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Case report

Multiple primary chordomas of the lung

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ABSTRACT

We here report the case of a 40-year-old man with primary pulmonary chordomas. Although an abnormality had been noted on a chest radiograph at age 26 years, the patient had not undergone further examination at that time because he was asymptomatic. Standard chest radiographs and computed tomography showed slow-growing, multiple bilateral pulmonary nodules. Two tumors were resected thoracoscopically to obtain a diagnosis. Pathologic examination resulted in a diagnosis of chordomas. Subsequent systemic examination revealed no additional lesions, not even in the axial skeleton. The patient is alive without any new lesions 38 months after surgery. These clinical and pathological findings suggest that our patient has multiple primary chordomas of the lung, which is an extremely rare condition.

1. Introduction

Chordomas are rare malignant bone tumors that display notochordal differentiation. They occur exclusively along the spinal axis with a predilection for the sacrococcygeal and spheno-occipital regions, and spine [1]. Here, we present a rare case of multiple extra-axial chordomas in the lungs.

2. Case report

A 40-year-old man with no prior symptoms presented to a community hospital because bilateral, multiple, pulmonary masses had been found in a chest radiograph that had been taken during a general checkup. He had been found to have similar abnormalities in his chest radiograph at the age of 26. Several radiographs taken since that time had revealed that the masses had gradually increased in sizes, but not in number. A chest computed tomography (CT) scan at the age of 40 years revealed eight nodules in the lungs, ranging in size from 4 to 23 mm. They were homogeneous and of regular shape; no enhancement was noted (Fig. 1). Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) did not show significant FDG accumulation in the mass (SUV max, 1.3). Serum concentrations of tumor markers (CEA, AFP, IL-2R and Beta-hCG) were all within normal limits. These findings indicated that the lesions were primary pulmonary tumors such as amyloidosis or hamartomas.

The patient underwent thoracoscopic surgery. Wedge resection, with wide margins at the lingular segment, of a cystic lesion in the left lingular segment and a nodule in the left apex was performed to obtain a diagnosis. Grossly, the specimen contained scattered 3–10 mm diameter nodules that were well-demarcated, solid to cystic, and had a yellowish clear gelatinous appearance on the cut surface. Microscopic examination of the nodules revealed solid sheets of neoplastic cells with lightly eosinophilic or vacuolated cytoplasm. Some cells had prominent cytoplasmic vacuoles and resembled physaliphorous cells. Alcian blue-positive myxoid extracellular matrix was observed in some areas (Fig. 2A–D). No vascular and/or lymphatic invasion was detected. Immunohistochemically, the tumor cells were positive for cytokeratin AE1/AE3, S-100 protein, epithelial membrane antigen, cytokeratin 19 and brachyury (Fig. 2E). These pathologic findings were consistent with a diagnosis of chordoma.

Based on these results, magnetic resonance and FDG-PET imaging of the whole body, including the skull, spine, liver, and sacral region, was performed; these procedures revealed no abnormalities. The postoperative course was uneventful and there has been no evidence of new lesions or enlargement of the existing tumors since surgery 38 months ago at the time of writing.

Abbreviations: AFP, alpha-fetoprotein; hCG, human chorionic gonadotrophin; BNCT, benign notochordal cell tumor; CEA, carcinoembryonic antigen; CT, computed tomography; FDG-PET, fluorine-18 fluorodeoxyglucose positron emission tomography; H&E, hematoxylin and eosin; IL-2R, interleukin-2 receptor

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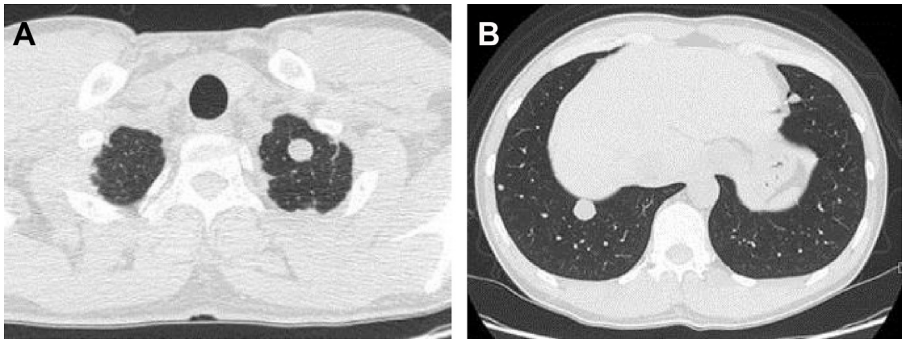

Fig. 1. Pre-operative chest computed tomography images showing solid tumors in the left upper lobe (**A**), right lower lobe, and left lingular segment (**B**).

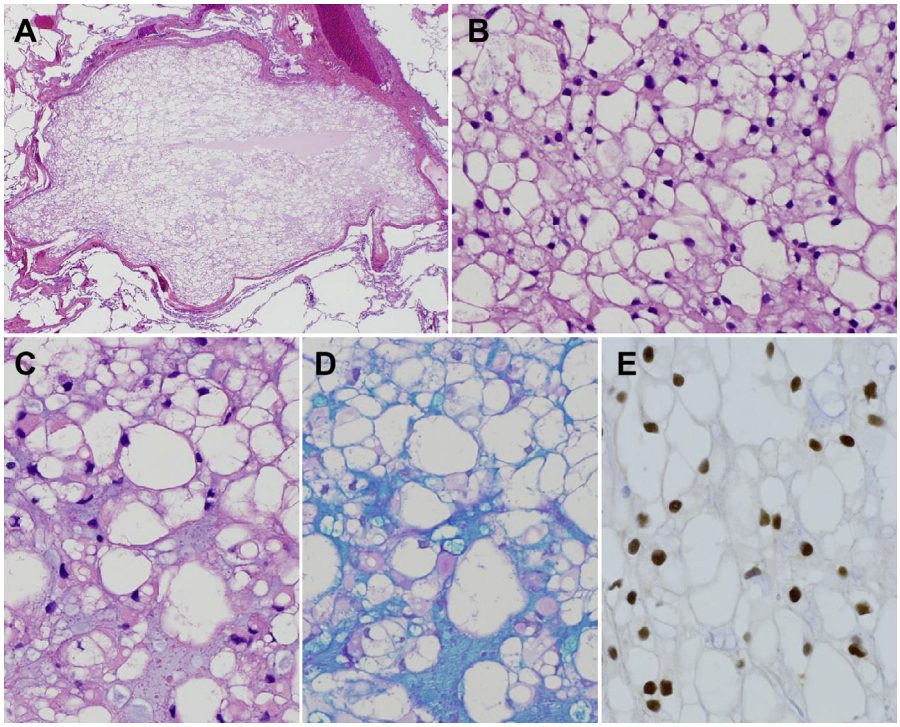

Fig. 2. Photomicrograph at low magnification revealing a well-demarcated nodule in the lung parenchyma (**A**). The nodule consists of a solid sheet of cells with lightly eosinophilic or prominent vacuolated cytoplasm (physaliphorous cells) (**B**). The tumor cells have hyperchromatic eccentric nuclei and are surrounded by a myxoid extracellular matrix that is Alcian blue positive (**C, D**). The nuclei of the tumor cells are positive for brachyury (**E**). **A–C**, H&E stain; **D**, Alcian blue–Periodic acid Schiff; **E**, immunostaining for brachyury.

3. Discussion

Chordomas are uncommon bone malignancies and extra-axial chordomas are extremely rare. To our knowledge, only two cases of primary pulmonary chordoma have been reported [2,3]. We believe that the present case is the first report of multiple chordomas of the lung. It was uncertain whether the multiple tumors were intrapulmonary metastases or multiple primary lesions; however, primary lesions were strongly favored because no new lesions have been detected in the 38 months since surgery.

A possible mechanism for development of pulmonary chordomas is that they have derived from multipotent cells in the lung parenchyma or a notochordal remnant with aberrant migration from the midline [2]. As to extra-axial chordomas in species other than human, intestinal chordomas have been reported in zebrafish [4]. In that study, the authors speculated that a specific gene mutation may drive tumorigenesis in both the intestine (extra-axial chordoma) and notochord (axial chordoma). However, such gene abnormalities have not been reported in humans. Interestingly, four cases of pulmonary benign notochordal cell tumors (BNCT) have been reported recently [5–7]. Although it has not yet been documented that chordomas arise from BNCTs in the lungs, pulmonary BNCT is considered a potential precursor of classic chordoma [5,6].

Because it is difficult to differentiate pulmonary chordomas from BNCTs on imaging studies, tumor resection and histological examination may be required for diagnosis. The histologic features that distinguish chordomas from BNCTs include lobular architecture, extracellular myxoid matrix, and a degree of nuclear atypia or mitotic activity [5]. However, both tumors have the same immunohistochemical profile, one that indicates notochordal differentiation. Thus, in the present patient, we diagnosed chordomas mainly on the basis of the lesions' morphological features together with confirmation of brachyury expression by immunohistochemistry.

The initial treatment for classic midline chordoma is wide local excision. Although chordomas are slow growing tumors, the incidence of local recurrence is high and distant metastases in the lungs, bone, pancreas, heart, and brain have been reported [1]. No effective chemotherapy has been identified [1,8]. Radiotherapy is mostly used in combination with surgery and may improve local control or increase the time to disease progression in some of the patients in whom wide resection cannot be achieved [1]. Our patient refused postoperative treatment with radiotherapy or resection of all tumors. Therefore, a policy of careful and detailed follow-up was adopted.

In conclusion, we here report a rare case of multiple chordomas in both lungs. This case and other reports [6] suggest that both benign and malignant primary notochordal tumors can present as multiple lung

nodules. Immunohistochemical staining for brachyury enables histological confirmation of the diagnosis. However, distinguishing between chordomas and BNCTs can be difficult because it depends mainly on morphological features [2,5]. Further studies are required to clarify the relationship between pulmonary chordoma and BNCT, how to distinguish them from each other, and differences in their clinical behavior.

Conflicts of interest

Conflict of interest: none declared.

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