

# Bilateral Spontaneous Pneumothorax During Cytotoxic Chemotherapy for Angiosarcoma of the Scalp

## : A Case Report

Spontaneous pneumothorax is a rare manifestation of metastatic lung cancers and described in advanced diseases or during cytotoxic chemotherapy which is manifested by sudden onset of dyspnea. The cause or mechanism of spontaneous pneumothorax has been unknown, as well as the association with site of metastases or type of cancers or side effect of chemotherapeutic drugs has been reported rarely. A 68-yr-old man underwent excision of angiosarcoma of the scalp. Chest radiography did not show any evidence of possible metastatic lung lesion at that time. Therefore, systemic doxorubicin and dacarbazine were given. After nineteen days of chemotherapy, he developed a bilateral spontaneous pneumothorax and palpable cervical lymph nodes. Both parietal and visceral pleura were intact and showed no evidence of metastatic and pathologic lesions on thoracoscopic evaluation. The patient managed with bilateral tube thoracostomy and both lungs were expanded. Lymph nodes became unpalpable during three cycles of the paclitaxel and doxorubicin, however, bilateral lung metastases were developed and progressed despite chemotherapy. The patient died due to respiratory failure after five months. This report underlines that spontaneous pneumothorax can occur as the first manifestation of metastatic angiosarcoma even if imaging studies do not show of a metastatic lesion.

Key Words : *Pneumothorax; Hemangiosarcoma; Scalp*

Chang Hwa Lee, Keon Uk Park,  
Deuk Young Nah, Kyoung Sook Won\*

Department of Internal Medicine, Dongguk University Medical Center, Gyeongju; \*Department of Nuclear Medicine, Keimyung University School of Medicine, Daegu, Korea

Received : 26 February 2002

Accepted : 17 June 2002

### Address for correspondence

Keon Uk Park, M.D.  
Department of Internal Medicine, Dongguk University Medical Center, 1090-1 Seokjang-dong, Gyeongju 780-350, Korea  
Tel : +82.54-770-8210, Fax : +82.54-770-8500  
E-mail : kupark@dumc.or.kr

## INTRODUCTION

Angiosarcomas are extremely rare high-grade malignant tumors, accounting for less than 2% of soft tissue sarcomas (1). Approximately one third of angiosarcomas occur in skin, one third in soft tissue, and remaining one third in other sites including breast, liver, and bone. Cutaneous angiosarcoma occurs most commonly on the face and scalp in elderly patients and is also seen in association with chronic lymphedema (2).

It is estimated that less than 1% of all spontaneous pneumothorax are tumor-associated (3). Development of a spontaneous pneumothorax in patients with metastatic soft tissue sarcomas has been described in advanced diseases or during cytotoxic chemotherapy. However, the spontaneous bilateral pneumothorax is a rare complication of cancer chemotherapy.

Here we report a case of bilateral spontaneous pneumothorax after systemic chemotherapy in a male patient with a localized angiosarcoma of the scalp.

## CASE REPORT

A 68-yr-old man is presented with an erythematous patchy

induration on his scalp. There were no history of smoking, radiation, and trauma. There were no evidence of underlying lung lesion or any metastasis on his chest radiography. On examination, there were 3 × 4 cm-sized pink-purple nodules with several small satellite lesions on scalp. There were no palpable lymph nodes on both supraclavicular and neck regions. Biopsy of the lesion showed a network of interconnecting capillary lumens lined by atypical endothelial cells with hyperchromic pleomorphic nuclei and collagen bundles in the deep dermis. The lining atypical endothelial cells showed a positive reactivity for CD34 and vimentin. Magnetic resonance imaging (MRI) revealed a tumor with an irregular boundary on vertex of parietal scalp (Fig. 2). Underlying cortical bones were intact and a mass containing a central necrotic portion was invading the skin, subcutaneous layer, and muscle layer. The patient underwent a wide excision of parietal scalp and a split-thickness skin graft from the thigh. On pathologic examination, a fragment of the scalp measuring 10 × 7.5 × 1 cm was indurated with central ulceration. On cross-section, the scalp was thickened and diffusely infiltrated by an ill-defined tannish firm lesions (Fig. 3). Numerous irregular shaped anastomosing vascular channels with the appearance of dissecting collagen bundles were seen in the

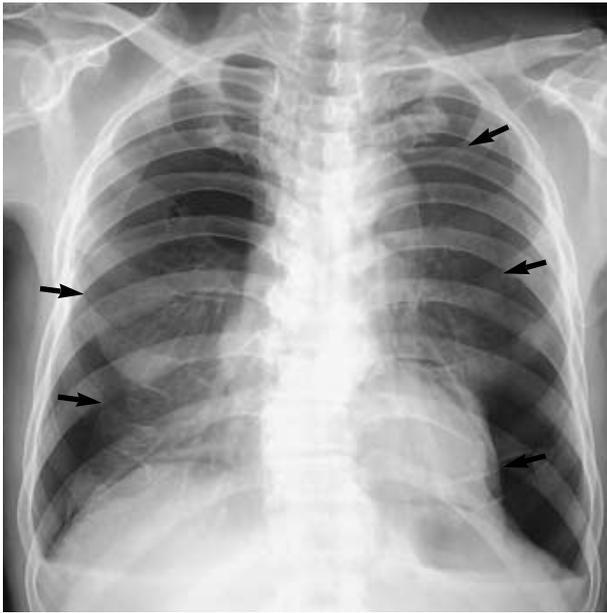


Fig. 1. Bilateral pneumothorax with both costophrenic angle blunting are observed.

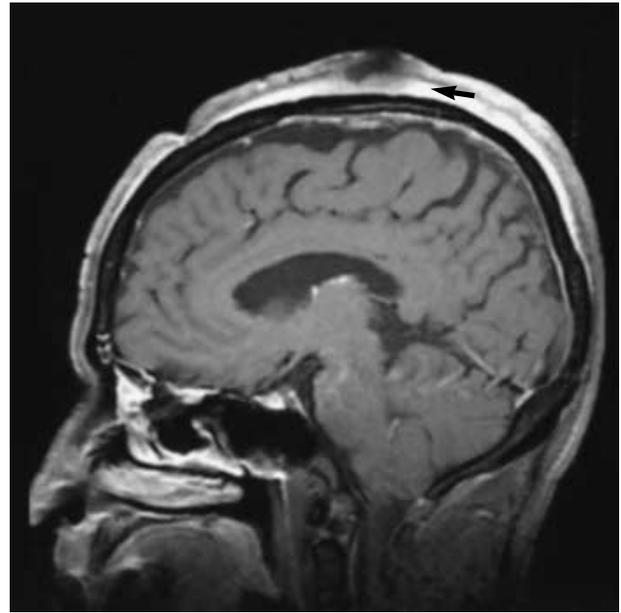


Fig. 2. T1-weighted sagittal view MRI shows heterogeneous signal intensity mass with an irregular boundary on the vertex of parietal scalp (arrow). Underlying cortical bone is intact and a mass containing a central necrotic portion is invading the skin, subcutaneous layer, and muscle layer.

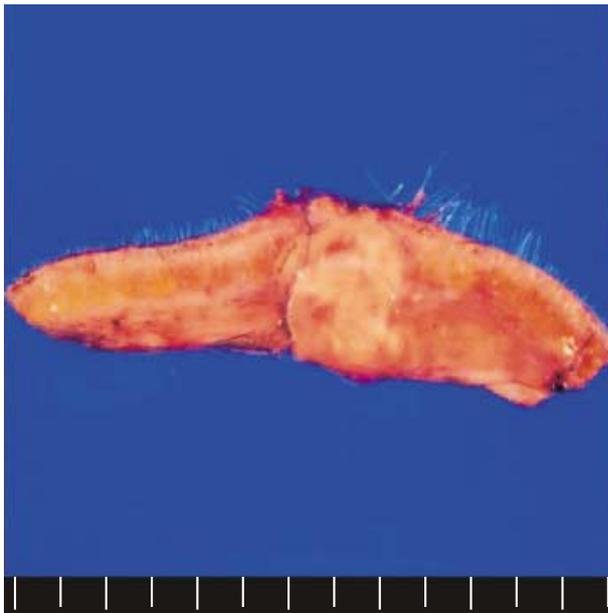


Fig. 3. On cross section, the parietal scalp is markedly indurated and diffusely infiltrated by an ill-defined tannish firm lesion.

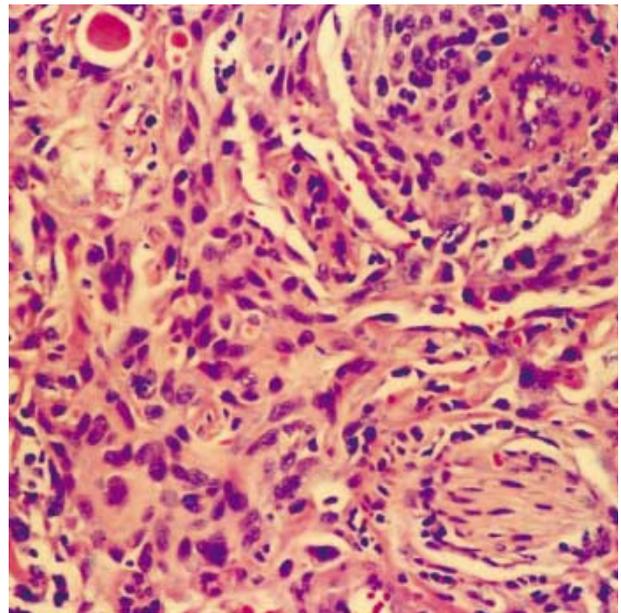


Fig. 4. Numerous irregular shaped anastomosing vascular channels are lined by endothelial cells with a cystic change and hemorrhage (H&E stain,  $\times 200$ ).

dermis. Microscopy showed anastomotic channels lined by the endothelial cells and a cystic change with hemorrhage (Fig. 4). Tumor cells showed a positive immunohistochemical staining for factor 8, CD34, and CD31 (Fig. 5). Due to diffuse local spread of tumor, complete excision was impos-

sible. The patient received combined systemic chemotherapy of doxorubicin ( $50 \text{ mg/m}^2$ ) and dacarbazine ( $400 \text{ mg/m}^2$ ). Nineteen days after the systemic chemotherapy, he was admitted to an emergency department with bilateral spontaneous pneumothorax (Fig. 1), and palpable cervical lymph

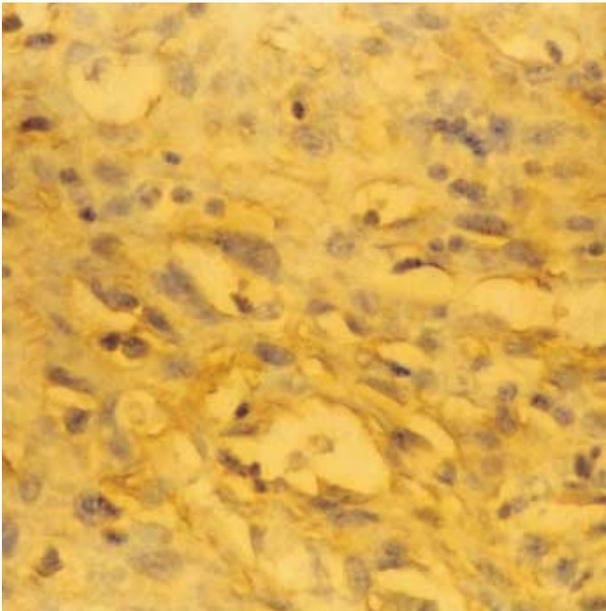


Fig. 5. Tumor cells show a positive immunohistochemical staining for CD31 ( $\times 400$ ).

nodes. Both parietal and visceral pleura were intact and showed no evidence of metastatic lesions on thoracoscopic evaluation. The patient was managed with bilateral closed thoracostomy and both lungs were expanded. Also he underwent pleurodesis with bleomycin and received three cycles of combined chemotherapy of paclitaxel ( $135 \text{ mg/m}^2$ ) and doxorubicin ( $50 \text{ mg/m}^2$ ). Lymph nodes disappeared, however, bilateral lung metastases were developed and progressed despite of systemic chemotherapy. He died of respiratory failure after five months.

## DISCUSSION

Angiosarcomas are extremely rare high-grade malignant tumors arising from the vascular endothelium (4). Approximately half of the cases involve head and neck regions. The disease occurs most frequent in the sixth and seventh decades of life, with a male predilection (5).

Angiosarcomas are highly invasive tumors with the capacity to spread locally as well as distantly and have a rapid clinical course. Most angiosarcomas are metastasized at the time of diagnosis and have a poor prognosis of 2-24 months of survival from the time of detection due to frequent recurrence and early hematogenous metastases. The most common distant metastatic sites include the lung, liver, lymph nodes, and the skin (5, 6).

Kitagawa et al. (7) subdivided 95 autopsies of patients with angiosarcomas into a scalp group and a non-scalp group. The patients of the scalp group had more frequent pulmonary complications including pneumothorax, pulmonary hemorrhage,

atelectasis, and pneumonia. In particular, pneumothorax was observed only in the scalp group, and was implicated in the extremely poor survival. Therefore, angiosarcomas of the scalp tend to metastasize to the lung, especially to the subpleural or pleural space, where these metastatic tumors are prone to necrosis, causing characteristic pulmonary complications.

Several theories regarding possible mechanisms of the bilateral pneumothorax in angiosarcomas have been put forward. First, the rupture of a subpleural bleb in a patient with an underlying chronic pulmonary disease is possible. Second, tumor nodules may act as ball valves to produce a partial bronchiolar obstruction and hyperinflation of alveoli. The rupture of an emphysematous bulla in an overexpanded portion of the lung produces a pneumothorax (8). Therefore, the disruption of peripheral visceral pleura or peripheral bronchioles causes a bronchopleural fistula (9). In our patient, thoracoscopic evaluation did not show any definite metastatic nodule or bulla. Third, the chemosensitivity of cancer may be considered. Tumors with an increased risk of developing a pneumothorax include Ewing's sarcoma, Wilms' tumor, teratoma, and synovial sarcoma (10). Osteosarcomas are thought to be the most common metastatic tumor causing a spontaneous pneumothorax (11). Fourth, the side effects of chemotherapeutic agents have been considered due to the temporal relationship between the use of combination chemotherapy and the development of pneumothorax. For example, Devereux et al. suggested that doxorubicin was the chemotherapeutic agent most likely to impair the wound healing with tissue repair, and may consequently predispose patients with pulmonary metastasis to pneumothorax (12). In this case, doxorubicin was included in the cytotoxic regimen, however, it is difficult to relate its direct effect on pneumothorax.

Until now, no established chemotherapy has been available for angiosarcomas, since systemic chemotherapy is ineffective in the disease with metastatic lesions. Therapy for angiosarcomas involves an early wide local excision, if possible. Early surgery and wide-field postoperative radiation therapy may offer the highest cure rate (1). Recently, however, paclitaxel showed a good response in 28 patients with scalp angiosarcomas with complete resolution of skin nodules and a partial response to metastatic lung lesions in phase II trials (13). Our patient was treated with paclitaxel (Taxol<sup>®</sup>) at a dose of  $135 \text{ mg/m}^2$  for three cycles. Lymph nodes were not palpated after three cycles with systemic chemotherapy but lung metastases were developed lately.

Fenlon et al. stated that a pneumothorax resulting from a bronchopleural fistula complicating chemotherapy may prove to be resistant to conventional treatment (repeated closed-tube thoracostomy, suction drainage, and pleurodesis), and thus required a bilateral thoracostomy and pleurectomy (10).

Metastases are sometimes confirmed by high-resolution computed tomography (CT) or transthoracic needle aspiration biopsy. Metastatectomy via thoracotomy or median sternotomy are sometimes employed (14). Early detection

of lung metastases is difficult, and Furrer et al. suggested that imaging studies such as chest radiography and CT are suboptimal for detecting micro-lesions and that sometimes pneumothorax could be the first and only evidence for metastases (9).

In this case, metastatic lesions could not be noted in the initial chest radiography and CT. However, with the delayed detection of diffuse bilateral lung metastases, we are able to presume that micrometastases were already occurred even before it could be detected by imaging studies.

This report underlines that pneumothorax can occur as the first manifestation of metastatic angiosarcoma even if imaging studies are not indicative of metastatic disease.

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