Ewing’s sarcoma family tumors (ESFT) have been reported to originate in a variety of sites, most commonly in the extremities. We herein report a case of a primary ESFT of the lung presenting in an 8-year-old boy. A histological examination of hematoxylin–eosin stained sections showed a homogeneous population of closely packed small neoplastic cells. The tumor cells were strongly positive for CD99/MIC2 and negative for the leukocyte common antigen, myoglobin, desmin, epithelial membrane antigen, AE1/AE3 and synaptophysin. The patient was treated with neoadjuvant chemotherapy and surgery. Nine months later, he is in good condition and chest CT scans have revealed no evidence of either local recurrence or distant metastasis. Cases of ESFT of the lung have been reported in recent years but there are still few reports of primary ESFT of the lung. To date, only eight cases of ESFT of the lung have been reported in the literature. This is the first report of an ESFT of the lung occurring in a patient under 10 years of age. The clinical course and therapeutic management of ESFT are also discussed.

Key words: Ewing’s sarcoma – lung – MIC2

INTRODUCTION

Ewing’s sarcoma family tumors (ESFT), which comprises Ewing sarcoma of the bone and primitive neuroectodermal tumors, is the second most common type of malignant bone tumor occurring in children and young adults, and it accounts for 10–15% of all primary bone tumors, following osteosarcoma (1). The annual incidence is estimated to be 0.6 per million population (2).

Most ESFT occur in the bone. As opposed to osteosarcoma, flat bones of the axial skeleton are more commonly affected, while in long bones, ESFT tend to arise from the diaphysis rather than the metaphysis. ESFT can affect any bone but the most common sites are the lower extremities (3).

Histologically, ESFT is a malignant, small, round-cell tumor. A classification scheme has been proposed for the differential diagnosis of ESFT based on the recognition of neural differentiation and characterized by the presence of Homer wright rosettes and/or immunohistochemically by the expression of at least two different neural markers (4). In addition, the glycoprotein p30/32 (CD99), which is encoded by the MIC2 gene, is strongly expressed on the surface of the tumor cells (5,6).

The identification of a non-random t(11;22)(q24;q12) chromosome rearrangement has been recently reported (7,8) in these aggressive malignant tumors, and this is considered to be strong evidence for their common histogenesis, while it is also a valuable characteristic that is useful in making a differential diagnosis from other small round cell tumors occurring in childhood and adolescence.

Cases of ESFT of the lung have been reported in recent years but there are very still few reports of primary pulmonary ESFT. To date, only eight cases of ESFT of the lung have been reported in the literature. Both the clinical course and the therapeutic management of this disease are discussed.
CASE REPORT

An 8-year-old boy was admitted to a regional hospital because of a low-grade fever and non-productive cough. His past and family history were noncontributory. The findings of physical and laboratory examinations on admission were normal with no evidence of lymphadenopathy, but a chest X-ray demonstrated a large consolidation in the right lung (Fig. 1). A computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed a contrast-enhancing mass lesion in his right upper lobe of the lung (Fig. 2). The patient underwent a needle biopsy which revealed a proliferation of malignant small, round cells. As a result, he was transferred to our hospital to receive further treatment. A histological examination of hematoxylin–eosin stained sections showed a homogeneous population of closely packed small neoplastic cells with fibrovascular stroma. Most of the individual cells had scanty cytoplasm and round or oval nuclei with fine powdery chromatin (Fig. 3). A panel of immunohistochemical staining was performed. The tumor cells were strongly positive for CD99/MIC2 (Fig. 3) and negative for leukocyte common antigen, myoglobin, desmin, epithelial membrane antigen, AE1/AE3 and synaptophysin. CD99/MIC2 stain exhibited strong membranous staining. The histological and immunohistochemical findings were compatible with ESFT. We could not perform reverse transcriptase-polymerase chain reaction to detect EWS associated chimeric mRNA, such as EWS-FLI1, because the biopsied specimen was too small to do so. The patient thereafter underwent abdominal, pelvic and cervical CT, a whole body technetium bone scan, a gallium scan and a bone marrow biopsy, in addition to chest CT. As a result, neither any evidence of another tumor that could be associated with the primary site nor distant metastasis was observed.

After making the diagnosis, the patient was treated with neoadjuvant and adjuvant chemotherapy, including ifosfamide, etoposide, vincristine, doxorubicin and cyclophosphamide, and surgery. The histological examination of the resected specimen after chemotherapy revealed an

Figure 1. Chest X-ray film showing a relatively circumscribed mass in the right lung.

Figure 2. Computed tomography (A) and magnetic resonance imaging (B, C) demonstrate a lobulated mass confined to the lung parenchyma.
incomplete disappearance of the tumor cells (Fig. 4). Nine months later, after surgery, he is in good condition and chest CT scans reveal no evidence of recurrence.

DISCUSSION

The ESFT is an uncommon malignant neoplasm. The family shares a common histological feature of closely packed small primitive round cells. ESFT most frequently arise in the bones followed by the soft tissue, but they have also rarely been reported at other sites, such as the ovaries, uterus, kidney, pancreas, colon, hard palate and lung (9–20). The morphological features of the present intrapulmonary tumors were closely similar to those of ESFT observed at a variety of other locations.

The histologic differential diagnoses comprised other small, round cell malignancies, including malignant lymphoma, embryonal rhabdomyosarcoma and neuroblastoma. Immunohistochemical and histochemical staining positive for glycogen (PAS, 80%), neuron-specific enolase (60%), S-100 protein (50%) and MIC-2 marker (90%) as well as negative findings for leukocyte common antigen, epithelial membrane antigen, cytokeratin, desmin, vimentin, myoglobin and glial fibrillary acidic protein all indicate a diagnosis of Ewing sarcoma (21). In our case, both the histological and immunohistochemical findings were compatible with ESFT, whereas a genetic analysis could not be performed due to the insufficient amount of the biopsy specimen.

In this report, we describe a primary ESFT of the lung, bringing the total number of reported ESFT described at this site to nine cases, including the present one. The clinical features of these cases are summarized in Table 1. The median age was 27.6 (8–64) years, including six males. Four out of nine cases occurred in adolescents.

They were treated with various combinations of surgery, chemotherapy and radiation therapy. Of the seven patients with a follow-up, three were treated with surgery and chemotherapy and are still alive without disease at 16 months, 22 months and 2 years, respectively, after surgery. On the other hand, two patients treated by surgery died due to widespread metastatic disease 2 years after the operation. Based on this small number of cases, ESFT of the lung is thus considered to be an aggressive neoplasm that has a clinical course similar to ESFT occurring in other organs. In general, patients who present with metastases at diagnosis have a 5-year survival rate of 20–30%. The treatment of choice is an early surgical removal with intensive chemotherapy and radiation therapy to ablate any residual microscopic disease.

In summary, we herein described an extremely rare case of ESFT of the lung which demonstrated immunoreactivity to the MIC2 gene product. This is the first report of an ESFT
of the lung occurring in a patient under 10 years of age. In addition, we also reviewed the eight cases of primary ESFT of the lung previously reported in the literature along with the present case. The optimal treatment of primary ESFT of the lung has not yet been clearly established. Adjuvant and/or neoadjuvant chemotherapy may thus be able to improve the treatment results in the future.

**Conflict of interest statement**

None declared.

**References**


**Table 1.** Previous reports of primary Ewing sarcoma family of tumors of the lung

<table>
<thead>
<tr>
<th>Reference</th>
<th>Year</th>
<th>Age</th>
<th>Gender</th>
<th>Metastasis at diagnosis</th>
<th>Treatment</th>
<th>Follow-up</th>
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<tr>
<td>Hammer et al.</td>
<td>1989</td>
<td>64</td>
<td>M</td>
<td>?</td>
<td>Ope/Chemo/RT</td>
<td>NE</td>
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<tr>
<td>Catalan et al.</td>
<td>1997</td>
<td>29</td>
<td>M</td>
<td>Multiple pulmonary nodules</td>
<td>Ope/Chemo</td>
<td>NE</td>
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<td>Tsuji et al.</td>
<td>1998</td>
<td>25</td>
<td>F</td>
<td>None</td>
<td>Ope</td>
<td>DOD, 2 years</td>
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<tr>
<td>Imamura et al.</td>
<td>2000</td>
<td>41</td>
<td>M</td>
<td>None</td>
<td>Ope/Chemo</td>
<td>NED, 22 months</td>
</tr>
<tr>
<td>Kahn et al.</td>
<td>2001</td>
<td>18</td>
<td>M</td>
<td>None</td>
<td>Ope</td>
<td>DOD, 2 years</td>
</tr>
<tr>
<td>Mikami et al.</td>
<td>2001</td>
<td>18</td>
<td>F</td>
<td>?</td>
<td>Ope/Chemo/RT</td>
<td>DOD, 3 months</td>
</tr>
<tr>
<td>Present case</td>
<td>2006</td>
<td>8</td>
<td>M</td>
<td>None</td>
<td>Ope</td>
<td>NED, 8 months</td>
</tr>
</tbody>
</table>

Ope, operation; chemo, chemotherapy; RT, radiotherapy; NE, not evaluable; DOD, dead of diseases; NED, no evidence of disease.