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CASE REPORT

Extensive calcification in adenocarcinoma of the lung: A case report

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Abstract

Calcification in lung nodules usually indicates a benign lesion. Here, we report the case of a 59-year-old male patient with a well defined 30 mm calcified nodule in his right upper lung lobe and calcified mediastinal lymph nodes. The mass was diagnosed as adenocarcinoma by transbronchial biopsy. He received systemic chemotherapy, followed by lobectomy and mediastinal lymph node dissection. During surgery, the lymph nodes were tightly adherent to the superior vena cava with invasion of the vascular wall. Pathological diagnosis confirmed acinar adenocarcinoma and psammoma bodies (PBs). Immunohistochemical analysis revealed tumor cells positive for parathyroid hormone-related proteins 1 and 2. Calcification of primary lung adenocarcinoma is rare. We report a calcified lesion where the secretion of parathyroid hormone by the tumor may have caused the accumulation of PBs. Calcification of metastatic lymph nodes may increase the risk of adhesion, requiring care during surgery.

Key points

Significant findings of the study

- Lung adenocarcinoma with extensive calcification in primary and metastatic lymph node lesions is rare and the mechanism involved is poorly understood. Of significance, calcification in our case was related to parathyroid hormone-related proteins 1 and 2 secreted by the tumor.

What this study adds

- This study suggests the potential role of parathyroid hormone-related proteins in lung tumor calcification. The implications for clinicians are that calcified metastatic lymph nodes and tumors might be tightly fused to tissues. Therefore, surgery should be conducted with care.

Introduction

Calcification in lung nodules is important for radiological evaluation, but the mechanism of lung calcification in tumors is often unclear. For example, calcification can occur in bronchogenic carcinoma via necrotic degeneration (dystrophic calcification), formation of psammoma bodies (Pb, concentrically laminated calcifications), or engulfment of benign calcified lesions by the carcinoma.[1–4] Malignancy cannot be ruled out for lung tumors with extensive calcification, but a benign tumor might be suspected because calcification might occur over a long period.[1] Computed tomography (CT) indicates that 6%–10% of lung cancers have calcification in the primary lesion.[1, 2] Tumors are considered benign if they have high attenuation values that exceed a critical level, and diffuse calcification throughout the lesion center with a welldefined edge.[3, 5] Lung

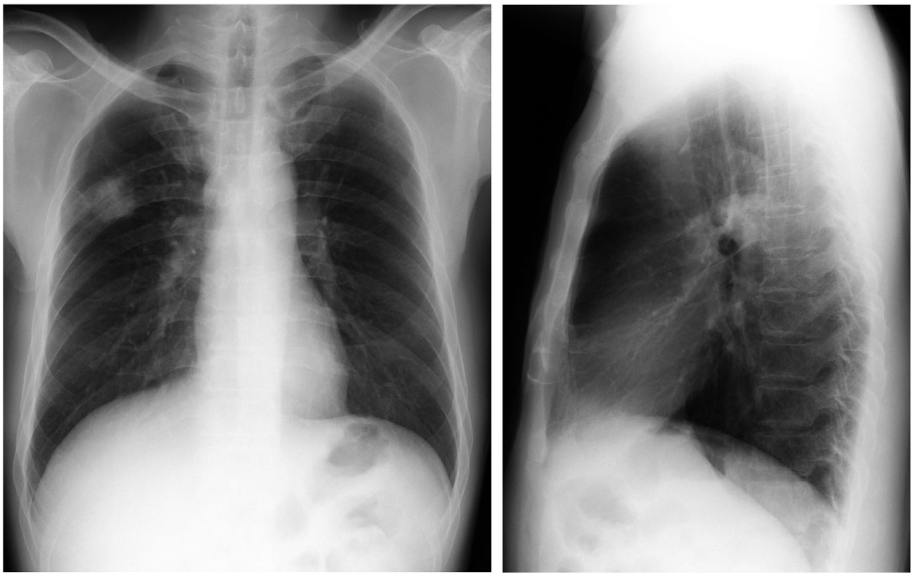

Figure 1 Chest radiograph showing a mass in the right upper lung field.

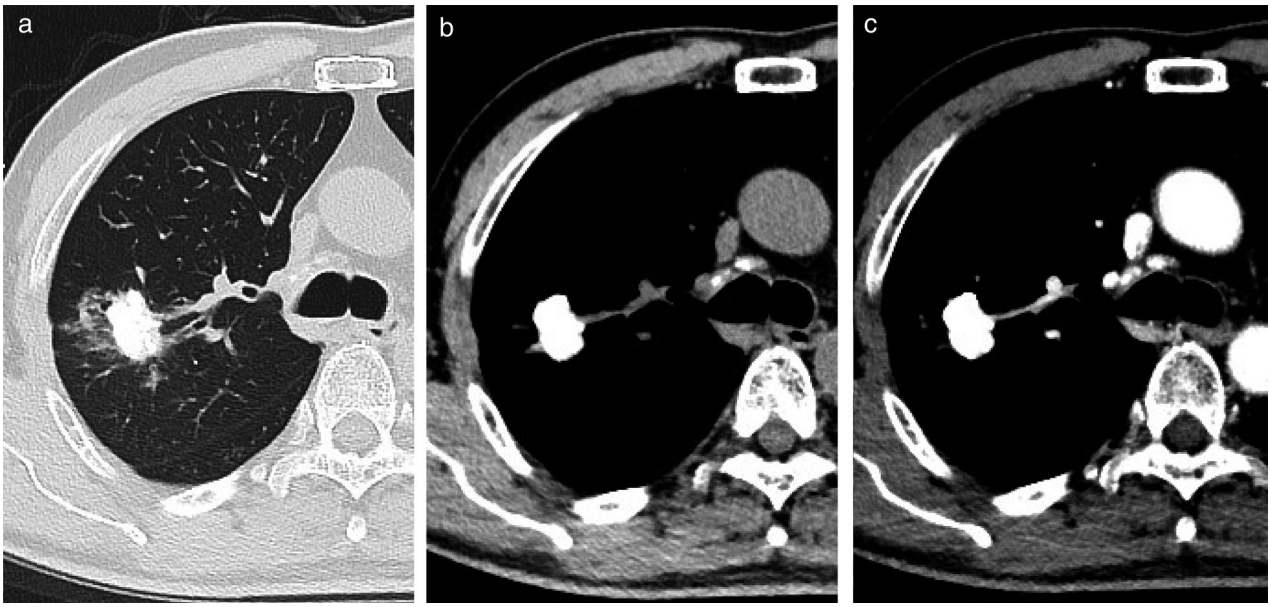

Figure 2 Chest computed tomography (CT) revealed a 30 mm mass in the right upper lobe and mediastinal lymph nodes with calcification. (**a**) Pulmonary window setting; (**b**) mediastinal window setting; and (**c**) enhanced CT.

carcinoma with extensive calcification is extremely rare. Here, we report a case of lung adenocarcinoma with calcification of the main lesion and metastatic lymph nodes.

Case report

A 59-year-old man was admitted to our hospital with abnormal findings on chest X-ray (Fig 1). On physical examination, he weighed 63.0 kg and was 176 cm tall. The patient had diabetes for 20 years and suffered from diabetic retinopathy. He had unremarkable medical and family histories, but a smoking history of 90 packs per year. Chest CT revealed a 30 mm mass in the right upper lung lobe and mediastinal lymph nodes with advanced calcification (Fig 2). Transbronchial biopsy resulted in a diagnosis of adenocarcinoma. [18F]-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) showed increased tumor uptake, with a maximum standardized uptake value of 6.16, and slight FDG uptake in the mediastinal lymph nodes. No metastases were detected by brain magnetic

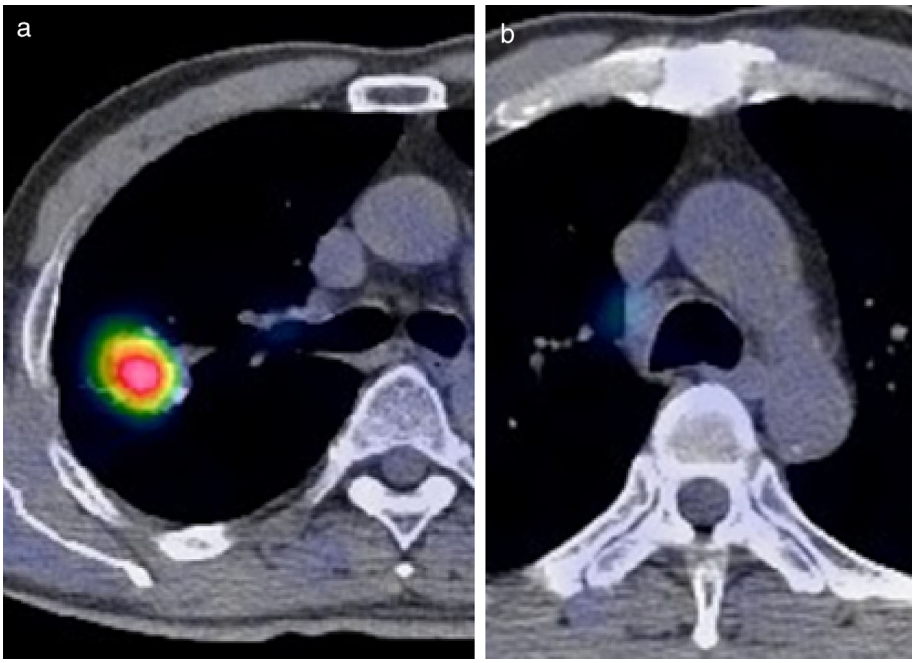

Figure 3 (**a**) 18F-fluorodeoxyglucose-positron emission tomography showing abnormal uptake in the mass; and (**b**) slight uptake in the mediastinal lymph nodes.

resonance imaging or FDG-PET (Fig 3). Mediastinal lymph node #4 had a short-axis diameter < 1 cm, but was considered potentially to be lymph node metastasis because of the slight accumulation of FDG-PET; therefore, preoperative adjuvant treatment was performed. HgbA1c of 10.5 indicated diabetes was poorly controlled and required treatment before surgery. Diabetic nephropathy did not coexist and blood calcium and phosphate concentrations were within the standard range. During diabetes treatment, he received neoadjuvant chemotherapy (pemetrexed (500 mg/m^2) plus cisplatin (75 mg/m^2). The patient achieved no significant radiological improvement with two courses of this regimen. Based on radiological findings, he was diagnosed with yc-T1cN0M stage 1A, and surgical treatment was planned. He underwent right upper lobectomy and dissection of the upper mediastinal lymph nodes (2R and 4R). The lymph nodes were firmly adherent to the surrounding tissue, the sidewall of the superior vena cava was firmly fused, and there was invasion of the vascular wall. Despite this, the lymph nodes and superior vena cava sidewall were removed. The chest drain tube was removed on postoperative day 3 and the patient was discharged on postoperative day 14. Macroscopically, the tumor was well circumscribed and most of the tumor was calcified (Fig 4). There was no bronchial or pleural involvement within the tumor. Acinar adenocarcinoma tissue was mixed with calcified tissue and PBs were confirmed. Similar features were found in calcified lymph nodes. The tumor was diagnosed as p-T2aN2M0 stage 3A (Union for International Cancer Control eighth edition). Immunohistochemistry revealed tumor cells positive for parathyroid hormone-related proteins (PThrP) 1 and 2. Postoperative examination indicated PThrP levels were within the standard range.

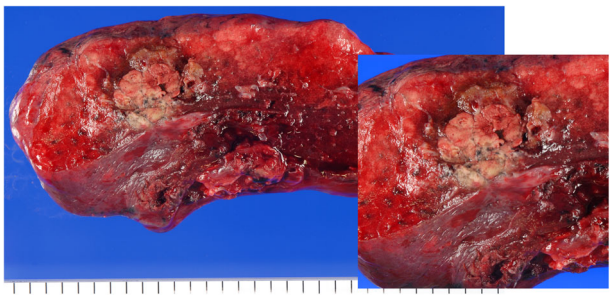

Figure 4 Macroscopically, the tumor was well circumscribed and most of the tumor was calcified.

Discussion

Typical nonmalignant lung disease often develops during the healing of infectious granulomatous disease.[6] Calcification within lung nodule shadows is considered negative for malignant tumors, but does occur rarely; for example, if lung cancer occurs near a calcified benign tumor.[1, 7]

Calcification occurs with amorphous (small-cell lung cancer), punctate (squamous cell carcinoma), or reticular patterns.[1, 4, 8] In primary lung cancer, extensive calcification is rare, and few studies have reported ossification and PBs.[9, 10] In the current case, lesions mainly contained diffuse calcification throughout the lesion center with a well-defined edge, and the tumor was considered benign.

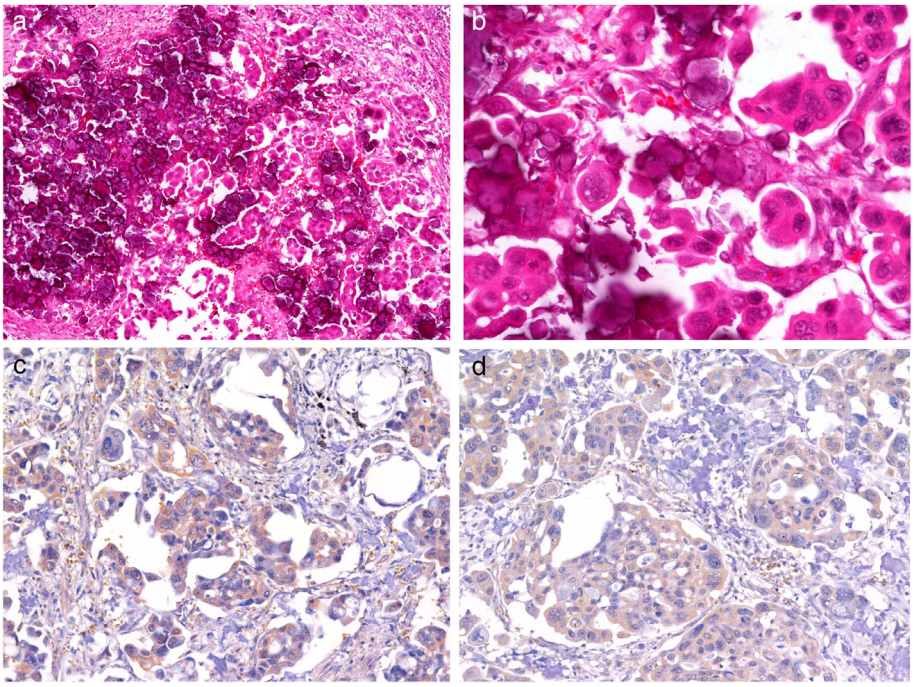

Figure 5 (**a**) Hematoxylin-eosin stained section showing adenocarcinoma comprising psammoma bodies and acinar growth pattern, and no sarcomatoid component; (**b**) high-power field; (**c**) strong immunostaining for PThrP1; and (**d**) immunostaining for PThrP2 confirming adenocarcinoma cells.

Effects of PTHrP, commonly expressed by non-small cell lung carcinomas,[11] on cancer cells include cell growth, apoptosis, and angiogenesis but its relationship with tumor calcification is unclear.[12] Although hypercalcemia was not present in our case, the calcified lesion contained many PBs, concentrically laminated calcific spherules usually associated with various organs and benign conditions.[13, 14] PBs, first identified in a benign meningeal tumor,[15] have been reported in thyroid cancer, ovarian cancer, uterine cancer, and meningioma,[16] but are rare in lung adenocarcinoma.[14] PBs appear as hydroxyapatite collections of 30–100 μm in diameter formed from acid mucopolysaccharides.[17, 18] PB formation might be related to necrosis, calcification of intravascular and intralymphatic thrombosis, or focal areas of infarction.[16] In the current case, the tumor was positive for PTHrP1 and PTHrP2, suggesting their involvement in tumor calcification and PBs (Fig 5).[19]

The calcified metastatic lymph nodes (<1 cm diameter) were tightly fused to the wall of the superior vena cava. Calcification induced by PTH might have also affected the surrounding blood vessel walls, and the fusion of calcified lesions associated with hormone production should be considered. PBs might be related to mutations in the epidermal growth factor receptor and anaplastic lymphoma kinase genes,[2, 20] neither of which were present in our case.

Here, we report a patient who underwent resection of lung adenocarcinoma with extensive calcification, apparently related to PTH-producing PBs. These tumors require surgery, especially if abnormal calcification is present. They might also be accompanied by strong inflammatory changes caused by necrosis in the surrounding tissues, and surgery should be conducted with care.

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Disclosure

The authors declare that they have no conflict of interest.

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