size. Histological examinations confirmed the absence of atypical cells such as carcinoma and the proliferation of enlarged clear cells in cords and sheets. Taking the swelling of only one parathyroid gland into consideration, the tumor was diagnosed as parathyroid adenoma (Fig. 3). The primary hyperparathyroidism was found to have resulted from parathyroid adenoma. Her postoperative course was uneventful, and the serum calcium level and intact-PTH level were reduced to normal.

Fifteen days after the operation for the primary hyperparathyroidism, left lower lobectomy for primary lung cancer was carried out under the video-assisted thoraco-

scopic approach. Histologically, the tumor was diagnosed as a moderately differentiated adenocarcinoma, and there was no metastasis to regional lymph nodes (pT2N0M0 stage IB) (Fig. 4). Four years and three months after the operation, the patient is alive and well with no sign of recurrence and without hypercalcemia.

Discussion

Lung cancer with hypercalcemia occurs in 2.5-12.5% of lung cancer patients.^{1,3,4)} Hypercalcemia is one of the most common metabolic problem associated with malignancy and arises in advanced stages of malignant neoplasms.¹⁻³⁾ Median survival after detection of hypercalcemia-complicated carcinoma of the lung is one month.³⁾ In our case, therefore, close examinations were performed because it was suspected that our patient was in an advanced stage of lung cancer. On the other hand, primary hyperparathyroidism is caused by adenomas in 83% of the patients, hyperplasias in 14.6%, and carcinomas in 2.5%.^{5,6)} The majority of adenomas are composed primarily of chief cells. Adenoma composed of clear cells is rare.^{5,6)}

Mechanisms of hypercalcemia in lung cancer are classified into local osteolytic hypercalcemia (LOH), humoral hypercalcemia of malignancy (HHM) and incidental complication of primary hyperparathyroidism.¹⁾ LOH is considered to be caused by osteoclast-activating factors such as TNF- α / β ,⁷⁾ IL-1⁸⁾ and IL-6⁹⁾ produced by tumor cells. On the other hand, the main causative factor of HHM is

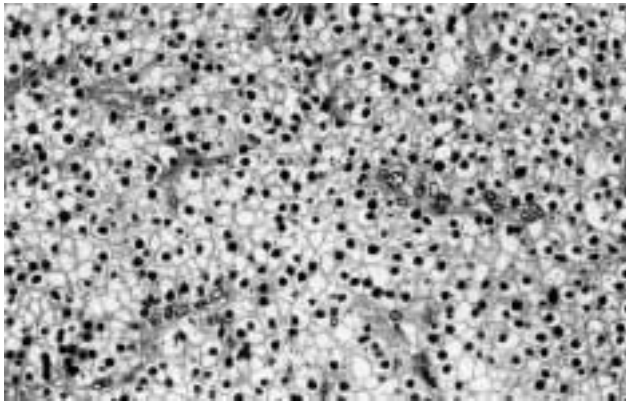


Fig. 3. Histologically, the parathyroid tumor is diagnosed as adenoma, mainly composed of clear cells.

PTHrP, which is produced by tumors, and most causes of hypercalcemia in patients with malignant neoplasm are elevated levels of PTHrP.^{2,10-12} Whereas the serum level of PTHrP is usually higher and that of PTH is lower than normal levels in the cases of HHM, in most patients with primary hyperparathyroidism the serum level of PTH is elevated.^{5,6,13}

Our patient did not have bone pain and bone scintigraphy did not show abnormal findings. Therefore, lung cancer was not considered to have metastasized to the bone. From the results of both the neck CT findings and the measurements of serum intact-PTH and serum C-PTHrP, it was determined that hypercalcemia was caused by incidental complication of primary hyperparathyroidism.

A patient with hypercalcemia may deteriorate abruptly. Hence, in our case, the hypercalcemia was treated prior to surgery. As a result, the following surgeries could be carried out safely. When a lung cancer patient is complicated with hypercalcemia, we need to consider that primary hyperparathyroidism is a possible cause of the hypercalcemia.

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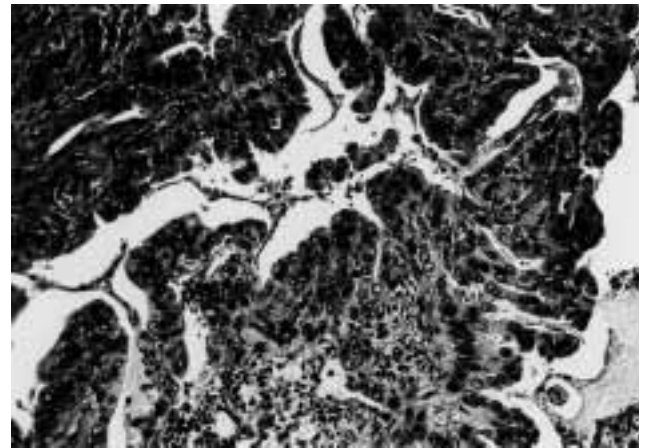


Fig. 4. Histologically, the lung tumor is diagnosed as a moderately differentiated adenocarcinoma.

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