

Primary Ewing's Sarcoma of the Lung

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Most cases of Ewing's sarcoma are reported in the bone, and extraosseous Ewing's sarcoma is an extremely rare disease. Here, we report a rare case of primary pulmonary Ewing's sarcoma in a patient with hemoptysis. The patient underwent right upper lung lobe lobectomy with adjuvant chemotherapy and radiation therapy and has been free of recurrent disease for 4 years.

Key words: 1. Ewing sarcoma
2. Lung neoplasms

CASE REPORT

A 41-year-old woman was admitted for hemoptysis of 4 days' duration. Her medical and family history was unremarkable. She visited a local clinic, where a chest radiograph revealed a radio-opaque mass in the right upper lung lobe. She was referred to Asan Medical Center. Computed tomography revealed several oval, smoothly marginated, and low attenuation lesions with ground-glass opacity in the right upper lung lobe (Fig. 1). Positron emission tomography with 18F-fluorodeoxyglucose (FDG) showed multiple round or oval lesions in the right upper lung lobe. The FDG uptake was increased in the lesions (maximal standard uptake value: 9.7) without any other abnormal uptake. She underwent bronchoscopy, and a transbronchial lung biopsy and wash with cytology were then performed. The pathological diagnosis of the specimen was a malignant small round cell tumor. Surgical resection was selected for definitive diagnosis and treatment.

The patient underwent right upper lobe lobectomy via post-

erolateral thoracotomy under one-lung ventilation. There were two relatively well-defined ovoid masses in the anterior and posterior segment of the right upper lobe (Fig. 2). These tumors were 5.5×5×3.5 cm and 4.5×4×3 cm in size, respectively. The cut surface was heterogeneously purplish, brown to yellowish, and pink in color. Focal hemorrhage and necrosis were evident. The tumors did not invade the visceral pleura. The surgical margins were not grossly involved. The small mass was approximately 3.3 cm from the bronchial resection margin, but the large mass abutted the bronchial margin. However, the remaining bronchus was too short to allow further resection, and the tumor was limited to the peribronchial soft tissue. Therefore, we decided to add radiation therapy.

Histologically, the tumor was composed of uniform, small, round cells with indistinct borders. The tumor cells had scanty clear cytoplasm and round nuclei with fine chromatin. Immunohistochemical staining for CD 99 revealed diffuse membranous positivity in the tumor cells, which is a characteristic feature of Ewing's sarcoma (Fig. 3). Immunohisto-

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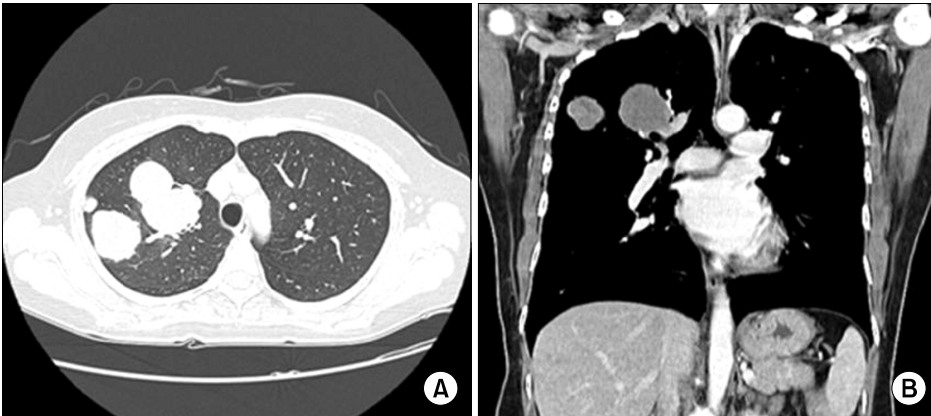


Fig. 1. Chest computed tomography of the patient showing masses in the right upper lung lobe. (A) Lung setting view. Coronal section. (B) Mediastinal setting view. Sagittal section.

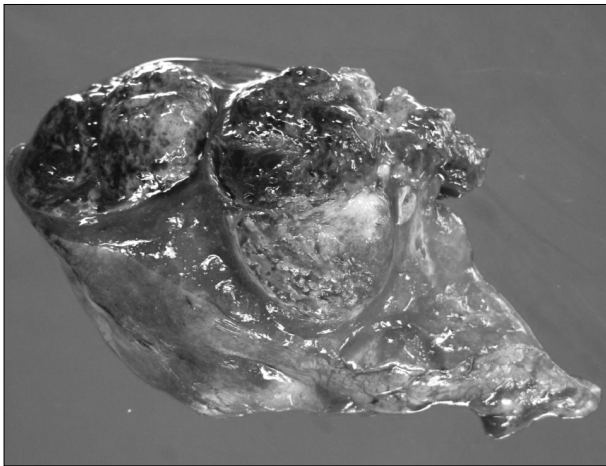


Fig. 2. There are 2 masses in the right upper lung lobe.

chemical staining for CD56, pancytokeratin, and leukocyte common antigen was negative for each.

Postoperatively, the patient was transferred to the intensive care unit, and then, the next day, to the general ward. The chest tube was removed on postoperative day 2. She was discharged from the hospital on postoperative day 4, without any complications. At the outpatient clinic, the patient underwent 6 cycles of chemotherapy consisting of vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide. She also underwent radiation therapy. The patient received 50 Gy to the right hilum. She experienced no recurrence or distant metastasis for 4 years after the surgery.

DISCUSSION

Ewing's sarcoma is a rare malignant disease. It generally occurs as a skeletal disease in pediatric patients. Adult patients are very rare and constitute only 5% of all cases [1]. Extrasosseous Ewing's sarcoma is even more uncommon in adults: only approximately 16% of all Ewing's sarcomas are extrasosseous, and therefore, less than 1% of all such tumors are extrasosseous tumors occurring in adults [2]. Only 12 cases of primary pulmonary Ewing's sarcoma (including 1 case in Korea) have been reported in the literature [3,4].

The pathological diagnosis of extrasosseous Ewing's sarcoma used to require the use of both standard light and electron microscopy to identify small, round, blue cells with abundant glycogen and an absence of cytoplasmic filaments. Because of the lack of any specific morphologic features or diagnostic histopathologic finding, the rate of misdiagnosis by histopathologic findings alone is exceptionally high [5]. Therefore, we used a more accurate diagnostic method, immunohistochemical staining. Staining for CD99 (a cell-surface glycoprotein encoded by the *MIC2* gene) has recently been used for the identification of Ewing's sarcoma, although it is not entirely specific for this disease [6]. Ewing's sarcoma should be differentiated from small-cell carcinoma, adenocarcinoma, squamous cell carcinoma, squamous cell carcinoma, and lymphoma. The cells in this case were small and round, as described above, and immunohistochemistry showed strong staining for CD99. Therefore, we readily diagnosed the case as Ewing's sarcoma.

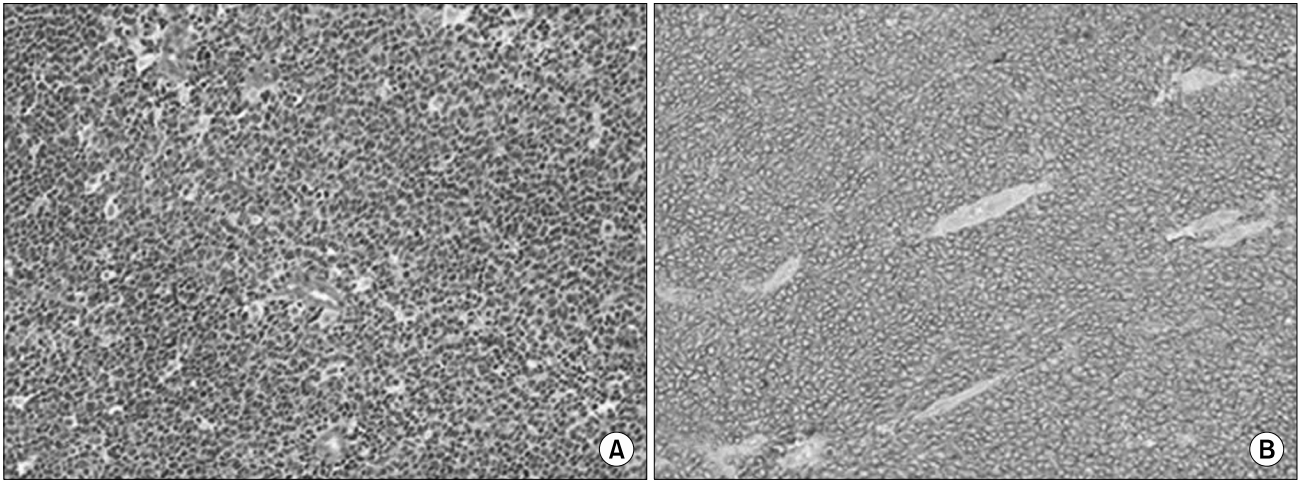


Fig. 3. (A) Hematoxylin and eosin-stained section of the tumor, which consists of highly proliferative, small, round cells (×200). (B) The tumor was strongly immunoreactive for CD99 (×200).

Advances in molecular diagnostics have allowed a highly specific diagnosis. Ewing's family of tumors is caused by chromosomal translocation $t(11;22)(q24;q12)$, which results in a hybrid gene product between the EWS gene located on the long arm of chromosome 22 and the FL-1 gene on the long arm of chromosome 11, which can be detected by reverse transcription polymerase chain reaction (RT-PCR) [3]. RT-PCR was not performed in this case because we had already diagnosed Ewing's sarcoma on the basis of the immunohistochemical staining results.

Extrasosseous Ewing's sarcoma is a curable disease. The disease-free survival rate has been significantly increased by managing these tumors with aggressive surgical resection in combination with multi-agent chemotherapy, with or without radiotherapy [7].

Currently, most protocols recommend surgical resection rather than radiation therapy if possible and reserve the use of postoperative radiation for positive margins or residual disease [8]. The 5-year disease-free survival rate is estimated to be 60% to 70% for localized disease managed with multi-agent chemotherapy and surgical resection [7].

In summary, we experienced a case of primary pulmonary Ewing's sarcoma. The patient underwent right upper lung lobectomy and postoperative chemoradiotherapy. She has exhibited no sign of recurrence to date; therefore, we report this as an outcome of the treatment of primary pulmonary

Ewing's sarcoma with surgical resection and combination therapy.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Shimada H, Newton WA Jr, Soule EH, Qualman SJ, Aoyama C, Maurer HM. *Pathologic features of extrasosseous Ewing's sarcoma: a report from the Intergroup Rhabdomyosarcoma Study*. Hum Pathol 1988;19:442-53.
2. Raney RB, Asmar L, Newton WA Jr, et al. *Ewing's sarcoma of soft tissues in childhood: a report from the Intergroup Rhabdomyosarcoma Study, 1972 to 1991*. J Clin Oncol 1997; 15:574-82.
3. Ichiki Y, Nagashima A, Chikaishi Y, Yasuda M, Yamamoto I, Toyoshima S. *Primary pulmonary Ewing's sarcoma: report of a case*. Surg Today 2012;42:812-5.
4. Lee YY, Kim DH, Lee JH, et al. *Primary pulmonary Ewing's sarcoma/primitive neuroectodermal tumor in a 67-year-old man*. J Korean Med Sci 2007;22 Suppl:S159-63.
5. Triche TJ, Askin FB. *Neuroblastoma and the differential diagnosis of small-, round-, blue-cell tumors*. Hum Pathol 1983;14:569-95.
6. Fellingner EJ, Garin-Chesa P, Triche TJ, Huvos AG, Rettig WJ. *Immunohistochemical analysis of Ewing's sarcoma cell*

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surface antigen p30/32MIC2. Am J Pathol 1991;139:317-25.

7. Hancorn K, Sharma A, Shackcloth M. *Primary extraskeletal Ewing's sarcoma of the lung*. Interact Cardiovasc Thorac

Surg 2010;10:803-4.

8. Zagar TM, Triche TJ, Kinsella TJ. *Extrasosseous Ewing's sarcoma: 25 years later*. J Clin Oncol 2008;26:4230-2.