Letter to the Editor

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Pulmonary Heterotopic Ossification Simulating a Pulmonary Hamartoma: Imaging and Pathologic Findings and Differential Diagnosis

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Heterotopic ossification is a diverse pathological process that is defined as the formation of extraskeletal bone in muscle and soft tissues [1]. Likewise, pulmonary heterotopic ossification (PHO) is a rare metaplastic condition in which dystrophic calcification occurs initially in areas of fibrinous or damaged lung tissue, and eventually changes over time to become heterotopic ossification. PHO is histologically differentiated into two distinct types: nodular and dendritic [2]. PHO cases are often reported in pathologic literature [3]; however, imaging findings of pulmonary ossification have occasionally been reported [4].

A 53-year-old man visited our hospital with a mass found incidentally on chest radiography (CXR). The patient was a current smoker (33 pack-years). On CXR, a mass approximately 34 mm in diameter was observed in the left parahilar area (Fig. 1A). Both non-enhanced and enhanced (Pamiray 300; Dongkook Pharm; 1.5 mL/kg; a total of 90 mL) CT scans were obtained. On CT, the tumor manifested as a fusiform lesion located in the anterior segment of the left upper lobe with a longest anterior-posterior diameter of 46 mm. The tumor contained internal stippled calcifications and air attenuations. It was surrounded by air (Fig. 1B, C). The leading bronchus sign was positive (Fig. 1C, D). The lung mass showed a net enhancement of 39 Hounsfield unit (HU) (24.2 HU before enhancement and 63.2 HU after enhancement). Our presumed imaging diagnosis was hamartoma, given the features of a well-defined margin, internal calcifications, and the presence of surrounding air.

The patient directly underwent video-assisted thoracoscopic wedge resection of the tumor without a biopsy procedure because he denied invasive diagnostic workup, knowing that the tumor seems to be benign but large enough to be resected (more than 3 cm in diameter). On gross pathology, the tumor appeared as a 5.0 cm x 3.0 cm x 2.8 cm-sized, well-defined, firm, yellowish mass (Fig. 1E). Histological examination revealed focal mature woven (not lamellar) bone with bone marrow proper that appeared normal. Also seen were bone forming lesions or abundant pinkish osteoid-like materials, mixed with osteoclast-like multinucleated giant cells, osteoblast-like mononuclear cells, and abundant fibroblastic stroma. An airway-like structure was observed in the peripheral portion of the tumor, which eventually connected to the main tumor (Fig. 1F, G).

Histologically, two distinct types of pulmonary ossification can be distinguished. Nodular ossifications are secluded into the alveolar space and are often round. Dendriform ossifications branch through the interstitium of the septa in a tree-like coral pattern. Even with thin-section CT, it is difficult to discern nodular from dendriform pulmonary ossification. Furthermore, differentiating between these two types clinically has little importance, as both may co-exist in the pulmonary tissue of the same patient [5]. However, it has been reported that dendriform PHO branches through the interstitium of the septa in a tree-like coral pattern. Dendriform PHO may appear as multiple tiny calcifications showing lattice-like or continuous branching patterns, usually in bibasilar subpleural lungs [4].

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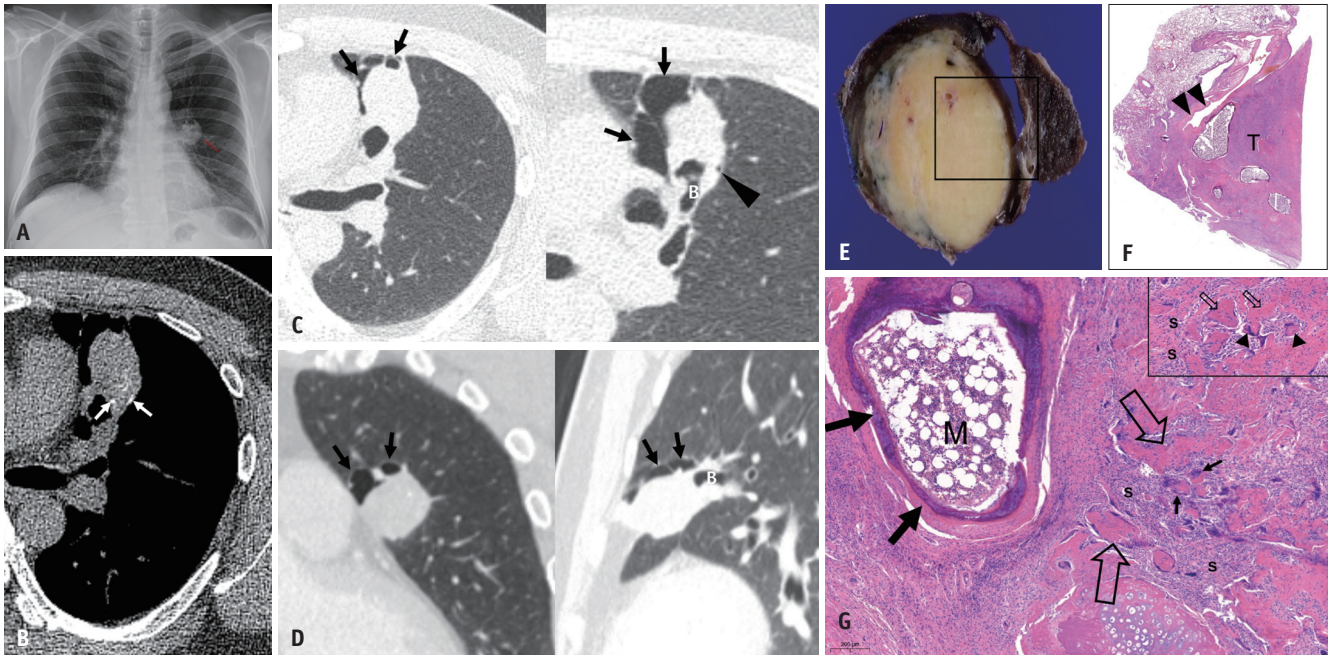

Fig. 1. Pulmonary heterotopic ossification in a 53-year-old male.
A. Chest radiograph shows a 34-mm-sized mass (arrow) in the left parahilar area. **B.** Mediastinal window image of 1.0 mm thin-section CT obtained at the level of the distal left main bronchus demonstrates a mass of 46 mm in anterior-posterior diameter in the anterior segment of the left upper lobe. Stippled calcifications (arrows) are observed within the tumor. **C.** Lung window images of consecutive thin-section CT scans depicts peritumoral air collection (arrows), leading bronchus sign (B), and intratumoral air attenuation (arrowhead). **D.** Coronal (left) and sagittal (right) reformation images reveal peritumoral gas collection (arrows) and leading bronchus sign (B) on the sagittal reformation image. **E.** Gross pathological specimen shows a well-defined, firm, yellowish mass. Histological specimens were obtained from the rectangular area covering one half of the gross specimen. The box in the gross specimen indicates the area where histological specimens **(F)** were obtained. **F.** Histological examination (hematoxylin-eosin staining; scan view, x 4) reveals focal mature bone formation containing bone marrow proper that appears normal. The remaining tumor (T) consists of pinkish osteoid-like materials mixed with osteoclast-like multinucleated giant cells, osteoblast-like mononuclear cells, and abundant fibroblastic stroma. Airway structures lined by respiratory epithelium-like cells (arrowheads) are observed in the periphery of the tumor. **G.** Medium power (hematoxylin-eosin staining; scan view, x 50) magnification view shows mature bony trabeculae (arrows) containing marrow proper (M). In addition, osteoid-like pinkish materials (open arrows) and osteoclast-like multinucleated giant cells are observed in the abundant fibroblastic stroma (S). Inset: osteoid-like materials (open arrows) rimmed by mononuclear osteoblast-like cells and multinucleated osteoblast-like giant cells (arrowheads) (x 200).

In our case, the PHO was surrounded by air on CT, the findings of which cannot be easily explained histopathologically. According to a report [6], air in the surrounding lung of or within a hamartoma is seen in five (26%) of 19 pulmonary hamartomas. The hamartomas were connected to the airways in four (21%) cases. The connection between the bronchi and epithelial lined clefts (located between mature cartilaginous lobules within hamartomas) is the presumed cause of air in and surrounding the hamartomas [6]. On histopathologic examination of our case, we could not identify the cleft-like structure observed in the hamartomas; however, we could see a connection between the PHO and the leading bronchus on CT. Moreover, we observed an airway-like structure leading to the tumor on histological examination and air attenuation within the tumor. We presume a similar connection between the tumor per se and the airway-like structure on histopathology in the PHO (as in the case of hamartomas) might have been the nidus of air in and surrounding the PHO.

Differential diagnosis includes benign solid tumors with ossification or calcification, such as hamartoma, pulmonary amyloidoma, and pulmonary osteoma. Hamartomas present as solitary lung nodules and occasionally as endobronchial tumors. Histologically, it consists of hyaline cartilage, fibromyxoid stroma, smooth muscle cells, and adipose tissues. One frequent and pathognomonic feature indicating the presence of hamartoma is the coexistence of mesenchymal elements and epithelial tubules (cleft), reminiscent of the bronchiolar epithelium [7]. On CT, fat and/or calcification are seen within the lesion; calcification(s) are seen in 5%–50% of cases, and fat is seen in up to 50% of cases [8].

Nodular pulmonary amyloidosis (amyloidoma) is a

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localized parenchymal type of amyloid deposition. On CT, it manifests as solitary pulmonary nodules, multiple nodular lesions, or more diffuse diseases without pathognomonic features. Histologically, the gold standard for diagnosis is the presence of apple-green birefringence upon Congo red staining under polarized light [9].

Osteoma is a radiologic term for a bone lesion that is histologically composed of lamellar bone with Haversian canals. The term osteoma should be reserved only for bone lesions. Osteomas, by definition, appear as very dense lesions (> 885 HU) on CT, similar in appearance to normal bone cortex [10], and mature osteomas may also demonstrate central marrow. There has been a report on pulmonary osteoma in which the tumor appeared as a solitary pulmonary nodule on CT [11]. However, we cautiously think that the case reported by Markert et al. [11] is not a case of true osteoma but rather a case of PHO, as in our case.

In conclusion, we report the imaging and histopathologic features of PHO in a healthy 53-year-old male with CT features of a fusiform mass containing internal stippled calcifications surrounded by air attenuation, thus simulating a large pulmonary hamartoma.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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