Extraskeletal Ewing Sarcoma of the Diaphragm Presenting With Hemothorax

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Ewing sarcoma is a relatively uncommon malignant bone neoplasm that usually occurs in children and young adults and involves the major long bones, pelvis, and ribs. Primary diaphragmatic Ewing sarcoma is extremely rare. To the best of our knowledge, only three cases of primary Ewing sarcoma of the diaphragm have been reported. A 12-year-old girl presented spontaneous occurrences of the right hemothorax. After drainage, a roentgenogram film, computed tomography, ultrasonography, and magnetic resonance image showed a giant mass on the right diaphragm. Primary diaphragmatic tumor was resected totally by right posterolateral thoracotomy, and histologically, an extraskeletal Ewing sarcoma was identified. The patient received adjuvant radiochemotherapy, and there was no evidence of disease 10 months after the operation. Although extremely rare, extraskeletal Ewing sarcoma should be kept in mind in the differential diagnosis of diaphragmatic soft tissue tumors.

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Extraskeletal Ewing sarcoma (EES) is simply Ewing sarcoma arising in soft tissues, which is now regarded as a member of the family of small, round cell neoplasms of bone and soft tissue, including primitive neuroectodermal tumor and neuroblastoma. The most frequent sites of occurrence are the chest wall, lower extremities, and paravertebral region. Less frequently, the tumor occurs in the pelvis and hip region, the retroperitoneum, and the upper extremities [1]. It occurs predominantly in adolescents and young adults between the ages of 10 and 30 years [1]. Extraskeletal Ewing sarcoma of the diaphragm presenting with hemothorax has not been reported until now. We describe a case of primary diaphragmatic Ewing sarcoma and its clinic, radiologic, and histopathologic findings.

A 12-year-old girl presented with dyspnea for 1 month. On admission, physical examination revealed decreased breath sounds in her right chest. Heart rate was 106 beats per minute, blood pressure was 100/70 mm Hg, and temperature was 37.1°C. Laboratory studies revealed a hemoglobin level of 10.8 g/dL and a platelet count of 360.000/mL. A chest radiograph showed a right pleural effusion (Fig 1A). Thoracentesis was performed and noncoagulated bloody fluid, with a hematocrit of 28%, was removed. No tumor cells were present. Gram stain of the fluid sediment showed no microorganisms, and cultures for bacteria and fungi produced no growth. A right intercostal drain was inserted and 1,600 mL of blood was evacuated. A computed tomography (CT) scan of the thorax after drainage showed a 9 × 6 × 5-cm solid extraparenchymal mass in the right recessus costodiaphragmaticus and a large pleural effusion (Fig 1B). Magnetic resonance imaging (Fig 1C) showed an extensive lesion, with the largest diameter of 10 cm, at the base of the right hemithorax compressing the liver and extending to the right thoracic wall. A CT scan–guided tru-cut biopsy was performed. The histology was quite characteristic of Ewing sarcoma.

At thoracotomy, the pleura-covered tumor was found completely apart from the liver and lung. Further exploration showed the tumor to be fixed to the diaphragm. A hard mass, 9 × 6 × 5 cm, arising from the right diaphragm had invaded the seventh, eighth, and ninth ribs and pleura, and no invasion of the liver was found. Because of the extent of the lesion, the main tumor, seventh, eighth, and ninth ribs, and right diaphragmatic muscle partially were resected. The diaphragmatic and thorax wall defects were closed with a Prolene patch (Fig 2A).

Microscopically, the lesion was composed of sheets of fairly uniform round-to-oval cells. The cytoplasm was relatively clear and indistinct, but contained large quantities of periodic acid-Schiff (PAS)-positive, diastase-digestible material, indicating high concentrations of glycogen (not shown). The tumor cells showed diffuse, intense membrane reactivity for CD99 (MIC 2) on immunohistochemical staining. The diagnosis was thus EES. The margins of resection were free of tumor and the following staging examinations showed no evidence of metastatic disease.

The postoperative course was uneventful, and the patient was discharged from the hospital on the 9th postoperative day. One month after discharge, chemoradiotherapy was carried out. Our patient received MAID (mesna, doxorubicin, ifosfamide, and dacarbazine) chemotherapy postoperatively, and the patient has had no recurrence of disease within 10 months of follow-up (Fig 2B).

Comment

Primary tumors of the diaphragm are rare. They can occur at any age but most cases occur in the fourth and fifth decades of life. Primary tumors may be benign or malignant. The most recent summary was published in 1998 and describes 106 cases, including cysts, benign neoplasms, and malign tumors [2]. Benign tumors are

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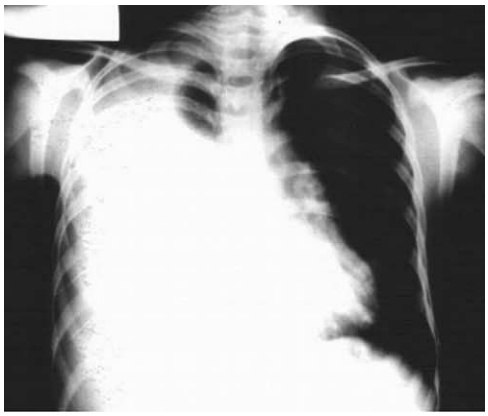

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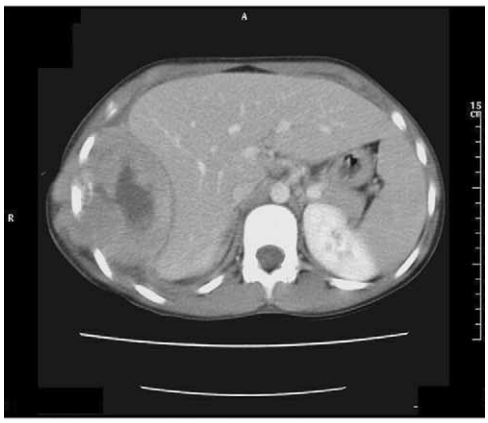

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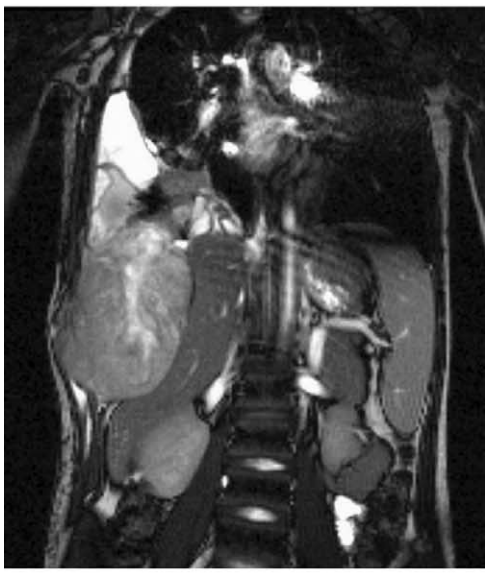
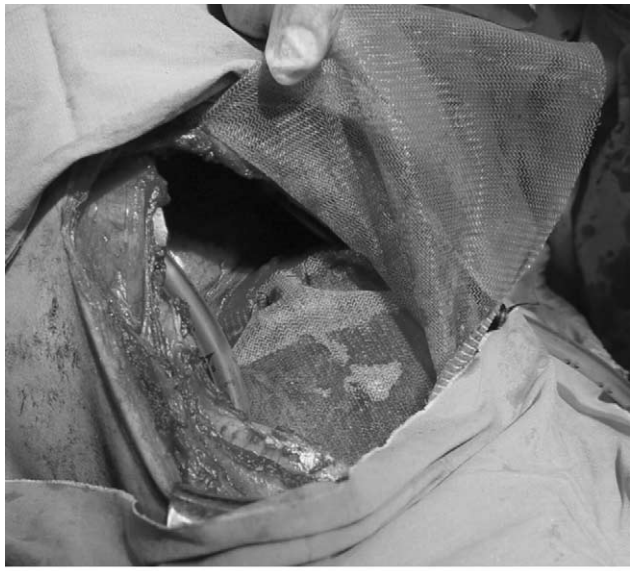


C

Fig 1. (A) Chest radiograph showed pleural effusion on the right hemithorax. (B) Contrast-enhanced thorax computed tomography scan showed an extrahepatic localization of the mass with compression of adjacent liver parenchyma and a centrally located area of necrosis. (C) Coronal T_2-weighted magnetic resonance imaging scan revealing an extrahepatic mass, growing from the diaphragm towards the thorax wall. The tumor compresses the liver parenchyma, which is indicated by the rounded edges of the liver adjacent to the tumor.



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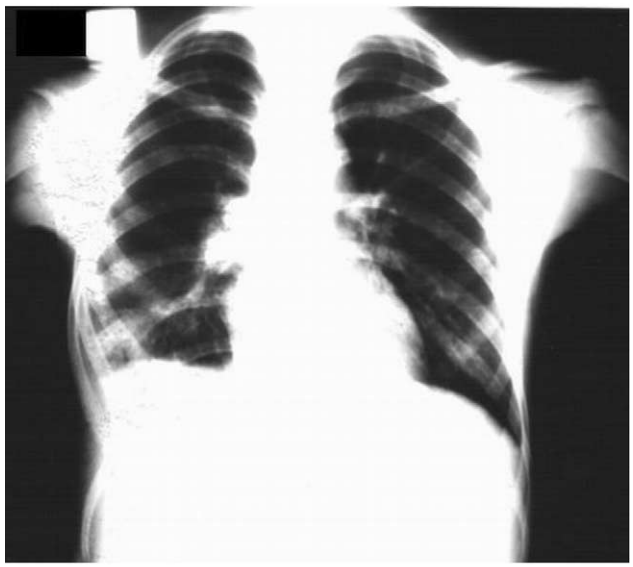

B

Fig 2. (A) The reconstruction of diaphragm and thorax wall defects with Prolene patch. (B) Chest radiograph after 10 months operation.

somewhat more frequent than malignant tumors, with fibrosarcoma being the most common malignant tumor. In a study of 71 primary tumors of the diaphragm, only five affected children below 15 years of age [3].

Sarcomas with diaphragmatic origin are extraordinarily rare in pediatric patients, with fibrosarcoma, rhabdomyosarcoma, and leiomyosarcoma representing the majority of cases. Raney and associates published a comprehensive review of soft tissue sarcomas arising in the diaphragm, which comprised 15 cases, three of which were EES [4]. The largest series of Ewing sarcoma originating from soft tissues was composed of 130 cases recorded from 1972 to 1991 [5]; all of the patients were aged less than 21 years. To the best of our knowledge,

only 3 patients with primary Ewing's sarcoma of the diaphragm have been reported [4], of whom, only 2 were children (aged 15 years; the third was 20 years old). Our patient is the youngest so far.

Almost 20% of patients with diaphragmatic tumors may be asymptomatic. Respiratory symptoms may include chest pain, cough, and dyspnea. Gastrointestinal symptoms are caused by left-sided tumors, which compress the gastric cardia and lead to anorexia, nausea, vomiting, and difficulty swallowing. Physical examination may reveal an abdominal or a chest wall mass, atelectasis, or pleural effusion. Our case presented with progressively increasing dyspnea due to right hemothorax. Diaphragmatic tumors presenting with hemothorax have not been published previously.

A certain preoperative discrimination of diaphragmatic tumors from other thoracic and abdominal neoplasms is difficult [6]. Sometimes, a typical diaphragmatic "hump" may be observed [6]. The sharp border to the liver and the close relation to the diaphragm in the upper parts of the neoplasm may lead to the suspicion of a primary diaphragmatic neoplasm, but these signs are also possible in other large abdominal or retroperitoneal lesions. Radiographs may show irregularity of the diaphragm [3]. The frequent occurrence of the normal variant of diaphragmatic lobulation, localized diaphragmatic eventration, and juxtadiaphragmatic abnormalities causing irregular diaphragmatic contour make discovery of diaphragmatic tumors difficult on plain radiographs. Tumors of the diaphragm may be difficult to differentiate from liver lesions in diagnostic imaging when located at the border of the liver. In the case presented, the MRI was the diagnostic tool showing precisely the rounded edges of the liver at the lateral margins of the lesion, indicating the growth of the depicted tumor from extrahepatic towards the liver with compression of liver parenchyma.

Ewing's sarcoma commonly arises from skeletal bone, but rarely may have an extraskeletal origin. Extraskeletal Ewing sarcoma can be confused with other small, round, blue cell tumors, including embryonal rhabdomyosarcoma, lymphoma, and neuroblastoma. This tumor shares histologic, immunohistochemical, and molecular findings with Ewing sarcoma of bone [7]. The classic histologic description of EES is of a tumor composed of small, uniform, round or oval cells in solid sheets divided by fibrous strands. Its cytoplasm is scanty, pale staining, and vacuolated because of the presence of glycogen, and the nuclei are round with "salt and pepper" chromatin and small nucleoli. Because no skeletal involvement was demonstrable in the present case, the diaphragm was considered the origin of this tumor. A sensitive and relatively specific antigen, CD99/MIC2, and a characteristic chromosomal translocation, t (11, 22)(q24; 12), have been identified in skeletal Ewing's sarcoma and EES [7].

The treatment of EES is aggressive because most patients with Ewing sarcoma die 2 or 3 years after diagnosis. The most effective treatment is surgery with combination chemotherapy and high-dose radiation therapy. When resectable, the surgical excision must be wide in accordance with the classic oncologic principles. The defect may be repaired by direct approximation of diaphragmatic edges, or this may require prosthetic repair of the diaphragm. Adjuvant chemotherapy and radiation have been used with variable results. When the tumor is unresectable, preoperative chemotherapy to cause complete or partial reduction of tumor is tried. Three prior cases with diaphragmatic EES [4] had been treated with debulking and postoperative radiotherapy and conbination chemotherapy with vincristine, actinomycin D, and cyclophosphamide and one additional doxorubicin. One patient survived more than 10 years and the other patients survived 2 years. In our patient, MRI and CT indicated the site of origin of the abdominal tumor, which was found resectable at thoracotomy. Our patient was treated successfully with surgery and multiple-agent, long-range chemotherapy, and high-dose radiation therapy, and there has been no recurrence during 10 months of follow-up. Survival has improved significantly in recent years, and current relapse-free survival is 55% at 5 years [8].

Extraskeletal Ewing sarcoma is a rare tumor and sensitive to multimodality treatment. Early surgical treatment followed by chemo- and radiotherapy has greatly improved the prognosis of this entity.

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