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Hypertrophic Pulmonary Osteoarthropathy Associated with Primary Adenocarcinoma of the Lung

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ABSTRACT : Hypertrophic pulmonary osteoarthropathy (HPOA) associated with primary lung cancer is reported in a fifty-four-year-old man. Symptoms of HPOA were makedly improved following lung resection for adenocarcinoma of the lung.

INTRODUCTION

Hypertrophic pulmonary osteoarthropathy (HPOA) was described independently by Bamberger[1] and Marie[2]. It is clinically characterized by clubbing of the fingers and toes, painful swelling of the joints and arthralgia. It is most commonly associated with malignant neoplasms. Primary lung cancer accounts for 80 per cent of cases, pleural tumors 10 per cent and other intrathoracic tumors 5 per cent[3]. The cause of HPOA remains unknown.

We report a patient with HPOA whose symptoms were markedly improved following lung resection for primary bronchogenic carcinoma.

CASE REPORT

A fifty-four-year-old man presented a three months history of bilateral knee and ankle pain and an abnormal shadow on a chest roentgenogram. He had no respiratory symptoms. He had smoked 20 cigarettes daily for 33 years before admission. On physical examination, the patient appeared well. There were marked clubbing of the toes and fingers (**Fig. 1**) and periarticular swelling of the foot ankles. There were no cervical lymphoadenopathy. Chest was clear.

Radiographs of the chest showed an ill-defined 6 cm mass lesion in the right upper lung field (**Fig. 2**). Bronchoscopy showed no endobronchial lesions, and cytological examination of a bronchial brushing and a sputum specimen gave negative results. Laboratory investigations gave results within normal limits except for mild anemia and elevation of c-reactive protein and erythrocyte sedimentation rate.

Computed tomographic scan of the chest revealed a large mass lesion with spiculation in contact with visceral pleura in the posterior segment of the right upper lobe (**Fig. 3**). Radiographs of the bones of legs showed subperiosteal bone deposition at the lower ends of the femur, tibia and fibura (**Fig. 4**). An isotopic bone scan demonstrated pericortical linear concentration of the nuclide along the bilateral femoral and tibial shafts together with icreased uptake in juxta-articular bones. The results of the computed tomographic scan of the brain and liver were negative.

Thoracotomy was performed under the diagnosis of lung cancer and revealed a large mass lesion in the right upper lobe which invaded to visceral pleura. There were no hilar and

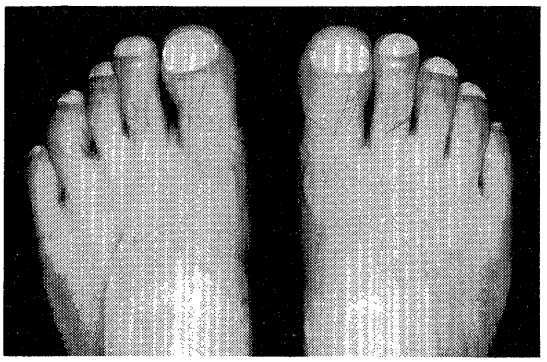

Fig. 1. Marked clubbing of toes

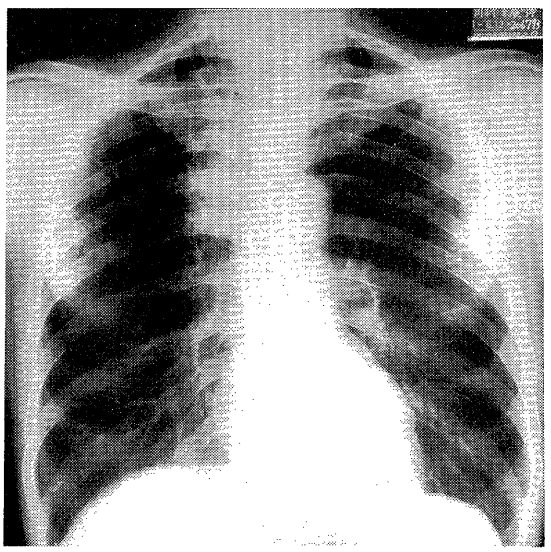

Fig. 2. Preoperative chast radiograph demonstrating a large mass shadow in the right upper lung field

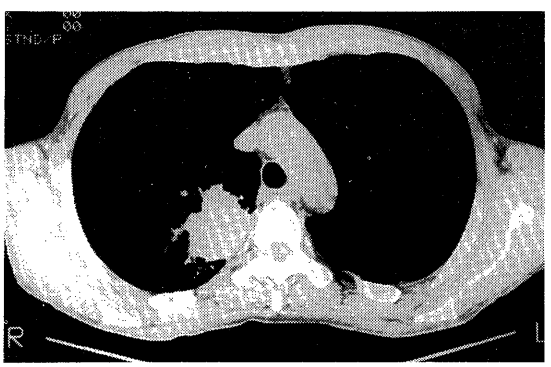

Fig. 3. Preoperative computed tomographic scan showing irregular round shadow

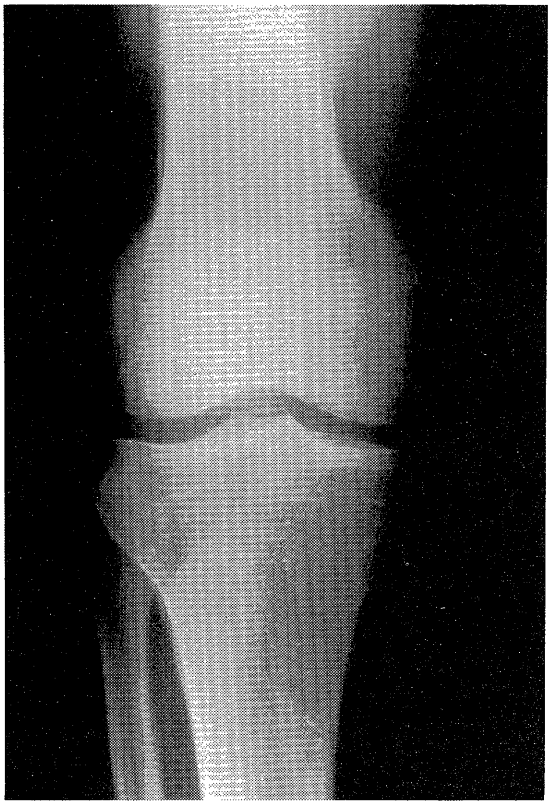

Fig. 4. Preoperative roentgenograph of right femur, tibia and fibula showing subperiosteal new bone formation

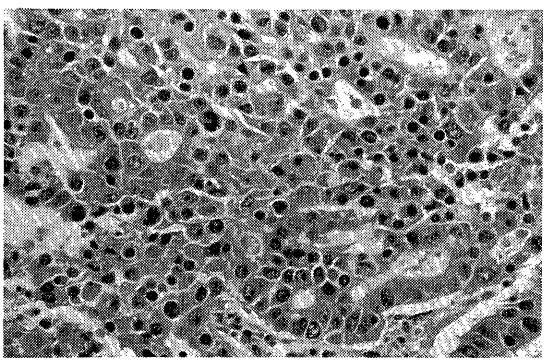

Fig. 5. Histological section of primary tumor showing undifferentiated adenocarcinoma (Hematoxylin and eosin stain 20X5)

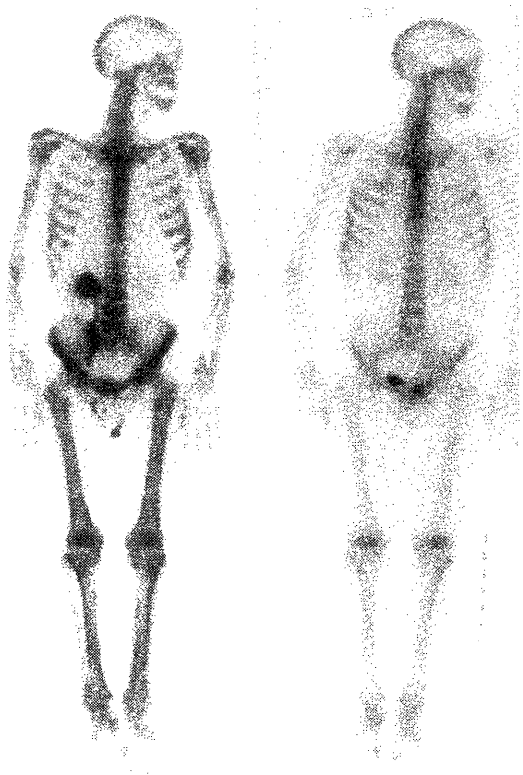

Fig. 6. a. Fig. 6. a.

Fig. 6. a) Preoperative bone scintigraphs of legs showing subperiosteal new bone formation b)Postoperative bone scan demonstrating disapperance of bone deposition

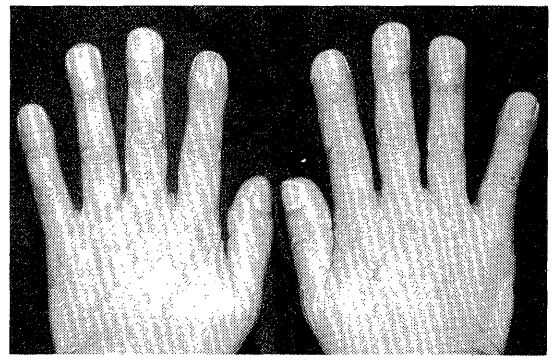

Fig. 7. a.

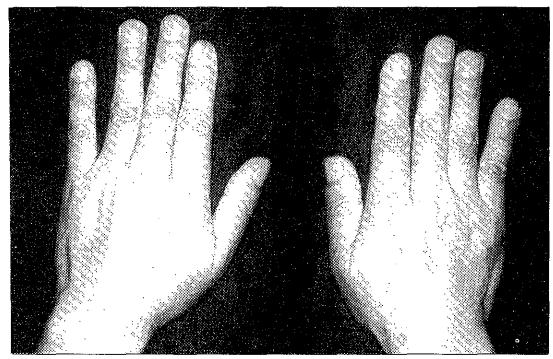

Fig. 7. b.

Fig. 7. Photographs of digits. a) preoperative marked clubbing of fingers b) postoperative finding one year and four months after operation

mediastinal lymph node enlargement and pleural effusion. Intraoperative needle aspiration biopsy confirmed an adenocarcinoma and a right upper lobectomy with mediastinal lymph node dissection was performed.

The lesion was a firm, subpleural irregular tumor of 5.2 X 5.0 X 3.0cm. Histology of the tumor showed a poorly differentiated adenocarcinoma (**Fig. 5**). There was no metastasis in hilar and mediastinal lymph nodes (p-$T_2N_0M_0$, Stage I).

His symptoms of arthralgia of knee and ankle joints improved markedly just after awakening from general anesthesia. His postoperative course was uncomplicated. No adjuvant chemothrapy or radiotherapy was given. He is well now without disease and complains no arthralgia two years after the pulmonary resection. A bone X-Ray examined one year after operation revealed a disappearance of subperiosteal new bone formation and an isotopic bone scan showed normalization of nuclide uptake of femoral and tibial shafts (**Fig. 6**).

A clubbing of his fingers and toes gradually improved after operation and his extremities are almost in normal apperance (**Fig. 7**).

DISCUSSION

Hypertrophic pulmonary osteoarthropathy is most commonly associated with primary lung carcinoma. It has also been associated with lung metastasis[4], pulmonary infections, achalasia and liver disease[5]. HPOA is said to occur in 0.7 per cent to 12 per cent of patients with bronchogenic carcinoma[6]. The pathophysiology of HPOA is characterized by a significant increase in peripheral blood flow in the distal

half of the extremities. However, the cause of this phenomenon is not known. There are several theories explaining this symptom. First, some kind of reflex through vagal nerve is thought to be the cause of HPOA, since vagotomy[7] or atropine improved this symptoms. The vagal nerve distributes widely over the visceral pleura and the pulmonary neoplasms are often large and in contact with pleural surface. Second, some authors stressed the endocrine substance as a cause of HPOA because a relativley high incidence of gynecomastia and over excretion of growth hormon, estrogen or gonadotropin were frequently observed in the patients with HPOA[8, 9]. Third, vasodilatic substances such as prostagrandine or bradykinine excreted form primary pulmonary neoplasms increase the blood flow of the extrimities. In the present case the hormonal assay was not performed and no endocrine disorders were observed. Therefore, the cause of HPOA of this patient was unknown, but some kind of neurogenic reflex may be suggested since his joint pain disappeared soon after lung resection.

In the histologic type of the patients with lung cancer associated with HPOA, squamous cell carcinoma and undifferentiated carcinoma were more frequent than adenocarcinoma[10]. However, oat cell carcinoma is rare in the patient with HPOA.

The symptoms are characterized by arthralgia, painful swelling of the limbs and clubbing of the fingers and toes. These symptoms appear early in the course of the disease, but do not relate to the extent of lung cancer[11].

Radiographic features of HPOA are subperiosteal new bone formation at the lower ends of the tibia, fibula, radius and ulna. However, these changes are uncommon at the finger, pelvic bone or vertebrum. The isotope scan of bones demonstrated high nuclide accumulation at the long bone[12, 13]. Ali[14] reported that these findings of high uptake of isotope were observed also at the skull and mandibulum at a rate of 40-60 per cent. To differentiate findings of high isotopic uptake between bone metastais and HPOA is important in the management of the patient with lung cancer. In the latter, the distribution of high uptake is even, diffuse and symmetric. On the other hand, in the former, high uptake is irregular, localized and asymmetric and commonly distributed at the vertebrum, rib or pelvic bone. On the clinical stand point, the differential diagnosis between two the pathologies is not difficult.

The symptoms of HPOA such as joint pain are commonly improved after resection of lung neoplasms[15, 16] as shown in the present case. However, there were several reports that symptoms decreased after simple thoracotomy, vagotomy, chemotherapy or indomethacin treatment. Relief of joint pain was gained without documented tumor response in some reports. This patient is free of disease and symptoms of HPOA two years after lung resection. As the estimation of the cause of HPOA, whether reappearance of symptoms of HPOA are observed or not is interesting when recurrence of lung cancer occurs. Because recurrence in the lung will cause the symptoms of HPOA, metastasis in extrapulmonary sites, symptoms will not appear, if the theory of neurogenic theory is true. If the endocrine theory is correct, symptoms of HPOA may appear regardless of the recurrent sites of cancer.

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