Asian Pac. J. Health Sci., 2017; 4(2):86-89 e-ISSN: 2349-0659, p-ISSN: 2350-0964

Document heading doi: 10.21276/apjhs.2017.4.2.13 Case Report

Cytodiagnosis of Ewings sarcoma, hip and its confirmation on immunohistochemistry: A case report

Shalini Bahadur[1], Shilpi[2]*, Akshi Katyal[3], Ruchi Bansal[3], Namrata Nargotra[4]

[1]Associate professor, Pathology, NDMC and Hindu Rao Hospital, New Delhi, India
[2]Junior Resident, Pathology, Hindu Rao Hospital, New Delhi, India
[3]Senior Resident, Pathology, NDMC and Hindu Rao Hospital, New Delhi, India
[4]Head of Department, Pathology, Hindu Rao Hospital, New Delhi, India

ABSTRACT

Ewings sarcoma is an important childhood malignancy. The patient usually presents in an advanced stage and before definitive or palliative therapy can be instituted, rapid and precise diagnosis is imperative. Fine needle aspiration cytology of the lesion aided with cell block preparation for immunohistochemical confirmation can serve as a rapid and inexpensive method for early diagnosis. Here we are presenting a case of Ewings sarcoma in the hip joint along with extraosseous extension in a young female which was diagnosed as well as confirmed on cytology.

Keywords: FNAC, Ewings sarcoma, Cell block, immunohistochemistry

Introduction

Ewings sarcoma (ES) / peripheral primitive neuroectodermal tumor (pPNET) along with neuroblastoma, retinoblastoma, hepatoblastoma, nephroblastoma, desmoplastic small round cell tumor, non Hodgkins lymphoma, rhabdomyosarcoma, and small cell neoplastic carcinoma form the potpourri of formidable majority of childhood malignancies[1]. Patients frequently present at an advanced stage and before definitive or palliative therapy can be instituted, rapid and precise diagnosis is imperative. Due to the morphological overlap with other small round cell tumors, diagnosis of ES may pose difficulty on cytology and is diagnostically challenging. We hereby report a case of ES arising in hip bone of a young girl utilizing simple diagnostic techniques: fine needle aspiration cytology (FNAC) aided with immunohistochemistry (IHC) on cell block preparation.

**Correspondence*
Dr. Shilpi
Junior Resident, Pathology, Hindu Rao Hospital, New Delhi, India
E Mail: drshilpihrh@gmail.com

Case report

A 12-year-old female patient presented to the orthopedic outpatient department with left hip swelling, pain, fever and associated difficulty in walking since one month. On examination, there was swelling and tenderness in the left hip region. Overlying skin was warm. Joint mobility was restricted. Magnetic resonance imaging of the hip joint showed a large expansile heterogenous mass, with solid and cystic areas, arising from left iliac bone. A large extraosseous component, with mild perilesional fluid was present. No obvious pathology was seen in the joint or pelvic viscera. Bilateralinguinal lymphadenopathy measuring less than 1cm each was reported. Cytological and histopathological correlation was advised. Fine needle aspiration yielded cellular aspirate. May Grunwald Geimsa smears showed dual population of cells in small clusters as well as lying singly. The larger cell population had moderate amount of pale fragile basophilic cytoplasm with cytoplasmic vacuolisation, round to ovoid nucleus with fine granular chromatin and 1-3 small nucleoli. Smaller cells were seen in clusters, having scant cytoplasm, high nuclear-cytoplasmic ratio, and irregular round nuclei with condensed chromatin. Few rossettes are also noted. Background showed mixed inflammatory infiltrate comprising of neutrophils, few lymphocytes and

tingible body macrophages. [Figure 1] Tumor cells showed brisk mitotic activity. PAS, CD99, NSE and LCA was put up on cell block prepared. PAS and CD99 turned out to be positive, NSE and LCA was negative. [Figure 2] In view of cellular morphology and intracellular PAS positivity as well as strong CD99 positivity of cells on cell block preparation, a diagnosis of Ewing sarcoma was rendered. Due to the limitations of the institution as well as limited affordability of the patient FLI-1 analysis could not be done.

Discussion

Ewing sarcoma(ES) is a highly malignant bone tumor, first described by James Ewing in 1921 as 'diffuse endothelioma of the bone'.[2] ES of the bone, extra skeletal Ewings sarcoma (EES) and primitive peripheral neuroectodermal tumor (pPNET), are considered tumors of the same spectrum as not much significant differentiation or biological and therapeutic distinction is found amongst these entities[3-6]. Derived from red bone marrow it's common in children and young adults with age incidence of 4-15 years. It's unusual below 5 years or beyond 30 years of age[7,8].Male to female ratio is 1.5:1. Following osteosarcoma, EWS is the most lethal, second most common malignant tumor in the young accounting for 23% of childhood cancers[9]. It presents in soft tissue and bone alike, anatomical sites being variable[10]. Frequently affected are bones of lower extremity; pelvis, ribs may also be involved commonly. Clinically it mimics osteomyelitis because of pain, fever and leukocytosis on presentation. Though bone is the most common site, EWS/PNET account for approximately 20% of soft tissue sarcomas in the first two decades of life, arising in a number of extraosseous sites, namely kidney, intestine, ovary, vagina, and skin[10,11].Radiologically, ill-defined, destructive intramedullary lesions involving diaphyses of the long tubular bones are seen in Ewings sarcoma. "Moth-eaten" pattern, accompanied by an onion skin type periosteal reaction, is characteristic.FNA biopsy is a reliable approach for the diagnosis of EWS/PNET regardless of site of clinical presentation[12].Smears and cell block preparation are cellular comprising of small, cohesive clusters as well as singly dispersed undifferentiated small round cells without nuclear molding. They have indistinct cell borders, and may form pseudorosettes. A dimorphic population of lighter and darker cells may be appreciable in Diff-Quik-stained smears. Lighter staining cells are larger (approximately the size of histiocytes) with moderate amount of finely vacuolated-to-clear cytoplasm that containing abundant glycogen (Periodic-Acid-Schiff-positive, diastase-digestible) and having round-to-oval nuclei, smooth nuclear membranes, fine, pale chromatin and 1 or 2 small nucleoli[13]. Second population is of darker staining or lymphocytoid cells having narrow rim of cytoplasm, small, irregularly contoured nucleus with dense chromatin and inconspicuous nucleoli. Lighter staining cells predominate and the two cell types usually are intermingled with no discernible pattern. Binucleation, multinucleation, multinucleated giant cells, and stromal matrix formation are not seen in a case of Ewing sarcoma.Various small round cell tumors are considered in the differential diagnosis of ewings sarcoma. These include malignant lymphoma, metastatic embryonal rhabdomyosarcoma, and metastatic neuroblastoma. Malignant lymphomas usually affect older patients, and cytosmears show completely dissociated cell population with lymphoglandular bodies. Metastatic embryonal rhabdomyosarcoma shows tadpole shaped cells on fine needle aspiration whereas eosinophilic fibrillar material, Homer Wright rosettes with cellular processes are seen in a case of metatstatic neuroblastoma [14].PAS stain is a useful adjunct for differential diagnosis as cells of Ewing's sarcoma contain large amount of cytoplasmic glycogen. CD99 shows characteristic perinuclear positivity in 90% cases of ES/PNET and it helps in differential diagnosis from neuroblastoma which is negative. Most lymphomas are positive for leucocyte common antigen and malignant rhabdomyosarcoma shows positivity for actin, myoglobin and desmin. However, CD99 is not entirely specific for Ewing's sarcoma as its positivity is also seen in a few cases of lymphoblastic lymphomas and rare cases of rhabdomyosarcoma[15,16]. Chromosomal analysis reveals balanced translocation at t(11;22) (q24;q12). This is the defining cytogenetic abnormality which results in expression of an aberrant hybrid protein in which the N-terminal part of EWS is linked to deoxyribonucleic acid binding domain (Ets domain) of the FLI-1 transcription factor. This EWS-FLI-1 protein is thought to be responsible for the origin of EWS[17].Ewing's sarcoma has a high propensity for distant metastases, primarily to the lungs, and nearly 50% of the patients present with disseminated disease.

Conclusion

X rays, computed tomography (CT) scan or MRI are helpful for aiding in the diagnosis of the tumor, however, definite diagnosis can be made on cytology along with cell block preparation. The latter gives equivalent results when compared to biopsy for applying immunohistochemical markers.

Immunophenotyping where economically feasible is an important adjunct in the diagnosis of these tumors. Early diagnosis of the disease on cytology can help in timely initiation of treatment and thus improve prognosis.

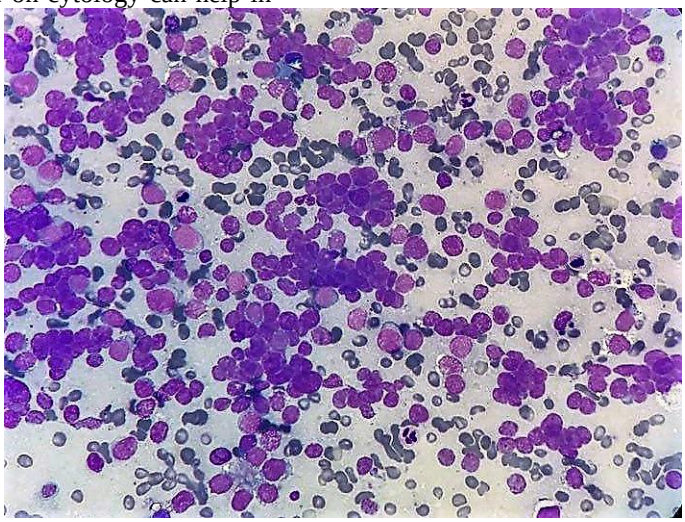

Fig 1: MGG stained cellular smear showing dual population of cells in tight clusters as well as singly along with presence of a rosette. [MGG, 40X]

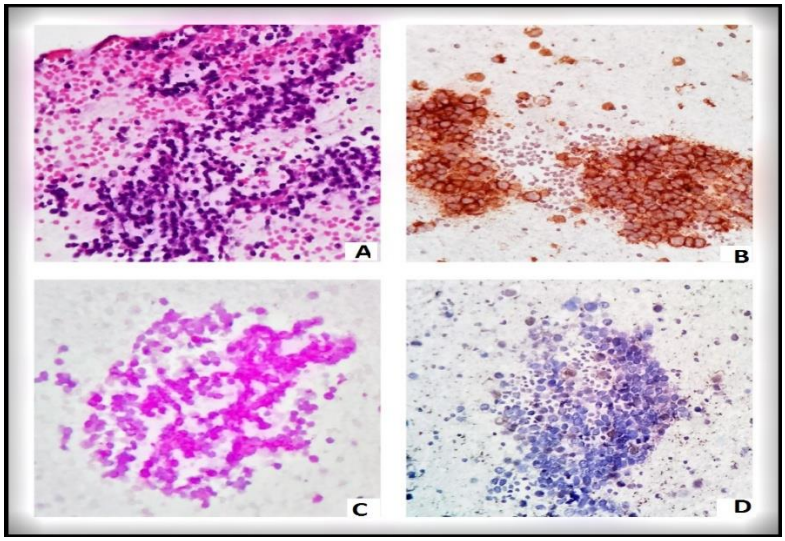

Fig 2: [A] Predominance of small round tumor cells in a hemmorhagic background on cell block preparation. [H&E, 10X] [B] CD99 strong positivity on cell block preparation [40X] [C] Diffuse cytoplasmic PAS positivity on cell block preparation [40X] [D] Negative NSE staining on cell block preparation [40X]

References

1. Asif N, Khan AQ, Siddiqui YS, Mustafa H. Metastasis from scapular Ewing′s sarcoma presenting as sutural diastasis: An unusual presentation. Int J Shoulder Surg 2010;4:1821.
2. Ewing D. Diffuse endothelioma of bone. Proc NY Pathol Soc. 1921;21:17–17
3. Ushigome S, Shimoda T, Nikaido T, Nakamori K, Miyazawa Y, Shishikura A, Takakuwa T, Ubayama Y, Spjut HJ. Primitive neuroectodermal

tumors of bone and soft tissue. With reference to histologic differentiation in primary or metastatic foci. Acta Pathol Jpn. 1992;42(7):483-93.

4. González-Cámpora R, Otal-Salaverri C, Panea Flores P, Hevia-Vázquez A, Gómez Pascual A, San Martín Díez V. Fine needle aspiration of peripheral neuroepithelioma of soft tissues. Acta Cytol. 1992;36(2):152-8.

5. Grier H E The Ewing family of tumors: Ewing's Sarcoma and Primitive Neuroectodermal Tumors. Pediatric Clin North Am. 1997; 44 :991-1004.

6. Siebenrock KA, Nascimento AG, Rock MG. Comparison of soft tissue Ewing's sarcoma and peripheral neuroectodermal tumor. Clin Orthop Relat Res. 1996;(329):288-99.

7. Ewing J. Classics in oncology. Diffuse endothelioma of bone. James Ewing. Proceedings of the New York Pathological Society, 1921. CA Cancer J Clin 1972;22:958.

8. Parija T, Shirley S, Uma S, Rajalekshmy KR, Ayyappan S, Rajkumar T. Type 1 (11;22)(q24:q12) translocation is common in Ewing′s sarcoma/peripheral neuroectodermal tumour in south Indian patients. J Biosci 2005;30:3716.

9. Delattre O, Zucman J, Melot T, Garau XS, Zucker JM, Lenoir GM, et al. The Ewing family of tumors A subgroup of small round cell tumors defined by specific chimeric transcripts. N Engl J Med 1994;331:2949.

10. Folpe AL, Goldblum JR, Rubin BP, et al. Morphologic and immunophenotypic diversity in Ewing family tumors: a study of 66 genetically confirmed cases. Am J Surg Pathol. 2005;29: 1025–1033.

11. Marley EF, Liapis H, Humphrey PA, et al. Primitive neuroectodermal tumor of the kidney—another enigma: a pathologic, immune histochemical, and molecular diagnostic study. Am J Surg Pathol. 1997;21:354–359.

12. Sanati S, Lu DW, Schmidt E, Perry A, Dehner LP, Pfeifer JD. Cytologic diagnosis of Ewing sarcoma/peripheral neuroectodermal tumor with paired prospective molecular genetic analysis. Cancer. 2007;111(3):192-9.

13. Demay RM. The Art and Science of Cytopathology. Chicago, Ill: ASCP Press; 1996.

14. Das DK. Fine-needle aspiration (FNA) cytology diagnosis of small round cell tumors: value and limitations. Indian J Pathol Microbiol. 2004 ;47(3):309-18.

15. Weidner N, Tjoe J. Immunohistochemical profile of monoclonal antibody 013: antibody that recognizes glycoprotein p30/ 32MIC2 and is useful in diagnosing Ewing's sarcoma and peripheral neuroepithelioma. Am J Surg Pathol 1994; 18:486-494.

16. Stevenson AJ, Chatten J, Bertoni F, Miettinen M. CD99 (p30/ 32MIC2) neuroectodermal/Ewing's sarcoma antigen as an immunohistochemical marker. Appl Immunohislochem 1994; 2: 231-240.

17. Ross KA, Smyth NA, Murawski CD, Kennedy JG. The biology of Ewing sarcoma. ISRN Oncol 2013:759725

Source of Support: Nil
Conflict of Interest: None