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A primary Ewing's sarcoma of pleura: Case report and literature review

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ABSTRACT

Ewing's sarcoma was first reported by J.Ewing in 1921, which is generally originated from soft tissue of the trunk or limbs. Primary Extraskeletal Ewing sarcoma (EES) of pleura is an uncommon condition, which is challenging to diagnose, and rarely reported. Herein, we present a previously 14-year-old male patient with fever and dyspnea for 1 month presented to the department of respiratory medicine in Binzhou Medical University Hospital. Radiology revealed a soft mass with massive pleural effusion in the right side of pleural cavity. After admission, we performed the transthoracic catheter drainage for the patient, followed by thoracoscopy and biopsy. Histopathology revealed a small round cell malignant tumor, combined with immunohistochemistry assay and the Fluorescence in-situ hybridization (FISH) detection of EWSR1 gene arrangement, Ewing's sarcoma was finally diagnosed. Despite receiving chemo- and radiotherapy, the patient died 1 year later after diagnosis. This paper reports a rare case that originated in parietal pleura with massive pleural effusion of Ewing's sarcoma, which was not previously reported. This rare tumor and its unusual clinical manifestations prompt us to report the current case.

1. Introduction

Ewing's sarcoma was first reported by J.Ewing in 1921, which is generally originated from soft tissue of the trunk or limbs. It is the second most malignant bone tumors in children [1]. EES was first reported by Tefft et al., in 1969 [2], it has been considered as a solitary solid tumor and is extremely rare. It mostly occur in the chest wall, paravertebral area, and lower limbs. EES has also been reported in the pelvis, buttocks, upper limbs, mediastinum, and abdominal organs [3]. This paper reports a rare case that originated in parietal pleura with massive pleural effusion of Ewing's sarcoma, which has never been reported in the previous literatures, and also reviews the literatures to further improve the understanding of EES.

2. Case presentation

A 14-year-old male patient complaining of fever and dyspnea for 1 month was admitted to Binzhou Medical University Hospital on October 13, 2019. The right lung auscultation showed breath sound disappeared, and trachea shifted to the left. Subsequently, we performed thoracic computed tomography (CT) scan for the patient, which showed a huge mass in the right chest with pleural effusion; there were no signs of adjacent bone destruction and mass calcification (Fig. 1). First, transcatheter thoracic drainage was carried out for the patients to determine the features of the pleural effusion, and routine examination showed hemorrhagic exudative pleural effusion with no malignant tumor cells.

Then, the patient underwent thoracoscopic examination, a large amount of bloody effusion was found, a solid mass with nodular appearance was located in the parietal pleura, and multiple metastatic solid nodules were distributed at the lateral wall of the parietal pleura with visceral pleura involvement (Fig. 2a–c). Thoracoscopic biopsy of multiple lesions was conducted (Fig. 2d). After operation, the patient received chest chest contrast-enhanced CT to describe the characteristics of pulmonary lesions (Fig. 3).

Histopathological examination confirmed a small round cell malignant tumor of pleura (Fig. 4). Immunohistochemical staining showed diffuse membranous CD99 positive cells (Fig. 5), which is of diagnostic significance for Ewing's sarcoma and primitive neuroectodermal tumor [4], followed by a FISH image of specimens confirmed the rearrangement of the 22q12 (EWSR1 gene), a potent and reliable auxiliary technology for the EES diagnosis [5]. The whole-body bone scan and abdominal ultrasound examination showed no abnormal lesions. Based

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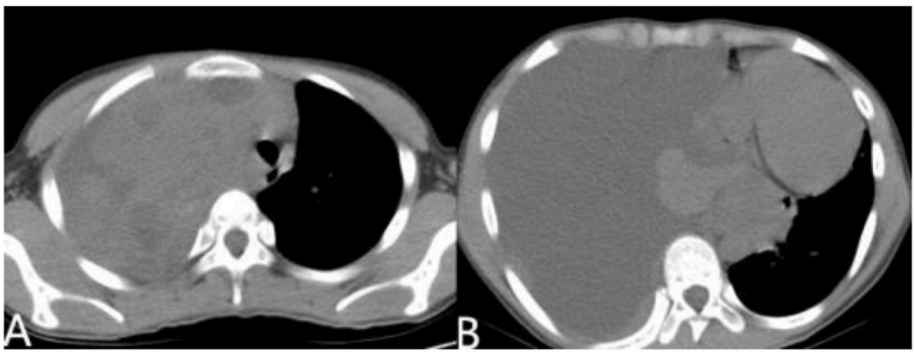

Fig. 1. Chest CT confirmed a huge mass (**a**) in the right chest and pleural effusion (**b**).

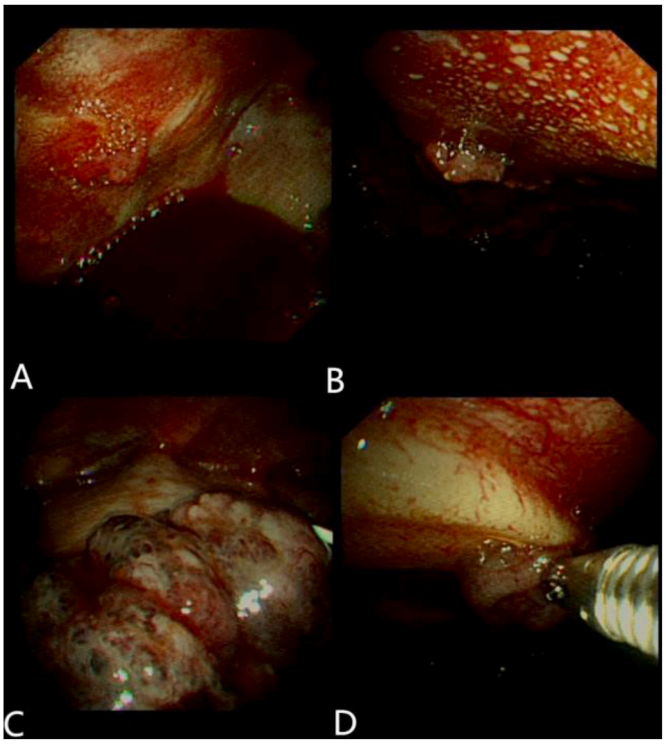

Fig. 2. Thoracoscopy and biopsy of the patient: **a** A large amount of bloody effusion was found; **b** A solid mass with nodular appearance and multiple metastatic solid nodules were distributed on the parietal pleura; **c** Multiple small nodules at the visceral pleura were also detected; **d** Thoracoscopic biopsy of multiple lesions were conducted.

on the above results, the patient was finally diagnosed as EES of pleura.

Given the large volume of the patient's mass and multiple pleural metastases, the current patient received radio- and chemotherapy (alternating regimens of vincristine, adriamycin, cyclophosphamide, ifosfamide and etoposide); unfortunately, the treatment effect was limited, and the patient died after 1 year.

3. Discussion

3.1. Clinical discussion

EES is considered a rare entity and has not been widely reported, but it is an essential factor for differential diagnosis considering the poor prognosis. This diagnosis should be considered when patients, especially children or adolescents, have unclear margins, uneven intrathoracic masses, and no primary bone lesions.

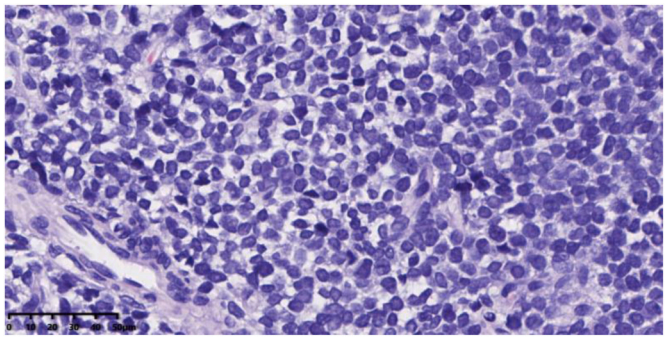

Fig. 4. Histopathological characteristics of the patient: pleomorphic tumor cells with scanty cytoplasm and hyperchromatic nuclei (hematoxylin and eosin, magnification × 40).

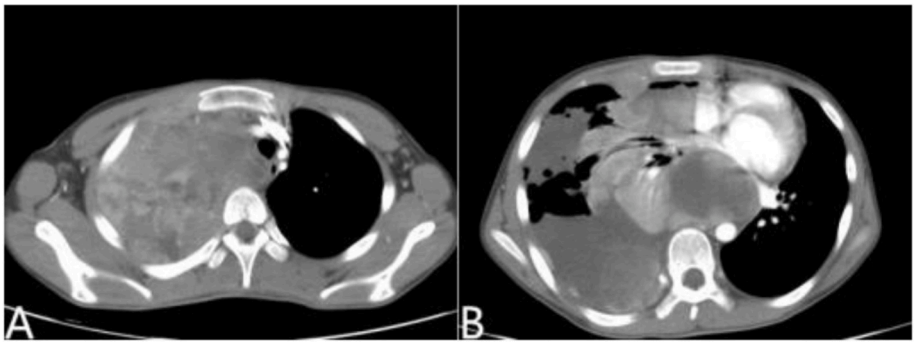

Fig. 3. Chest contrast-enhanced CT confirmed a huge heterogeneous mass (**a**) in the right chest and pleural effusion (**b**).

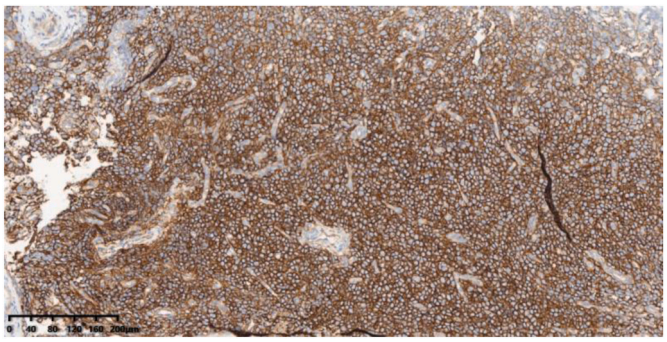

Fig. 5. Immunohistochemical staining: the neoplasm was stained with antibody to CD99.

3.2. Imaging discussion

EES adjacent to bone can show osteolytic bone destruction on X-ray, generally without osteosclerosis and periosteal reaction, and lack of onion skin-like X-ray changes (periosteal reaction or reflective needle bone) unique to bone Ewing's sarcoma.

CT showed soft tissue density masses in different sites with necrotic cystic areas and mild heterogeneous enhancement after contrast medium. Despite the lack of characteristics, CT showed the location, size, and internal tissue structure of the tumor, which is of great importance in evaluating the feasibility of tumor resection and formulating the treatment plan.

18-Fluorodeoxyglucose positron emission tomography showed that Ewing sarcoma of the lung often showed large volume, smooth edge, and high fluorodeoxyglucose uptake [4]. In addition, it can also be used as a tool for initial staging, efficacy evaluation, and recurrence detection and help to exclude the possibility of secondary extrapulmonary Ewing sarcoma [6].

Due to the lack of specificity in clinical manifestations and imaging examination, the diagnosis is challenging and easy to be misdiagnosed. Therefore, the final diagnosis must depend on pathological examination.

3.3. Brief review of literature

Using "intraporacic tumor, extra skeletal ewing sarcoma, pleural effusion" as the keywords, we have searched the literatures about related topics published in PubMed and Excerpta Medica Database in recent 10 years, the results showed a total of merely 5 cases of EES with pleural effusion in PubMed and Excerpta Medica database [7–11] (Table 1). All 5 cases were young patients, including 2 males and 3 females. The average age was 16.6 years, with the youngest 7 years old and the oldest 21 years old. Almost every individual complained of chest pain and dyspnea as the primary symptoms. In terms of diagnostic methods, one case was diagnosed by thoracoscopy [9], and the others were diagnosed with the help of pleural biopsy. One case of pleural effusion was caused by pleural metastasis of Ewing's sarcoma of the ribs [10], and the others were diagnosed as primary Ewing's sarcoma of the pleura. Our patient is the second case of primary Ewing's sarcoma of pleura confirmed by thoracoscopy, unlike the first case, the primary site originated from parietal pleura, and multiple metastases of visceral and diaphragmatic pleura were also observed during operation, suggesting a very poor prognosis.

Ewing sarcoma family tumors are an entity composite of malignant small round blue cell tumors with different degrees of neuroectodermal differentiation [12], including Ewing sarcoma of bone, EES, peripheral primitive neuroectodermal tumor and Askin tumor [13]. EES accounts for 1.1% of soft tissue malignant tumors, with common pathology, gene phenotype, and chromosome translocation with bone Ewing sarcoma and primitive neuroectodermal tumors. At present, it is considered that they all originate from the neuroectoderm and belong to the family of peripheral primitive neuroectodermal tumors. Translocation chromosome t (11; 22) (q24; q12) and the positive expression of CD 99 can distinguish it from the other small round cell tumors [14].

3.4. Pathologic discussion

The diagnosis of EES is mainly based on histopathology and immunohistochemistry of tumor specimens. Under a light microscope, the tumor cells are small and round, uniform in size with a round to oval in the nucleus, and sparse in the cytoplasm. Tumor cells are arranged in flakes or lobules, which are separated by vascular fibrous tissues. Under an electron microscope, there are few organelles and abundant glycogen granules in the cytoplasm. Immunohistochemical staining of CD99 shows tumor cells with positive diffuse membrane, which is a typical manifestation of Ewing's sarcoma. The immunohistochemical staining for S-100 protein, neurofilament protein, GFAP, desmin, F8, UEA-1, and keratin is negative. Finally, Ewing sarcoma can be diagnosed by detecting the rearrangement of EWS gene and related oncogene [15].

4. Conclusions

Considering that EES is a highly invasive malignant tumor, the most effective treatment is surgical resection combined with postoperative chemotherapy and high-dose radiotherapy [16]. Complete tumor resection is the first treatment to be considered as long as there is no clear surgical contraindication. It has also been proved that preoperative chemotherapy with vincristine, adriamycin, cyclophosphamide, and etoposide combined with surgery can significantly improve the prognosis of patients.

This report presents a rare case of primary pleural Ewing's sarcoma, which is characterized by a large number of pleural effusions. Previous literature showed that the incidence rate of EES is very low, and it has a high degree of malignancy and poor prognosis. There are few reports and reference experiences on the disease; thus it leads to insufficient

Table 1
Pleural Ewing's sarcoma with massive effusion.

First author	Publication date	Age (y)	Gender	Country	primary site	clinical manifestation	Diagnosis method	therapy	outcome
Gerald Wolf	2002	17	Male	Austria	Pleura	Chest pain dyspnea	Biopsy	NS	NS
Cengiz Ozge	2004	18	Female	Turkey	Pleura	Back pain cough dyspnea	Pleural needle biopsy	NS	NS
Karatziou C	2011	21	Female	Greece	Left visceral pleura	Fever productive cough sternal pain	Thoracoscopy and biopsy	Chemo-therapy	NS
Kushwaha	2011	20	Female	India	Left 7th rib	Fever Chest pain dyspnea	Transthoracic needle biopsy and pleural biopsy with cope needle	Chemo-therapy	Follow up
Denny Mathew	2019	7	Male	South Africa	Pleura	Dyspnea	Biopsy of the mass	Chemo-therapy	NS

NS: not stated.

clinical understanding. According to routine diagnosis and treatment processes after admission, this patient also missed the opportunity of early diagnosis and radical operation. Moreover, the diagnosis of the disease needs to be discussed and analyzed jointly with radiologists, pathologists, thoracic experts and oncologists to prevent misdiagnosis and inaccurate diagnosis of the disease.

Ethical approval statement

Written informed consent was obtained from the patient. Ethics committee approval was not necessary for this case report because it does not constitute research where it was conducted.

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Authors' contributions

Conceptualization: Xuexue Zou, Hengxing Gao. Data curation: Wenli Chang. Supervision: Hengxing Gao.Writing-original draft: Xuexue Zou. Writing-review & editing: Hengxing Gao.

Declaration of competing interests

The authors declare that they have no competing interests.

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