Two Cases of Lung Carcinoma with Osteoplastic Bone Metastasis

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Two cases of lung carcinoma with osteoplastic bone metastasis are reported. The bone roentgenogram of a 66-year-old woman with pleuritis carcinomatosa revealed multiple sclerotic changes in the right forearm, lumbar spine, and pelvis. Biopsy at internal fixation of the left humerus revealed metastatic adenocarcinoma with osteoplastic change. In a 77-year-old man with small cell carcinoma of the lung, after chemotherapy, osteoplastic bone changes were detected in roentgenograms. An ivory vertebra formation was seen in L1, L2 and L4, and bone scintigram showed, additionally, uptake in the ilium. (Internal Medicine 32: 416-420, 1993)

Key words: adenocarcinoma, small cell carcinoma, bone scintigram

Introduction

Metastasis to bone is not uncommon with lung cancers. In the literature, the incidence of bone metastasis varies from 15.7 to 51 percent (1, 2). Whereas the incidence of osteolytic metastasis is frequent, osteoplastic bone lesions are rare (3-11). We present here two cases of osteoplastic bone metastasis from bronchogenic carcinoma.

Case Report

Case 1

A 66-year-old woman was admitted to our hospital with a three-month history of right forearm pain and swelling; she also had right iliac pain. She had no cough, dyspnea, or cyanosis. She had been in good health, and her past medical history was unremarkable, except for hysterotomy because of uterine myoma. She was a non-smoker. There was no family history of neoplasms. Physical examination showed a fairly well nourished woman, whose right forearm was swollen with slight tenderness. Decreased breath sounds were audible over the left posterior lower chest. An enlargement of the thyroid gland, lymphadenopathy and hepatosplenomegaly were absent. The neurologic findings were normal except for decreased deep tendon reflexes.

A chest roentgenogram revealed a large left pleural effusion

(Fig. 1). Cytology of the effusion showed an adenocarcinoma. Chest CT scan after thoracic drainage revealed a nodule, 2.0 cm in diameter, with spiculated, irregular margins in the left posterior basal segment, and invasion of mediastinal lymphnodes (Fig. 2). Retrospectively, the nodule was identified in a screening chest roentgenogram of two years previously; the nodule had increased slightly in a roentgenogram of one year later.

Laboratory investigation revealed an erythrocyte sedimentation rate of 78 mm in the first hour. The hemoglobin was 13.2 g/dl, WBC 10,400/mm³ with 65% neutrophils, and platelets were 415,000/mm³. Fasting blood sugar was 202 mg/ml, HbA_{1c} 13.3%, HbA_{1c} 10.5%, and urine sugar was 2.1 g/dl. Serum calcium and phosphorus levels were normal. Serum level of parathormone was 610 pg/ml, and 1,25(OH)₂Vit.D, 33 pg/ml. LDH was 1,298 IU/l, and alkaline phosphatase (ALP), 3,372 IU/l with 85% of ALP₃ isozyme. CEA levels were 99.9 ng/ml in blood, and 42.3 ng/ml in the effusion, and neuron-specific enolase (NSE) was 13 ng/ml.

Bone roentgenograms revealed multiple sclerotic changes, especially in the right forearm, lumbar spine, and pelvis (Fig. 3a and 3b). Bone scintigram also showed multiple uptake (Fig. 4). CDDP at 150 mg and OK432 at 6.0 KE were administered intrathoracically after thoracic drainage. While at home she experienced progressive anorexia and malaise. After four months, pathological bone fracture of the left arm was detected. Biopsy at internal fixation of the left humerus revealed

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Fig. 1. Chest roentgenogram on admission (case 1). A large left pleural effusion was noted.

Fig. 2. A chest CT scan after thoracic drainage revealed a nodule, 2.0 cm in diameter, with spiculated, irregular margins, in the left posterior basal segment.

Fig. 3. Bone roentgenogram revealed sclerotic changes, especially in the right forearm (a). Spine (Th12 and L4), and right pelvis were also sclerotic (b).

osteoplastic bone metastasis (Fig. 5).

Case 2

A 77-year-old man was admitted to our hospital because of

lumbago. His chest roentgenogram revealed a mass-like shadow in the left anterior basal segment (Fig. 6). The diagnosis of small cell carcinoma was made by aspiration lung biopsy. The NSE level was 40 ng/ml. Before treatment, bone roentgenograms

Fig. 4. A bone scintigram also showed multiple uptake.

Fig. 6. Chest roentgenogram on admission (case 2). The chest roentgenogram revealed a mass-like shadow in the left anterior basal segment. The diagnosis of small cell carcinoma was made by aspiration lung biopsy.

Fig. 5. Biopsy at internal fixation of the left humerus revealed osteoplastic bone metastasis (HE stain, ×200).

were normal, but a bone scintigram showed multiple uptake in the spine (L4). As the possibility of bone metastasis was not ruled out, a combination chemotherapy of carboplatin and etoposide was performed. After four courses of chemotherapy, the mass-like shadow had almost disappeared, but osteoplastic changes were detected in roentgenograms. An ivory vertebra formation was seen in the L1, L2 and L4 (Fig. 7), and bone scintigram showed, additionally, uptake in the ilium (Fig. 8).

Fig. 7. Bone roentgenograms revealed osteoplastic bone changes. An ivory vertebra formation was seen in L1, L2 and L4.

Fig. 8. Bone scintigram of case 2. Left (on admission), uptake in the spine (L4). Right (after four courses of chemotherapy), uptake in L1, L2, L4 and the right ilium.

Discussion

The rate of metastasis to bone has been shown at autopsy to be as high as 83.3 percent in prostate, 61.1 percent in breast, and 51.1 percent in lung cancer (1). In women, the most frequent origin of metastatic carcinoma is carcinoma of the breast, followed by carcinoma of the lung. In men, carcinoma of the lung is the most frequent cause of metastatic bone disease (1).

Tumor cells which enter the circulation are carried to the vascular bone marrow. This is followed by invasion of the bone tissue matrix, and finally by invasion of the cortical bone (12). It is known that bone itself contains growth factors and angiogenesis factors, such as fibroblast growth factor, platelet-derived growth factor, transforming growth factor beta and insulin-like growth factors I and II, each of which is important for the local growth of the tumor (13). Although most carcinomas tend to cause osteolytic metastasis, prostate cancer and breast cancer occasionally provoke osteoplastic metastasis in the affected bone, producing an increase in osseous density on the radiograph. In prostate cancer extracts, osteoblast stimulatory factors were found which could be responsible for the stimulation of new bone formation (13).

Whereas osteolytic metastasis is frequent in lung cancers, 26 cases (including our two cases) of osteoplastic metastasis from primary bronchogenic carcinomas have been reported by several authors (3–11). Of these cases, 13 were adenocarcinomas, 9 were small-cell carcinomas, 3 were anaplastic, and one was a

Table 1. A Summary of Case Reports in the Literature of Lung Cancer with Osteoplastic Bone Metastasis

Patient	Author	Age and sex	Cell type
1	Feld	56 M	Adenocarcinoma
2	Sackner	56 M	Adenocarcinoma
3	Beer	37 M	Anaplastic
4		44 M	Anaplastic
5		53 M	Adenocarcinoma
6		48 M	Adenocarcinoma
7		61 M	Adenocarcinoma
8	Napoli	51 M	Small-cell
9		59 M	Small-cell
10		41 M	Adenocarcinoma
11		47 M	Small-cell
12		58 F	Adenocarcinoma
13		42 M	Small-cell
14		57 M	Small-cell
15		69 M	Small-cell
16		73 M	Small-cell
17	Kimoto	25 F	Adenocarcinoma
18		55 M	Adenocarcinoma
19		68 F	Anaplastic large cell
20		59 M	Anaplastic
21	Araki	68 M	Adenocarcinoma+hepatoma
22	Itoh	62 M	Small-cell (Oat cell)
23	Ueno	56 F	Adenocarcinoma
24	Matsumura	50 F	Adenocarcinoma
25	Our case	66 F	Adenocarcinoma
26		77 M	Small-cell

large-cell carcinoma (Table 1). It is notable that osteoplastic bone metastasis was not seen in squamous-cell carcinoma of the lung. Elaboration of a parathyroid hormone-related protein, which stimulates osteoclastic bone resorption in vitro and in vivo, was confirmed in a squamous-cell carcinoma of the lung (14). This fact leads one to speculate that the production of parathyroid hormone-related protein may account for the apparent lack of osteoplastic lesions in this tumor (6, 9). However, recent clinical studies of serum parathyroid hormone-related protein level in patients with lung cancer support the view that a wide variety of cell types can produce parathyroid hormone-related protein (15). Histochemical study using anti-parathyroid hormone-related protein antibody also revealed that all lung cancer cell types produce parathyroid hormone-related protein (Sakamoto et al., unpublished observation). Nevertheless, further investigation is needed to determine whether parathyroid hormone-related protein molecule has not only immunologically reactivity but also biologically activity.

The roentgenographic appearance of the bone lesions in case 2 was indistinguishable from those due to metastasis from prostatic cancer. Histologic examination of the bone lesion was not performed, but a primary carcinoma of the prostate was considered unlikely based on the following findings: 1) normal size, shape and consistency of the prostate and 2) normal levels of serum acid phosphatase.

The treatment of skeletal metastasis from a primary lung cancer depends on the patient's general condition, the radiosensitivity of the lesion, the site and extent of the involvement, and the proximity of the tumor to vital organs such as the spinal cord. Most skeletal metastasis of pulmonary carcinomas are radiosensitive and a partial response can be achieved in some patients by radiation therapy (1, 2).

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