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CASE REPORT

A pulmonary metastatic breast phyllodes tumor and clinicopathology analysis

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Abstract

Objective Breast phyllodes tumors (PTs) are rare fibroepithelial tumors that are characterized by formation of foliation patterns. Behaviorally, only relatively poor prediction of PTs is possible based on their histological appearance. PTs are frequently misdiagnosed because they are difficult to differentiate from soft tissue tumors. In this report, we describe the pathological features of a rare case of PT and review the relevant literature, summarizing the essentials of the diagnosis and differential diagnosis, while attempting to avoid misdiagnosis or missed diagnosis of the tumor to the best of our abilities.

Methods We present a case of pulmonary metastatic lobular tumor, analyzing the morphological [hematoxylin-eosin (HE) staining] and immunohistochemical (streptavidin perosidase method, SP) features of the tissue.

Results Long spindle-shaped tumor cells were observed using microscopy. The cells were arranged in bundles, with a whirlpool pattern, and braided. The proliferation of the spindle cells was markedly atypical and karyokinesis was elevated. Residual ductal epithelium was detected in some areas, and the margins of the tumor tissues showed invasive growth. Immunohistochemical studies of the spindle-shaped tumor cells were positive for actin, PR, CD10, SMA, Bcl-2, and negative for CKP, S-100, CD34, ER. The Ki-67 index was 40%.

Conclusion The spindle cell tumor identified in the lung should first be considered as a metastatic neosplasm, because most soft-tissue sarcomas commonly metastasize through the bloodstream to the lungs. Although malignant breast PTs are rare, a detailed medical history that includes prior surgical history is required to avoid wrongful or missed diagnosis.

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Phyllodes tumors (PTs) are a group of well-demarcated fibroepithelial tumors, accounting for 0.5–1% [1] of primary breast tumors. PTs are classified as benign, borderline, or malignant. Although most PTs are benign, the recurrence rate is relatively high, and malignant PTs may metastasize to multiple organs through the bloodstream [2]. We report a case in which PT metastasized to the lungs.

Case report

A 51-year-old woman was admitted to the surgical department of our hospital for a tissue mass in her right lower lung. No symptoms, such as chest tightness, asthma, or chest pain, were detected, and she had no history of chronic coughing, asthma, excessive phlegm accumulation. Her clinical diagnosis was pulmonary tumor, and a wedge-shaped resection was performed on the right lower lung mass under general anesthesia. The postoperative routine involved pathological examination: the lung excision measured 7 × 3 × 4 cm, with a clear border, and a tough ashen tubercle that measured 3.6 × 3.7 × 3 cm was observed in the cut section. Microscopic examination showed a fibroepithelial neoplasm composed of residual ductal epithelium in the background of a markedly hypercellular spindle cell stroma (Fig. 1). A leaf-like architecture and stromal overgrowth were

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observed, which also showed fibroepithelial stromal hypercellularity, nuclear pleomorphism, mitoses (Fig. 2), and necrosis (Fig. 3). We observed 11 mitoses per 10 high-power fields of view; the spindle-shaped tumor cells were arranged in bundles, whirlpools, and braided. The tumor had a pushing and infiltrative margin. Immunohistochemical studies of the spindle-shaped tumor cells were positive for actin,PR, CD10, SMA, Bcl-2,and negative for CKP, S-100, CD34, ER. The Ki-67 index was 40%. A review of the medical history showed that the patient had previously undergone a right breast lump resection in August 2011. The postoperative pathology demonstrated that this was a case of malignant PT, and the mastectomy specimen was examined. Microscopic examination showed the disappearance of breast lobules, stromal hypercellularity, a pushing and infiltrative margin, and cleft-like ductal epithelium by compression. The spindle-shaped tumor cells were arranged in bundles, with a whirlpool pattern, and braided (Fig. 4). The tumor cells were characterized by an uneven distribution, showing a dense and heteromorphic pattern. Additionally, we observed tumor giant cells like those found in sarcoma (Fig. 5), mitoses ≥ 10/10 HPF (high power field). Using an immunohistochemistry approach, we observed the following spindle cells: were positve for CKP, EMA, Vimentin, Act, SMA, PR, P53, and nagative for CD117, Des, NSE, the Ki-67 index was 40%. The staining intensity of Ki-67 was also strongly apparent around the catheter (Fig. 6). Combined with the clinical history and primary pathological diagnosis, this patient was diagnosed as having pulmonary metastases arising from malignant PT.

Discussion

PTs are rare tumors of the breast accounting for 2.5% of all breast fibroepithelial tumors, most of which occur in middle-aged women [3]. Clinically, PTs tend to be present as continually growing, painless breast masses [4]. The median size of PTs are usually 4 cm. The two clinical characteristics of PTs are recurrence and metastasis. PTs of any grade have the potential for recurrence; moreover, during local recurrence, the classification grade can worsen. Another characteristic of PTs is metastasis; the rate of PT metastasis is about 6.2–25% [5]. The main metastatic mode is by blood, and an intravenous tumor embolus could be detected (Fig. 7). Metastatic sites are mainly limited to the skeleton, lungs, kidneys, and heart [6- 9]. Classically, it was noted that metastases from PTs were consistently preceded by a primary malignant diagnosis, but there are exceptions. Abdalla had reported that metastases occurred in 3.2% of benign PTs, which remains controversial [10]. Although metastasis is a rare occurrence in benign PTs, metastases may be of great diagnostic value in malignant diagnosis; however, they cannot be used as evidence for final diagnosis.

Because clinical manifestations of PTs are not distinct, there are several methods such as shear wave velocity and different probe orientations that have been used in its diagnosis [11]. Pathology is the major diagnostic modality, which is also the gold standard used for diagnosis [12]. The cut surface of the mass has a brownish pink appearance, with a structure of mucoid or flesh; additionally, a whirlpool structure with a leaf bud-like curved fissure can be seen. Microscopic examination showed leaf-like fronds protruding into cystically dilated ducts and stromal hypercellularity. PTs are classified by the World Health Organization (WHO) into the categories benign, borderline, and malignant. These grade categories are based on stromal cellularity and atypia, mitotic count, stromal overgrowth, and the nature of their tumor borders [13]. Apart from grading, however, is a compound problem in clinical practice. In general, benign PT interstitial cells are mostly spindle shaped and mitotic figures are rare. As interstitial cells have more pleomorphism with increased mitotis, and with the appearance of permeable margins, PTs are often considered to be malignant. In addition, the expression rate of multiple biological markers, such as P53, Ki-67, CD117, EGFR, VEGR, and P16 also increased gradually as the PT grade progresses. These tests can be helpful for differential diagnosis of PT. In addition, when the tumor appears to be heterogeneous, the malignancy should be diagnosed even if the above features are lacking [14]. In terms of pathogenesis, PTs are thought to originate from intralobular or periductal stroma, which may be primary or evolved from fibroadenoma. In the case reported here, which belongs to the latter, there is a fibroadenoma area around the tumor (Fig. 8).

There are several diseases that must be differentiated from PTs. First, PTs should be differentiated from leiomyoma and rhabdomyosarcoma. Lung spindle cell nodules must be ruled out for the diagnosis of several primary tumors, including leiomyoma sarcoma and rhabdomyosarcoma. This exclusion can be made by immunohistochemistry. In addition, the cytoplasm of rhabdomyosarcoma spindle cells has a red appearance. By microscopy, rhabdomyoblasts can be detected by careful observation. Second, they should be distinguished from spindle cell carcinoma. A solitary mass, located at the edge of the lung, excludes spindle cell carcinoid. The keratin and neuroendocrine markers are always positive for spindle cell carcinoids, and can be differentiated from PTs. Third, PTs can be easily misdiagnosed as an inflammatory myofibroblastic tumor (IMT). The main characteristic of this tumor is the presence of spindle cells. The immunohistochemical and ultrastructural characteristics are consistent with myofibroblasts and are often accompanied by severe mononuclear cell

infiltration (mainly lymphocytes) and closely associated with spindle cells. ITM constant appears to involve 2p23 chromosome translocation and the overexpression of the ALK gene regulatory protein [15], but this is not observed in PT. Finally, the morphologic form of metaplastic cancer is sometimes similar to that of poorly differentiated malignant PTs. The identification of the two is mainly dependent on immunohistochemistry.

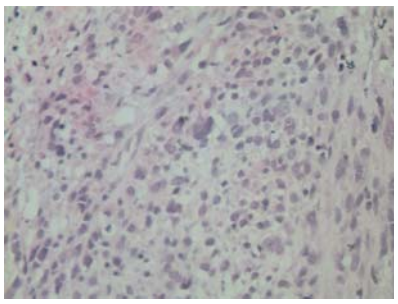

Fig. 1 Microscopic examination showed a fibroepithelial neoplasm composed of residual ductal epithelium in the background of a markedly hypercellular spindle cell stroma (HE × 400)

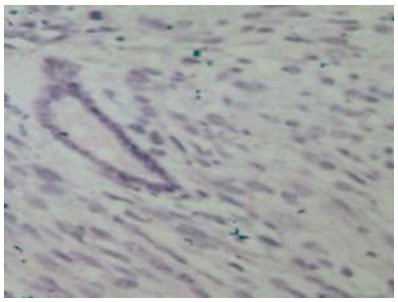

Fig. 3 Necrosis were observed (HE × 100)

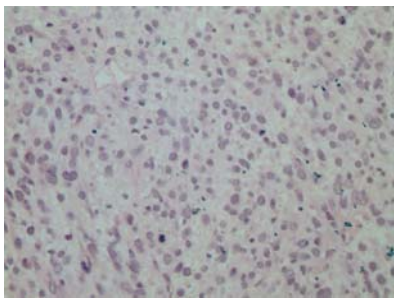

Fig. 5 Tumor giant cells like those found in sarcoma were visible (HE × 400)

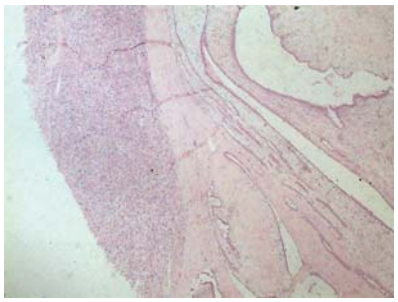

Fig. 7 an intravenous tumor embolus could be detected(HE × 200)

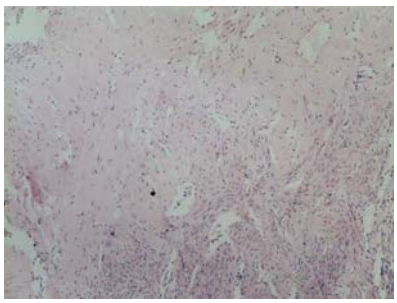

Fig. 2 Mitoses were observed (HE × 400)

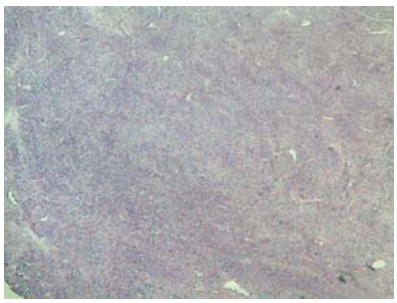

Fig. 4 The spindle-shaped tumor cells were arranged in bundles, with a whirlpool pattern, and braided (HE × 100)

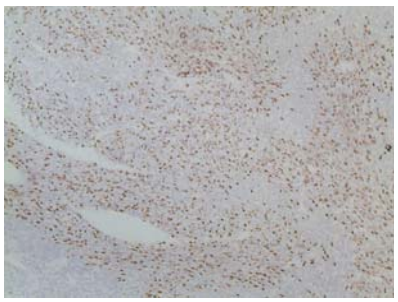

Fig. 6 The staining intensity of Ki-67 was strongly apparent around the catheter (SP × 100)

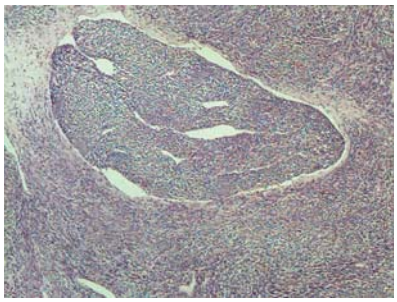

Fig. 8 There was a fibroadenoma area around the tumor (HE × 100)

In conclusion, spindle cell tumors in the lung should first be considered as metastatic neosplasm, because most soft-tissue sarcomas that metastasize through bloodstream commonly metastasize to the lungs. Although malignant breast PTs are rare, a detailed medical history that includes prior surgical history is required in order to avoid wrongful and missed diagnosis. For the treatment of malignant PT, the international recognized surgical resection approach and postoperative chemotherapy are recommended as the most effective forms of therapy, which is similar to the chemotherapy program used for soft tissue sarcoma [16].

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