Case Report

A rare mediastinal tumour in a young male mimicking massive pleural effusion

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ABSTRACT

A 30-year-old male, carpenter by profession, presented with a history of dry cough and progressive shortness of breath for two months along with right-sided chest pain for one and a half months. The clinico-radiological picture was suggestive of right-sided massive pleural effusion. Computed tomography (CT) scan of the thorax showed a huge mediastinal mass occupying the entire right hemithorax with very small amount of pleural effusion. CT-guided fine needle aspiration cytology and tru-cut biopsy from the mass both revealed small round-cell tumour, possibly small cell carcinoma of the lung. However, on immunohistochemistry tumour cells expressed Mic-2 and it was consistent with a diagnosis of primitive neuroectodermal tumour.

KEY WORDS: Ewing's sarcoma, immunohistochemistry, mediastinal tumour, primitive neuroectodermal tumour

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INTRODUCTION

The Ewing's sarcoma/primitive neuroectodermal tumour (ES/PNET) family of tumours is part of a rare group of malignant neoplasms with small round-cell morphology. ES/PNET is an uncommon primary malignancy of the bone primarily affecting children and young adults with more than 80% of patients being younger than 20 years of age at the time of presentation.[1] Less frequently, ES/PNET arises from soft tissues and then the neoplasm is classified as extraskeletal ES/PNET. Involvement of the mediastinum as the primary site of origin is extremely uncommon in the literature, only four cases were reported in a span of 20 years in a large case series from a tertiary care centre in India.[2,3] A rare case of primary PNET tumour of the anterior mediastinum mimicking massive pleural effusion in a young male is reported here.

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CASE HISTORY

A 30-year-old male, carpenter by profession, presented with dry cough and progressive shortness of breath for two months, right-sided severe chest pain for one and half month and low-grade fever for one month. He had lost two kilograms of weight in the last one month. The patient was a non-smoker, non-alcoholic and non-diabetic. There was no history of similar illness in the family. General examination revealed pallor and raised but non-pulsatile jugular venous pressure. Clubbing was absent and there was no peripheral lymphadenopathy.

On examination of the respiratory system features of right hemithoracic volume enlargement were present. Mediastinum (both upper and lower) was grossly shifted to the contralateral side. Percussion note was dull all over the right hemithorax with presence of tenderness on superficial percussion. Anterior de'Espion sign was positive but there was no sternal tenderness. On auscultation, a tubular breath sound was heard near the right infraclavicular area parasternally, in all other areas on the right side vesicular breath sound was markedly diminished. Examination of other systems including the lymphoreticular system and testicular examination were all within normal limits.

Chest X-ray postero-anterior view revealed right-sided homogenous opacity involving all three zones with loss of costophrenic and cardiophrenic angles along with contralaterally shifted mediastinum [Figure 1], suggesting right-sided massive pleural effusion; but on thoracentesis, only 50 ml hemorrhagic fluid could be aspirated from the right infrascapular area after repeated attempts. Pleural fluid study yielded reddish-coloured, predominantly lymphocytic, exudative fluid with high adenosine deaminase (ADA) [Total cell count– 170/cmm, lymphocyte-80%, neutrophil-15%, ADA-122 IU, protein-3.7g/dl, sugar- 86 mg/dl] and pleural fluid for PAP stain was negative. No acid-fast bacillus was found in sputum smear microscopy. Subsequently contrast-enhanced CT (CECT) scan of the thorax was done and showed a huge non-homogenous mass of heterogeneous density with multiple foci of necrosis occupying the entire right hemithorax, possibly arising from the anterior mediastinum, causing shifting of the mediastinum to the left and compression of the superior venacava (SVC), there was minimal pleural effusion [Figure 2].

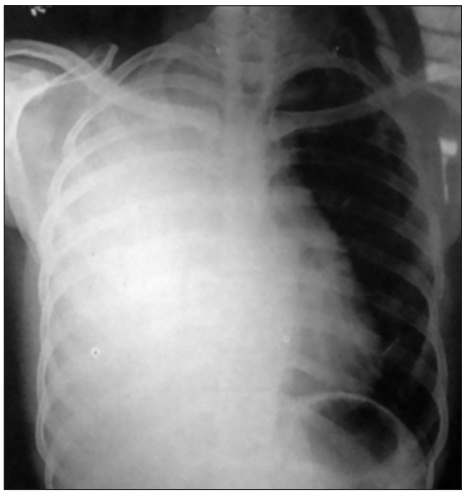

Figure 1: Chest X-ray PA view showing homogenous opacity on the right side involving all zones with obliteration of the costophrenic angle and contralateral mediastinal shift

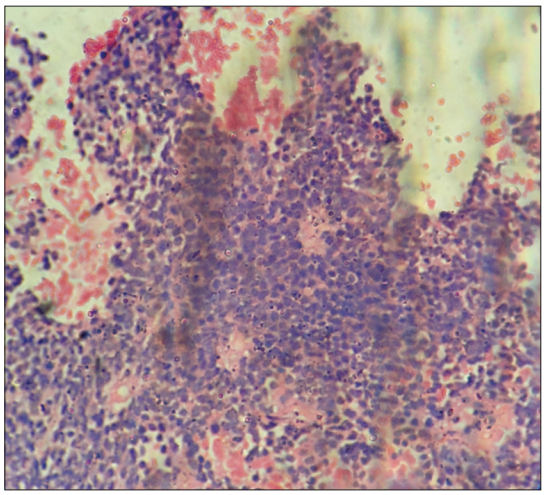

Figure 3: Cytology of CT-guided FNAC slide under high-power field showing highly cellular smear with small round cells with hyperchromatic nuclei and scanty cytoplasm (Hematoxylin-eosin, ×400)

CT-guided fine needle aspiration cytology (FNAC) was performed and the pathologist opined it as small round-cell tumour, possibilities: Non-Hodgkin's lymphoma or small-cell carcinoma of lung [Figure 3]. CT-guided tru-cut biopsy of the lesion was performed next and it revealed a tumour composed of round, oval or fusiform cells with hyperchromatic nuclei and scanty cytoplasm, mitotic figures were present [Figure 4] and it was reported again as small round-cell tumour, possibly small-cell carcinoma of the lung. Subsequently, fibreoptic bronchoscopy was done and it showed narrowing of the right bronchial tree possibly due to external compression but no intraluminal growth was noted. On immunohistochemistry of the histology block of tru-cut biopsy, tumour cells expressed MIC-2 and were immunonegative for cytokeratin, synaptophysin, chromoganin a, CD 20, CD 3, tdt, and the findings were consistent with primitive neuroectodermal tumours (PNETs).

Finally, a diagnosis of PNET of the mediastinum was made.

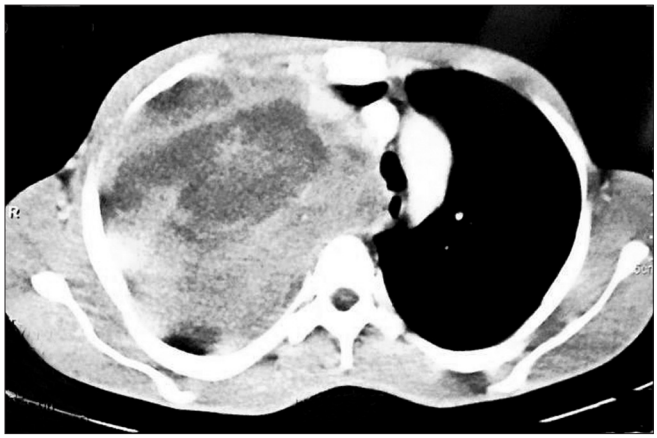

Figure 2: CT scan of the thorax (CECT) showing a large mass of heterogeneous density with foci of necrosis occupying the entire right hemithorax

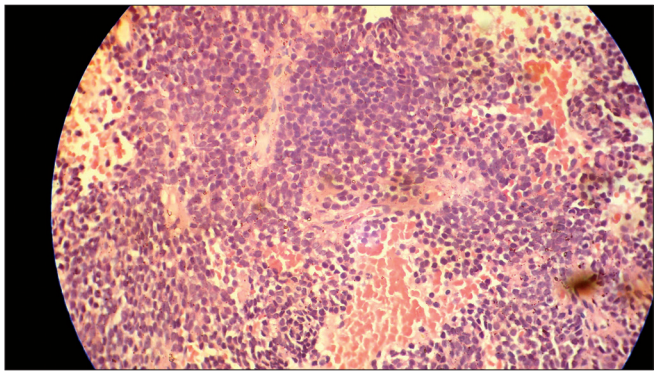

Figure 4: Histopathology of CT-guided tru-cut biopsy slide under high-power field showing sheets of small round or oval cells with hyperchromatic nuclei and variable amount of cytoplasm, tumour cells showing rosette formation at places (Hematoxylin-eosin, ×400)

CT scan of brain was performed subsequently and it was within normal limit. So it was an extremely rare case of peripheral PNET arising from the anterior mediastinum.

DISCUSSION

In 1973, Hart and Earle[4] first coined the term primitive neuroectodermal tumour (PNET), which drew attention to the primitive nature of the tumour rather than histogenesis. This entity is primarily a disease of childhood and young adults with a median age at diagnosis being nine years, and 80% of the cases are under 20 years of age.[1] PNETs are highly malignant, undifferentiated neoplasms of the ES/PNET family, arising from the germinal matrix cells of the primitive neural tube. PNETs are a variety of small round blue cell tumors (SRBCT) and may involve more than one site at presentation. When located in extraosseous sites, supratentorial brain, spinal canal, and soft tissues of the thigh are the usual sites; primary involvement of extracranial sites like the mediastinum, chest wall, kidney is very rare.[5,6] In a study of extraskeletal ES by Ahmad *et al.*,[7] only one of 24 patients presented with the tumor involving the mediastinum. Kuzucu *et al.*,[8] reported a case of a multifocal intrathoracic ES that involved the mediastinum and lingula. Primary mediastinal PNETs are mostly located in the posterior mediastinum like other neurogenic tumours, primary involvement of the anterior mediastinum is extremely uncommon. These neoplasms are usually seen in young males who predominantly present with chest pain as in our case.[9] Radiologically, it is very difficult to differentiate these neoplasms from other common anterior mediastinal tumours, CT scan of the thorax reveals an ill-defined, heterogeneous mass with necrotic foci within, calcification is usually absent.[10] The cytological appearance of classic ES/PNET is usually distinctive. Smears are generally highly cellular and are composed of both single cells and groups of loosely cohesive cells with a high nuclear/cytoplasmic ratio, hyperchromatic nuclei without prominent nucleoli, distinctively smooth nuclear membrane contour, finely granular chromatin, one or two small nucleoli and scanty but almost always present perinuclear clear cytoplasm suggesting epithelial differentiation. Homer-Wright rosettes may be seen but are absent in undifferentiated tumours.[11] In atypical ES and PNET the cellular and nuclear atypia is more marked than in conventional ES, rosette- like structures are more common, the distinction between large light and small dark cells less obvious and cells with thin cytoplasmic processes are present.[12] In atypical cases diagnosis on FNAC is quite challenging and the extraskeletal variant of ES/PNET is more often difficult to diagnose on cytopathology,[13] and a histology with immunohistochemistry can only clinch the diagnosis in these cases.The classic histological pattern of ES/PNET consists of solid sheets of small uniform "primitive" cells with round nuclei and scanty cytoplasm that lack significant differentiation. In more differentiated ES/PNET, Homer-Wright rosettes may be identified. Due to the lack of characteristic morphologic features, ES/PNET is difficult to distinguish from histologically similar small round-cell tumours including rhabdomyosarcoma, desmoplastic small round-cell tumour, poorly differentiated synovial sarcoma, mesenchymal chondrosarcoma, neuroblastoma and lymphoma.[14] Immunohistochemical expression of the Mic2 gene product (CD99) in ES/PNET is helpful in separating this entity from other small round-cell tumours.[15] However, CD99 expression is not specific for ES/PNET, as it can be expressed by other sarcomas, including poorly differentiated synovial sarcoma[16] and mesenchymal chondrosarcoma. Other ancillary techniques, including cytogenetic analysis, reverse transcriptase polymerase chain reaction and fluorescence *in situ* hybridization may provide further aid in confirming the diagnosis of ES/PNET. Unfortunately, these specialized molecular tests are available in very few centers. Demonstration of the t(11;22)(q24;q12) chromosomal translocation (EWS-FLI1 gene rearrangement) is highly specific for ES/PNET as it is encountered in more than 90% of the neoplasms.[1,15] Management is usually multimodal: surgery followed by ifosfamide or doxorubicin-based chemotherapy and radiotherapy. Overall, PNETs are aggressive neoplasms that have less than 20% five-year survival,[17] but the overall prognosis of extraskeletal ES/PNET seems to be better. A retrospective study of 24 patients with extraskeletal ES showed an overall five-year survival rate of 61%. Wide tumor-free resection margins in conjunction with multi-agent chemotherapy are necessary for good clinical outcomes.

Although, a rare entity, extraskeletal ES/PNET should be considered in the differential diagnosis of primary mediastinal neoplasms, especially in children or young adults and if a primitive small round-cell tumour is encountered in cytology or histology. Histopathology with immunohistochemistry, cytogenetic analysis and other molecular tests to identify chromosomal translocations, are invaluable to establish specific diagnosis.

REFERENCES

1. Ushigome S, Machinami R, Sorensen PH. Ewing's sarcoma primitive neuroectodermal tumour (PNET). In: Fletcher CDM, Unni KK, Mertens F, editors. WHO Classification of Tumours. Pathology and Genetics. Tumours of Soft Tissue and Bone. Lyon: IARC Press; 2002. p. 298-300.
2. Sculman H, Heinman-Neuman N, Kurtzbart E, Maor E, Zirkin H. Thoracoabdominal peripheral primitive neuroectodermal tumours in childhood: Radiological features. Eur Radiol 2000;10:1649-52.
3. Bubasi B, Cyriac S, Tenali SG. Clinicopathological analysis and outcome of primary mediastinal malignancies-a report of 91 cases from a single institute. Ann Thorac Med 2009;4:140-2.
4. Hart MN, Earle KM. Primitive neuroectodermal tumors of the brain in children. Cancer 1973;32:890-7.
5. Roberts RO, Lynch CF, Jones MP, Hart MN. Medulloblastoma: A population based study of 532 cases. J Neuropathol Exp Neurol 1991;50:134-44.
6. Zhang L, Wang T, Zheng L, Wu G. Primitive neuroectodermal tumor of the kidney with inferior vena cava thrombus. J Natl Med Assoc 2009;101:1291-4.
7. Ahmad R, Mayol BR, Davis M, Rougraff BT. Extraskeletal Ewing's sarcoma. Cancer 1999;85:725-31.
8. Kuzucu A, Erkal HS, Soysal O, Serin M. Extraskeletal Ewing's sarcoma

presenting with multifocal intrathoracic mass lesions associated with mediastinal shift. Ann Thorac Surg 2006;81:1487-8.
9. Saifuddin A, Robertson RJ, Smith SE. Radiology of Askin's tumour. Clin Radiol 1991;43:19-23.
10. Zhang WD, Zhao LL, Huang XB, Cai PQ, Xu GX. Computed tomography imaging of anterior and middle mediastinal ewing sarcoma/primitive neuroectodermal tumors. J Thorac Imaging 2010;25:168-72.
11. Kocjan G. Diagnostic Dilemmas in FNAC Cytology: Small Round Cell Tumours. In: Schroder G, editor. Fine Needle Aspiration Cytology: Diagnostic Principles and Dilemmas. 1st ed. Berlin, Heidelberg: Springer; 2006. p.133-49.
12. Akerman M. Bone. In: Orell SR, Sterrett GF, Whitaker D, editors. Fine Needle Aspiration Cytology. 4th ed. New Delhi: Elsevier India; 2005. p. 433-44.
13. Halliday BE, Slagel DD, Elsheikh TE, Silverman JF. Diagnostic utility of MIC-2 immunocytochemical staining in the differential diagnosis of small blue cell tumors. Diagn Cytopathol 1998;19:410-6.
14. Manduch M, Dexter DF, Ellis PM, Reid K, Isotalo PA. Extraskeletal Ewing's sarcoma/primitive neuroectodermal tumor of the posterior mediastinum with t(11;22)(q24;q12). Tumori 2008;94:888-91.
15. Folpe AL, Goldblum JR, Rubin BR, Shehata BM, Liu W, Dei Tos AP, *et al*. Morphologic and immunophenotypic diversity in Ewing family tumors: A study of 66 genetically confirmed cases. Am J Surg Pathol 2005;29:1025-33.
16. Zamarron C, Abdulkader I, Alvarez UC, Baron FJ, Prim JM, Ledo RL, *et al*. Primary synovial sarcoma of the lung. Intern Med 2006;45:679-83.
17. Gladish GW, Sabloff BM, Munden RF, Truong MT, Erasmus JJ, Chasen MH. Primary thoracic sarcomas. Radiographics 2002;22:621-37.

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