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Primary pulmonary Ewing sarcoma: a rare case report

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ABSTRACT

Ewing sarcoma (ES) is a malignant soft tissue tumor that consists of undifferentiated neuroectodermal cells. The anatomical sites of ES are commonly the pelvis and long bones. Metastasis is the cause of the most prevalent pulmonary ES. The primary lung origin of ES is extremely uncommon. Here, we report a rare case of primary pulmonary ES diagnosed from cytology and biopsy material. A chest X-ray revealed a lesion with a 9×7.5 cm diameter in the pericardiac area of the right lung. Clinical and radiological examinations (computed tomography and positron emission tomography) demonstrated that the lesion was a primary lesion. No distant metastasis was detected. Bronchoscopy-guided fine-needle aspiration and cytological analysis of the lesion revealed uniformly shaped small round cell morphology. Immunohistochemistry performed on the cell block produced positive results for CD99 and FLI-1. These immunohistochemical findings support the ES diagnosis.
Keywords: Ewing sarcoma, primary pulmonary Ewing sarcoma, fine-needle aspiration, cytopathology

Ewing sarcoma (ES) is a malignant small round cell tumor that is commonly localized to the diaphysis and metaphysis of long bones. Extra-bone localization of ES is less frequently observed [1-3]. The first case of primary ES of the lung was described by Hammar *et al*. [4] in 1989, and since then, less than 40 cases have been reported in the literature [5]. It features a distinctive immunophenotype that combines diffuse and membranous CD99 expression with FLI-1 nuclear positivity [6]. Due to its extreme rarity, similar presentation to other lung tumors, and nonspecific symptoms, primary pulmonary ES can be challenging to distinguish from other pulmonary tumors [7]. Based on our best literature reviews, this is a quite rare case of ES where the diagnosis was made on fine needle aspiration cytology (FNAC) and cell block, with immunohistochemistry (IHC) [3]. Here, we presented a case of primary pulmonary ES, emphasizing its diagnosis from cytology and cell block.

CASE PRESENTATION

A 48-year-old non-smoker male was admitted with a five-month history of dry cough and no contributory past or family history. He denied any history of fever and dyspnoea.

Direct chest radiography revealed radio-opaque irregular margins mass in the para-cardiac area of the right lung (Fig. 1A). The thoracic-computed tomography (CT) scan revealed a 9 × 7.5 cm hypodense lesion that extended from the perihilar segment to the medial segment of the right middle lobe of the lung and there no chest wall invasion was detected (Fig. 2).

After such radiography and CT findings, a bron-

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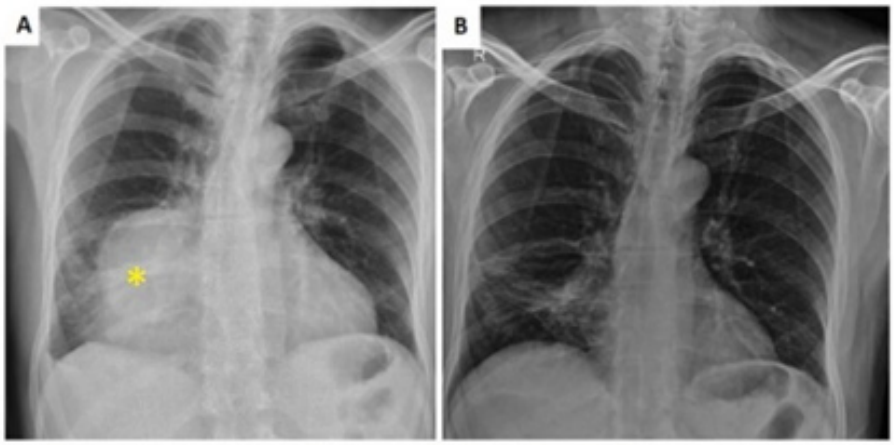

Fig. 1. **(A) A direct chest radiography revealed a radio-opaque mass in the pericardiac area of the right lung (asterisk). (B) After initiation of chemotherapy, a direct chest radiography demonstrated a response with only minimal residual disease.**

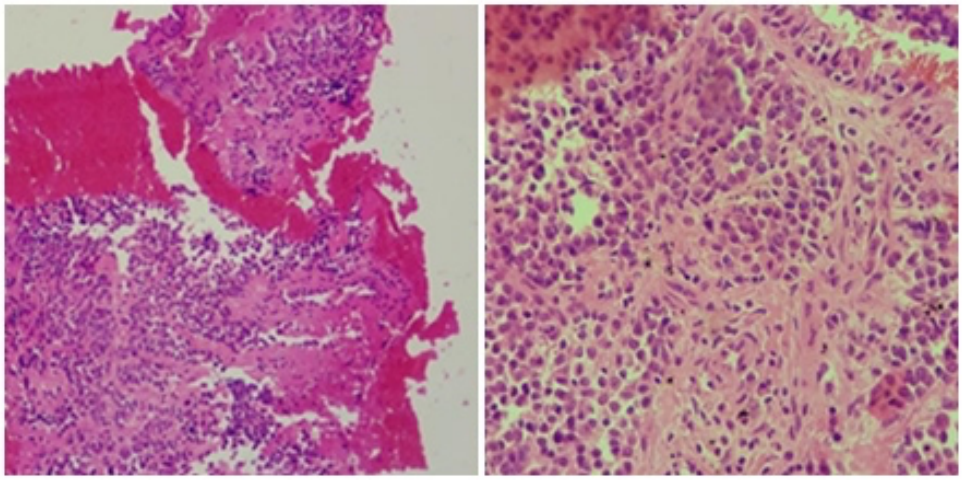

Fig. 3. **Cell block of the tumour (H&E) demonstrating atypical pleomorphic cell groups with small, round to oval nuclei and scant cytoplasm. There is respiratory epithelium in the right upper corner of the last picture. Magnification: 10× and 20×, respectively.**

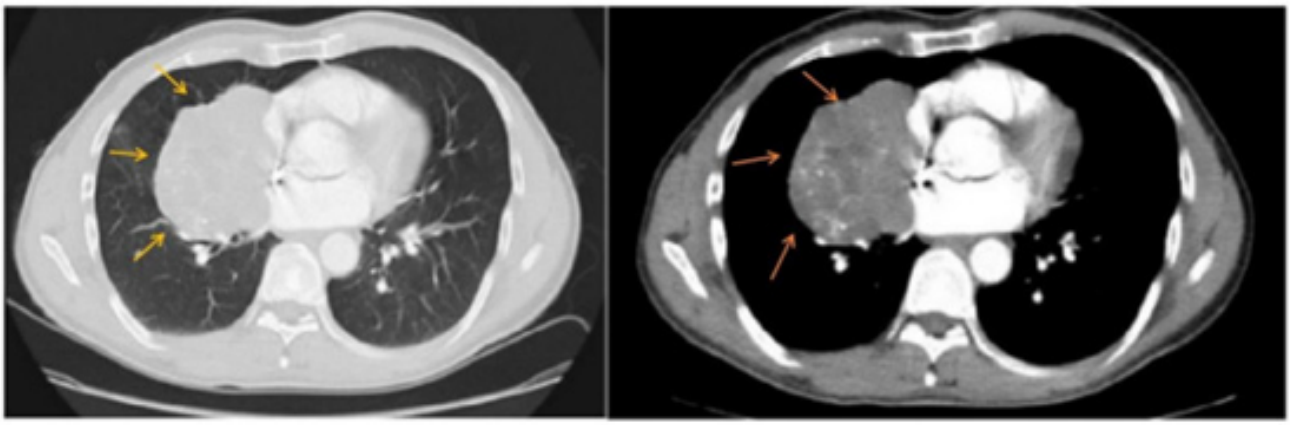

Fig. 2. **The thoracic-computed tomography (CT) scan revealed a 9 × 7.5 cm hypodense lesion that extended from the perihilar segment to the medial segment of the right middle lobe of the lung (arrows).**

choscopy detected that the middle lobe was almost completely occluded by a nodular infiltrative solid mass. From this location, FNAC, lavage, and forceps biopsy procedures were performed, and the smears were stained with hematoxylin-eosin (H&E). A cell block study was made with the remaining aspirate. The biopsy demonstrated a few atypical cells with enlargement and hyperchromatic oval nuclei with scant cytoplasm on the wide necrotic area. However, these biopsy sections were small and not diagnostic. FNAC and cell block showed atypical pleomorphic cell groups with small round to oval nuclei and scant cytoplasm was observed within the wide bleeding areas. A rosette-like pattern of arrangement was observed (Fig. 3).

Immunohistochemical analysis of the cell block revealed that the atypical cells were CD99 positive, FLI-1 focal nuclear positive, TTF-1 negative, pan CK negative, vimentin focal positive, Ki-67 positive, synaptophysin focal dot-like positive, LCA negative, CD56 negative, CD34 negative, and Melan-A negative (Figs. 4A-4F). Initial histological and immunohistochemical findings demonstrated that this was compatible with ES.

A new biopsy was attempted on the patient a month later. The repeated biopsy material was stained

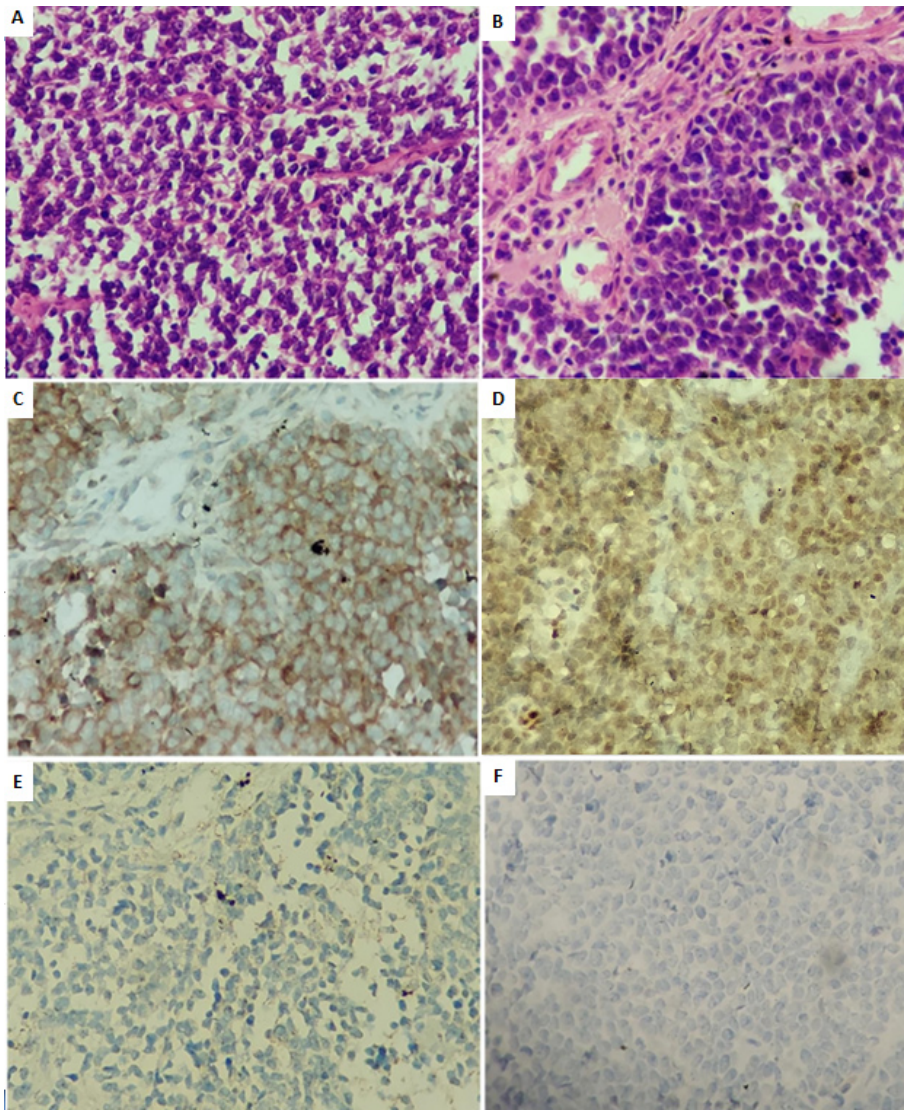

Fig. 4. (A, B) Cell block of the tumour (H&E). (C) Tumor cells showing diffuse membranous positivity for CD99. (D) Tumor cells showing focal nuclear FLI-1 positivity. (E) Immunohistochemical staining for pan CK showing negative staining. (F) Immunohistochemical staining for TTF-1 showing negative staining. Magnification: 20×, 20×, 40×, 40×, 40×, and 40×, respectively.

with H&E stains. A tumoral structure consisting of atypical cells with small round to ovoid cells, nuclear enlargement, hyperchromatic nuclei, and lots of mitotic figures was observed. A panel of IHC stains was performed; FLI1 diffuse nuclear positive, CD99 diffuse membranous positive which are characteristic findings of Ewing sarcomas, Ki-67 positive, TTF-1 negative, pan CK negative, S100 negative, synaptophysin negative, LCA negative. These findings were compatible with our previous definition of ES in the cell block and cytology material.

The patient thereafter underwent a positron emission tomography scan. As a result, neither evidence of another tumor that could be associated with the primary site nor distant metastasis was observed. The presence of any primary tumor in another focus was ruled out through radiological investigations. This confirmed the diagnosis of primary pulmonary ES. After the treatment plan, chemotherapy was initiated for the patient. After 2 months, a repeat of the chest X-ray showed a response with only minimal residual disease (Fig. 1B).

DISCUSSION

ES which were first described by James Ewing in 1921 is neuroectodermal tumors characterized by monotone small round cells arranged in sheets. ES is a rare sarcoma of bone and soft tissue and may involve any location. The most common anatomical sites of ES are the pelvis and long bones [2]. Metastasis is the cause of the most prevalent pulmonary ES. An extraskeletal primary source of this condition from the lung is extremely uncommon [1]. ES most often occurs in children and young adolescents [2].

In the differential diagnosis of pulmonary ES, small round cell malignant tumors, such as carcinoid, small cell carcinoma, desmoplastic small round cell tumor, malignant lymphoma, and poorly differentiated synovial sarcoma are included [8]. These neoplasms can be distinguished from other small round cell tumors in large part by the use of immunohistochemistry in combination with cytogenetics and molecular research [3]. On hematoxylin-eosin stain, diffuse sheets of small, round, blue cells with oval to round nuclei revealing finely dispersed chromatin and sparse, mildly eosinophilic or pale cytoplasm make up the typical histologic morphology of ES. The tumor is immunoreactive to CD99, FLI-1 [1]. In intractable cases, FLI-1 protein is more sensitive and specific and is convenient in confirming this diagnosis. Other markers (Chromogranin A, S-100 protein, CD56, Synaptophysin) are only rarely positive [9].

In this case, our patient had only a dry cough and a mass in the right lung on X-ray and CT imaging. FNAC and a cell block study showed atypical pleomorphic cell groups with small, round to oval nuclei and scant cytoplasm. When evaluating tumors with small round cell morphology presenting these histomorphological findings, ES should be included in the differential diagnosis.

To our current knowledge, extremely rare cases of ES are diagnosed by FNAC. Auxiliary tests are carried out on the cell block to establish a definitive diagnosis of ES. Most of the cases in the literature were diagnosed with tissue biopsies [3]. Here, we show that cytomorphology offers sufficient information and that IHC may be conducted on the cell block, raising the likelihood that the diagnosis is correct. We confirmed the diagnosis of ES with immunohistochemical studies performed on the rebiopsy material. After our diagnosis, the patient received chemotherapy and initially, most of his mass regressed without a surgical procedure.

CONCLUSION

Although primary pulmonary ES is a rare tumor, it should be considered in the differential diagnosis of pulmonary soft tissue tumors with small, round cell morphology. We reported a rare case of primary pulmonary ES with early detection from cytological material. This case emphasizes the importance of considering unusual differentials and the convenience of FNA with IHC techniques as the primary procedure in the diagnosis of such a rare case. With our diagnosis in the cytology material, the tumor largely regressed with chemotherapy without the need for surgery.

Authors' Contribution

Study Conception: N/A; Study Design: RA; Supervision: RA; Funding: N/A; Materials: HDT, ANT; Data Collection and/or Processing: HDT, ANT; Statistical Analysis and/or Data Interpretation: HDT,

ANT; Literature Review: HDT, ANT; Manuscript Preparation: RA, HDT, ANT and Critical Review: RA.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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