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CASE REPORT

Blastomatoid pulmonary carcinosarcoma: A rare case report and review of the literature

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Abstract

A 65-year-old never-smoking woman presented to a local hospital, because an abnormal shadow was detected at the right lower lung field by annual chest X-ray. Computed tomography (CT) revealed a 5-cm tumor in segment 6 of her right lung and an enlarged subcarinal lymph node, suggesting metastasis. The lung tumor was diagnosed as adenocarcinoma by a CT-guided percutaneous needle biopsy. She was referred to our hospital and underwent right lower lobectomy with lymph node dissection (ND2a-2). A histopathological examination of the tumor showed a biphasic proliferation made of carcinomatous and sarcomatous components. The carcinomatous component consisted of glandular structures of atypical cells that possessed chromatin-rich nuclear and clear cytoplasm, confirming high-grade fetal adenocarcinoma. The sarcomatous component consisted of immature spindle cells that differentiated into chondrosarcoma. Immunohistochemically, the glandular structures expressed membranous beta-catenin, and the ultimate diagnosis was blastomatoid variant of pulmonary carcinosarcoma. She received four courses of cisplatin plus vinorelbine as adjuvant chemotherapy and remained alive with neither recurrence nor distant metastasis at two and a half years after the operation. We experienced a rare case of blastomatoid pulmonary carcinoasarcoma.

Introduction

Blastomatoid pulmonary carcinosarcoma is one of the rarest histologic types of carcinosarcoma of the lung.[1] Although there have been only a few reports on this histologic type so far, there might be some cases in which a definitive diagnosis of blastomatoid pulmonary carcinosarcoma was not obtained.[2–5] Advances have been made in recent years in ancillary diagnostic techniques for this histologic type, such as immunohistochemistry and gene mutation analyses.[2,3]

We herein report a case of blastomatoid pulmonary carcinosarcoma.

Case report

A 65-year-old never-smoking woman presented to a local hospital, because an abnormal shadow was detected at the right lower lung field by annual chest X-ray. She had no subjective symptoms. Computed tomography (CT) revealed a 5-cm well-circumscribed tumor in segment 6 of her right lung, which was in wide contact with the parietal pleura (Fig 1a,b). An enlarged subcarinal lymph node was suspected of being metastasis (Fig 1c). A CT-guided percutaneous needle biopsy of the lung tumor was performed, and a diagnosis of adenocarcinoma was made. She was referred to our hospital for treatment. Since there was no evidence of distant metastases, we performed right lower lobectomy with lymph node dissection (ND2a-2), and combined resection of the parietal pleura with video-assisted thoracoscopic surgery.

Macroscopically, the lesion was a well-circumscribed tumor of 7.0 × 4.5 × 4.2 cm in size with a soft, fleshy, and pale tan-white cut surface. A histopathological examination showed biphasic proliferation with carcinomatous and sarcomatous components with a sharp border between both

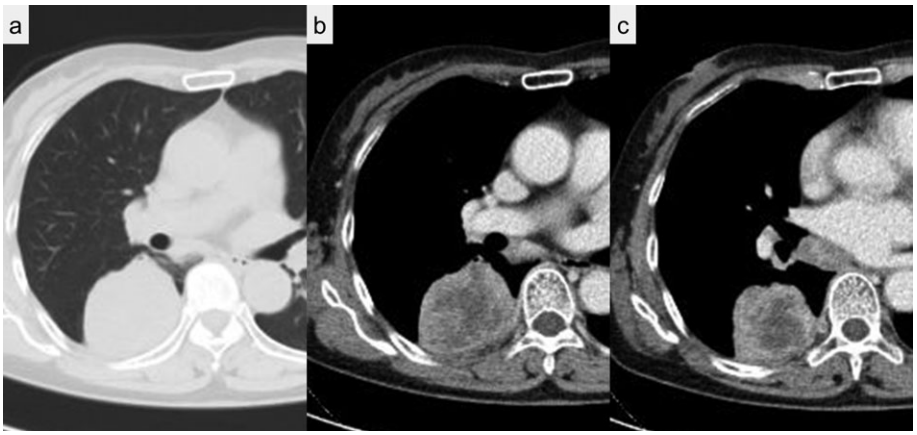

Figure 1 Computed tomography showed a tumor in segment 6 of patient's right lung, which was in wide contact with the parietal pleura in a pulmonary window image (**a**) and in a mediastinal window image (**b**). An enlarged subcarinal lymph node suspected of being metastasis was also detected (**c**).

components (Fig 2). The carcinomatous component consisted of glandular structures of atypical cells that possessed chromatin-rich nuclear and clear cytoplasm, confirming high-grade fetal adenocarcinoma (H-FLAC) (Fig 2a,b). Morule formation was not seen in the carcinomatous components. In contrast, the sarcomatous component consisted of immature spindle cells that differentiated into chondrosarcoma (Fig 2c–e). Immunohistochemically, the glandular structures expressed membranous beta-catenin and focal α-fetoprotein (Fig 3). The expression of p53, murine double minute 2 (MDM2), cyclin-dependent kinase 4 (CDK4), and thyroid transcription factor 1 (TTF-1) were not confirmed. A diagnosis of the blastomatoid variant of pulmonary carcinosarcoma was thus established.

The tumor infiltrated the parietal pleura, but there was no invasion of tumor cells on the detached surface of the parietal pleura. As expected before surgery, the involvement of the subcarinal lymph node was confirmed, although no other lymph node metastases were confirmed. The tumor was ultimately staged at pT3, pN2, M0, G3, R0, UICC stage 3A by the UICC 7th classification.[6] The mutations in epidermal growth factor receptor (*EGFR*) gene and v-Ki-ras2 Kirsten rat sarcoma viral oncogene homolog (*KRAS*) gene, and the anaplastic lymphoma kinase (*ALK*) translocations were not detected. She received cisplatin (80 mg/m^2, Day 1) plus vinorelbine (25 mg/m^2, Day 1 and 8) every three weeks for four cycles as adjuvant chemotherapy six weeks after the operation and remained alive

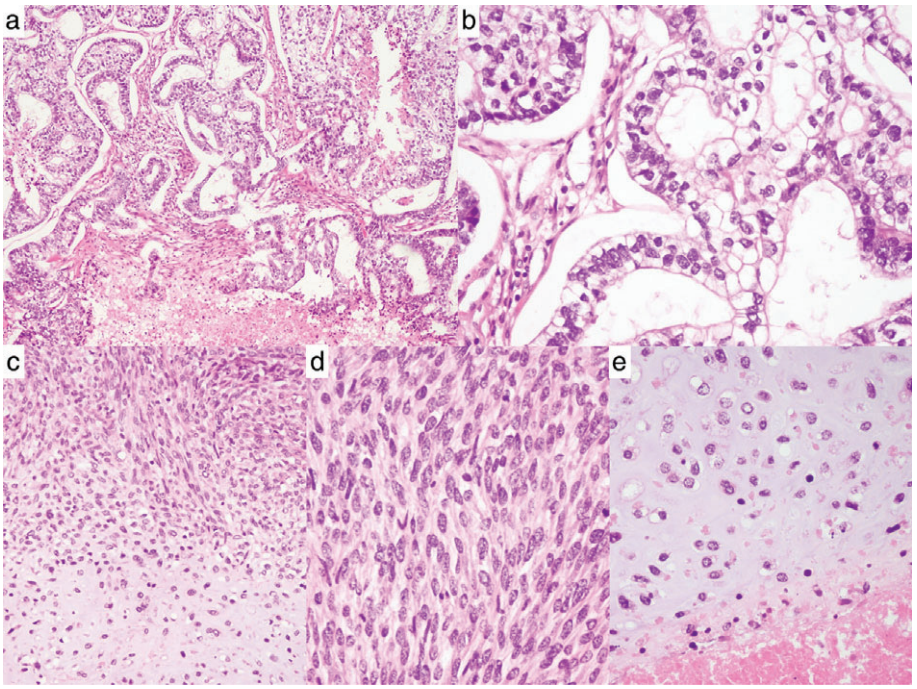

Figure 2 A hematoxylin and eosin-stained specimen showing biphasic proliferation with carcinomatous and sarcomatous components. The carcinomatous component consisted of glandular structures of atypical cells without morules, confirming high-grade fetal adenocarcinoma (**a**, magnification, ×100; **b**, magnification, ×400). The sarcomatous component consisted of immature spindle cells (top) that differentiated into chondrosarcoma (down) (**c**, magnification, ×200). A high-power view of the immature spindle cells (**d**) and chondrosarcoma (**e**) (magnification, ×400).

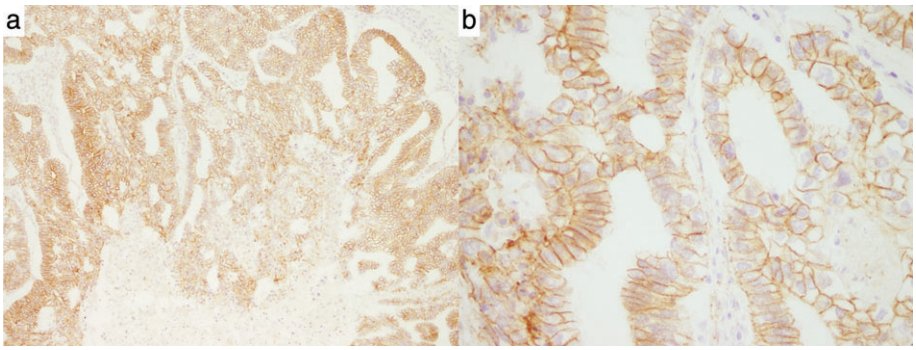

Figure 3 Immunohistochemistry demonstrating the membranous expression pattern of beta-catenin in the glandular structures of the carcinomatous components (**a**, magnification, ×100; **b**, magnification, ×400).

two and a half years after surgery with no evidence of local recurrence or distant metastasis.

Discussion

Sarcomatoid carcinomas are estimated to account for only 0.1–0.4% of all lung cancers, and of these, only 4% are pulmonary carcinosarcomas.[1,7] According to the recent World Health Organization (WHO) classification of lung tumors, carcinosarcoma is defined as a malignant tumor that consists of an admixture of non-small cell lung carcinoma and sarcoma-containing heterologous elements.[1,8] Koss *et al.* reported that 18% of 66 carcinosarcoma cases contained H-FLACs as epithelial components.[9] These carcinosarcomas, including H-FLACs, are defined as blastomatoid pulmonary carcinosarcomas, but they are not yet recognized as a distinct entity by the WHO classification and are only obliquely referenced in the section on carcinosarcoma.[1]

H-FLACs are referred to by Nakatani *et al.* as a type of pulmonary adenocarcinoma of the fetal lung.[10] Those authors divided pulmonary adenocarcinomas of the fetal lung into low- and high-grade forms, and low-grade adenocarcinomas of fetal lung type (L-FLACs) are also known as well-differentiated fetal adenocarcinomas (WDFAs) in the WHO classification at present.[10] Currently, both L-FLACs/WDFAs and H-FLACs are included as a subtype of adenocarcinoma in the WHO classification.[11] Although both groups show similar histological findings, H-FLACs show high nuclear atypia and typically lack morules.[12] The pathogenesis of these two groups has been discussed, and the up-regulation of the Wnt signaling component, including gene mutations of beta catenin, is suggested to be important for L-FLACs/WDFAs but not for H-FLACs.[2,7,12] Furthermore, immunohistochemical analyses have demonstrated aberrant nuclear and cytoplasmic staining of beta catenin in the epithelial cells of L-FLACs/WDFAs, while membranous staining in H-FLACs.[2,3,11,12] These findings with ancillary techniques support our diagnosis in the present study. In addition, α-fetoprotein staining is often positive and TTF-1 staining negative in H-FLACs.[5,12]

No valid therapy has yet been proposed for the treatment of carcinosarcomas, other than complete resection as for other types of sarcomatoid carcinomas, and the role of chemo- and radiation therapy remains controversial.[13,14] At least seven cases of blastomatoid pulmonary carcinosarcoma have been reported (Table 1). All were advanced cases (stage 2 or more), reflecting the difficulty of early detection due to the disease's rapid progression.

According to the previous reports, pulmonary carcinosarcomas occur seven to eight times more often in men than in women, particularly in elderly smokers predominantly in their 60s.[1,5,9,15] The prognosis of carcinosarcoma is generally very poor. Indeed, most of the above-mentioned seven cases of blastomatoid pulmonary carcinosarcoma were males with smoking history, and they also showed a poor prognosis.

It is well known that smoking is one of the most important risk factors in the etiology of lung cancer including

Table 1 A summary of the clinicopathologic features of blastomatoid pulmonary carcinosarcomas from the present and previous series

Year	Age (years)/Gender	Smoking history	TNM	Stage	Treatment	Outcome	Reference
2004	65/Male	+	T2aN2M0	IIIa	Surg, RT	Died of disease at 10 months	[3]
2004	21/Male	–	T3N1M1	IV	Surg, CT	Alive and well at 108 months	[3]
2004	62/Male	+	T3N0M0	IIb	Surg	Died of other disease at 1 month	[3]
2004	69/Female	+	T3N0M0	IIb	Surg	Died of other disease at 1 month	[3]
2004	71/Male	+	T4N3M0	IIIb	Surg	Died of disease at 14 months	[3]
2012	58/Male	+	T3N0Mx	IIb	Surg	Alive and well at 30 months	[4]
2013	54/Male	+	T2aN2M0	IIIa	Surg	Alive and well at 24 months	[5]
2018	65/Female	–	T3N2M0	IIIa	Surg, CT	Alive and well at 24 months	Present case

+, yes; –, no; Surg, surgery; RT, radiation therapy; CT, chemotherapy.

carcinosarcoma[1,9,16] However, the present case was a never-smoking female, and she remained alive without recurrence for at least two and a half years after complete resection followed by adjuvant chemotherapy. Because there is no established chemotherapy for blastomatoid pulmonary carcinosarcoma, we used the regimen of cisplatin plus vinorelbine, which is used for non-small cell lung cancer as adjuvant therapy. Our selected chemotherapy regimen as adjuvant therapy after complete resection may be effective against blastomatoid pulmonary carcinosarcoma.

In summary, we herein described a particularly rare case of blastomatoid pulmonary carcinosarcoma. Due to the similarity in the histopathological findings between H-FLACs and L-FLACs/WDFAs, and the rarity of the disease, the exact behavior of blastomatoid pulmonary carcinosarcoma remains unclear. The accumulation of more cases and long-term follow-up data leading to a more objective assessment is needed.

Disclosure

The authors have no conflicts of interest to declare.

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