Rare Presentation of Ewings Sarcoma in Sinonasal Region: A Case Report

John Winkle Medida[1], Joseph Benjamin Gandi[2], Bala Sankar Ramavath[3], Fatema[4]

ABSTRACT

Introduction: Ewings sarcoma (ES) is highly malignant round cell tumor of childhood and infancy. It has both skeletal and extra skeletal manifestations. It most commonly involves long bones and extra skeletal forms generally involve soft tissues of extremities, retroperitonium, paravertibral tissues and rarely head and neck region. Involvement of sinonasal region is very rare and few cases were reported till date.

Case Report: We report a case of Ewings sarcoma involving sinonasal region in 34 year old male, who presented with epistaxis, nasal obstruction and pain in facial area. He was received conformal radiotherapy to stop epistaxis and followed by chemotherapy. Patient responded subjectively and objectively.

Conclusion: The small round cell tumors like olfactory neuroblastoma, lymphoma, undifferentiated carcinoma, sinonasal melanoma, acute leukemia, embryonal rhabdomyosarcoma, sinus mesenchymal chondrosarcoma, osteosarcoma small cell and small neuroendocrine cell carcinomapose difficulties in diagnosis and management. Therefore, this study aims to focus on the features of ES and other small round cell tumors and the differentiating features for the accurate diagnosis and proper treatment. We present this case due to its rare presentation and few cases were reported till date and also to focus on the clinical, histopathological and immunohistochemical features, to differentiate among all the round cell tumors for accurate diagnosis and proper treatment.

Keywords: Ewings Sarcoma, Sinonasal Region, Radiotherapy, Chemotherapy.

INTRODUCTION

Ewings sarcoma (ES) is highly malignant round cell tumor which originates from mesenchyme.[1] It can arise from bone (skeletal) as well as soft tissues (extra skeletal). Skeletal forms are more common than extra skeletal forms which most commonly involves long bones of extremities. Extra skeletal forms mostly involve soft tissues of extremities, retroperitonium, paravertibral tissues and rarely head and neck region.[4] The incidence in head and neck region is 2-7% and frequently involves maxilla and mandible.[2] Involvement of sinonasal region is very rare and few cases were reported till date. ES belongs to family of blue, small round cell tumors which have different clinical manifestations. They pose difficulties in diagnosis and management. Therefore, this study aims to focus on the features of ES and other small round cell tumors and the differentiating features for the accurate diagnosis and proper treatment.

CASE REPORT

A 34 year old male presented to oncology OPD with chief complaints of epistaxis, pain in right side of face and nasal obstruction. He was examined thoroughly. No growth was seen in nasal cavity and tenderness noted in right malar area. Slight swelling was noted in right cheek. Oral cavity, oropharynx and neck examination was normal. He was further investigated with CT Scan Head and Neck, which showedlarge lobulated sino nasal mass seen predominantly in maxillary sinus extending into nasal cavity and sphenoid sinus with bony erosion. Mass is also involving right inferior turbinate and extending into infra temporal fossa (Fig 1 and 2) Biopsy was taken from the mass and histopathology revealed collections of monotonously appearing small round cells with hyper chromatic nuclei and scant cytoplasm (Fig 3 and 4). Immunohistochemistry was positive for Mic-2 (CD 99) and CD 56. Viamentin was focally positive. IHC was negative for chromogranin, synaptophysin, CD 45, Desmin, Neuron specific enolase (NSE) and Pan cytokeratin. It was also negative for MYOD 1 and CD 138. Haemotological and biochemical investigations were normal. Chest radiograph and ultrasound of abdomen and pelvis were normal. Finally, it was diagnosed as Ewings Sarcoma of Sinonasal region. Patient complaining of recurrent episodes of epistaxis for which we forwarded with upfront conformal radiotherapy to stop bleeding. There was improvement both subjectively and objectively.

Patient is now on chemotherapy with VAC/IE regimen for total of 12 cycles. (vincristine,adriamycin,cyclophosphamide,iphosphomide,etoposide)

DISCUSSION

ES Family Tumors include tumors with varied histology. They have different ultrastructural and immunohistochemical features too. James Ewings described Classic ES in 1921, as monotonous population of small round cells with high nuclear to cytoplasmic ratios arrayed in sheets.[1] The cells

[1]Senior Resident, [2]Professor, [3]Assistant Professor, [4]Junior Resident, Department of Radiation Oncology, MNJ Institute of Oncology and Regional Cancer Centre, Hyderabad, India

Corresponding author: Dr. John Winkle Medida, Room no 7, MNJ Institute of Oncology and Regional Cancer Centre, Redhills, Hyderabad – 500004, India.

How to cite this article: John Winkle Medida, Joseph Benjamin Gandi, Bala Sankar Ramavath, Fatema. Rare presentation of ewings sarcoma in sinonasal region: a case report. International Journal of Contemporary Medical Research 2016;3(2):462-465.

Tumor	Clinical features	Microscopy	IHC
Neuroblastoma	Solid tumor of infancy and child-hood	Uniform small round cells with indistinct borders, arranged in nests and sheets having sparse cytoplasm, round nuclei, Higher-grade tumors with nuclear pleomorphism, prominent nucleoli, increased mitotic activity, Rosettes of the Homer Wright type (pseudorosettes) in up to 30% of tumors, and Flexner-Wintersteiner type (true neural rosettes) in 5%.	Positve: Neuron specific enolase (NSE), Synaptophysin, Neurofilament pro-tein(NFP), Class III beta-tubulin, and Microtubule-associated protein (majority of cases). S-100 protein staining limited to the sustentacular cells situated along the periphery of the neoplastic lobules (may be sparse in the higher-grade tumors)
Desmoplasticsmall round cell tumor	Tumor of infancy and childhood	Small round cells with hyperchro-matic nuclei and increased nuclear cytoplasmic ratio	Positive: Cytokeratin, Desmin, Viamentin, Nueron specific enolase.
Medulloblastoma	Childhood tumor	Small round cell tumor with sheets of undifferentiated cells withhyperchro-matic nuclei and increased nuclear cytoplasmic ratio	Positive: NSE, Synaptophysin, Focal GFAP(glial fibrillary acidic protein)
Rhabdomyosarcoma	Children and young adults	Cells of variable size and shape which stain deep blue,small cytoplasmic vacuoles,Strap cells or tadpole cells strongly associated with RMS	Positve: Desmin, Muscle specific actin, Myoglobin and MyoD1.
Synovial sarcoma	Adolescents and young adults.	Tumor cells were small to medium in size, with rounded, ovoid, or fusiform bland nuclei with inconspicuous nu-cleoli. Small glandular or acinar-like structures were seen in some biphasic variant cases. The cytology of the small cell variant of synovial sarcoma shows numerous, small round cells with high nuclecytoplasmic ratio	Negative: Cytokeratin and Epithelial membrane antigen. Diagnosed mainly by presence of t(X:18) translocation by molecular techniques.
Wilms tumor	Childhood tumor of kidney	Cells have scanty deep blue cytoplasm with ill defined borders round to oval nuclei having fine, regular, evenly distributed chromatin.	Positive: Cytokeratin, NSE, Epithelial membrane antigen and Viamentin.
Retinoblastoma	Childhood eye tumor	Sheets and nests of small blue cells with scanty cytoplasm, hyperchromat-ic nuclei. Rosettes of the Homer Wright type and Flexner-Wintersteiner type	Positive: NSE, Synaptophysin, S-100,Leu-7, Myelin basic protein, GFAP(glial fibrillary acidic protein).
Small cell lymphoma	Old age tomor, male	Small round mature lymphocytes and prolymphocyets.	Positive: CD-5,CD-9,CD-20,CD-23,CD-43 and CD-79a.
Small cell lung cancer	Old age tumor, male	Sheets,clusters,rosettes of small round to oval cells with minimal cytoplasm, salt and pepper chromatin, hyperchro-matic and indistinct nucleoli.	Positive: Pan keratin(100%) TTF1(89%), NSE(77%), CD-117(75%) Chromogranin Synaptophysin, Calretinin, Keratin5.
Mucosal Melanoma	Old age,male	Small uniforem blue cells,70% of cells with melanin pigment, nesting growth pattern	S-100, HMB 45, Melan A/Mart1, Tyrosinase, Viamentin.
The main differentiating features among small round cell tumors are as follows:			

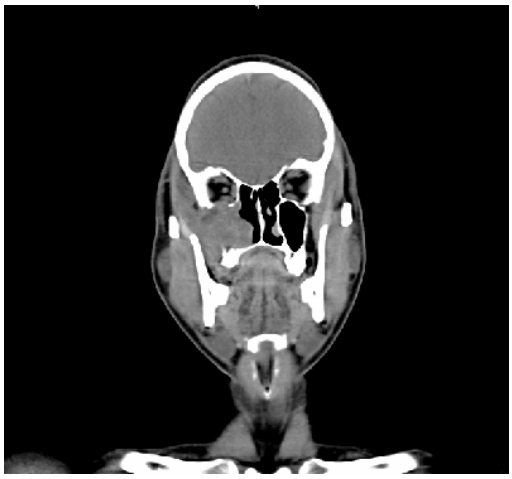

Figure-1: CT Scan head and neck coronal view showing lobulated mass in sino nasal region

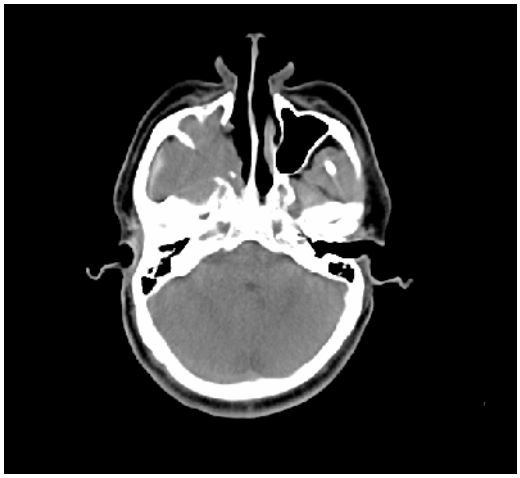

Figure-2: CT Scan head and neck axial section showing mass in sinonasal region.

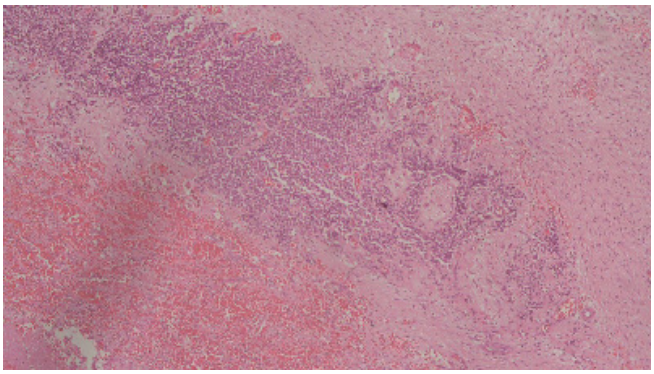

Figure-3: Monotonous clusters of small round cell with scanty cytoplasm and hyperchromatic nuclei.

have scant, faintly eosinophilic to amphophilic cytoplasm, indistinct cytoplasmic borders, and round nuclei with evenly distributed, finely granular chromatin and inconspicuous nucleoli.[2]

CD-99 is expressed in most of the ES tumors, which is a cell surface glycoprotein and is a characteristic feature of Ewing's sarcoma. Diffuse membrane staining is positive for CD-99 in a chain-mail pattern in 95-100% of Ewing's sarcoma

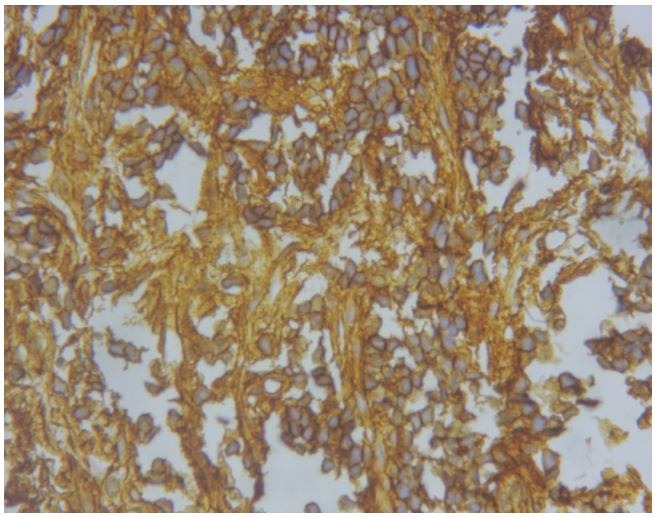

Figure-4: IHC slide showing cells of CD-99 positivity in high power (40X)

cases.[3] ES is also positive for other cell surface proteins like viamentin sometimes.[4] Peripheral Primitive Neurectodermal Tumors (pPNET) which are more differentiated variety of ES Family Tumors express markers like NSE(neuron specific enolase),S-100 protein, Leu-7 which shows evidence of neural differentiation.[6] 20% of cases of ES are immune reactive for cytokeratin focally and 10% of cases show diffuse immunoreactivity.[7]

Ewing's sarcoma is characterized by a reciprocal chromosomal translocation between chromosomes 11 and 22. It is considered as the pathognomonic feature of Ewing's sarcoma as it is present in 85% of tumors. Other translocations involving chromosomes like 22q12, 21q22, 7p22, 17q12, and 2q36 are seen in rest of the cases.[8] The rearrangement results in the translocation of the 3′ portion of the friend leukemia virus integration site 1 (FLI1) gene from chromosome 11 to the 5′ portion of the Ewing's sarcoma gene EWS on chromosome 22. As result of this translocation, a chimeric EWS-FLI1 RNA is expressed which results in a fusion protein.[9] This is useful for molecular detection methods like RT-PCR and FISH. The presence of t(11;22) (q24;q12) is present in 85% of ES cases and found to correlate with high expression of CD-99. About 15% of histopathologically defined CD99 positive Ewing's sarcomas lack the classical Ewing's sarcoma- specific translocation.[10]

As the histologic and immunophenotype characters of ES overlap with other small round cell tumors, an expanded panel of immunohistochemical studies may be required to rule out other entities. Olfactory neuroblastoma is also positive for NSE, S-100, and Leu-7 like Ewing's sarcoma but it is negative for vimentin and immunoreactive for neurofilament protein. Lymphoblastic lymphoma is also strongly positive for CD-99 but it is also immunoreactive for leukocyte common antigen (CD45) which is not seen in ES. Rhabdomyosarcoma is also focally positive for CD-99 and is also immunoreactive for myogenin, myoD1, desmin, and actin which is not seen in ES. The differentiation between poorly differentiated synovial sarcoma and Poorly differentiated Ewing's sarcoma is difficult sometimes as both express same

markers like CD-99.

In our case, the histology showed small round cell tumor with hyperchromatic nuclei and scant cytoplasm. IHC was positive for MIC-2(CD-99) and CD-56. Viamentin was focally positive. Olfactory neuroblastoma was ruled out as the tumor was not arising from cribriform plate and superior turbinate as well as the histologically there were no Homer wright rosettes which are characteristic features of nueroblastoma. Moreover the tumor is negative for NSE. Rhabdomyosarcoma is ruled out as it is most common in children, histologically small round cells should present in subepithelial layer and IHC is positive for Myo-D. By the above features the Rhabdomyosarcoma is ruled out. Sinonasal melanoma was ruled out due to absence of prominent eosinophilic nucleoli, absence of melanin pigmentation and negativity for HMB45. Lymphomas especially lymphoblastic type can be confused with ES and it was ruled out by absence of single prominent nucleoli and CD45 negativity. Synovial sarcoma is rulled out due to absence of cytokeratin and presence of CD-99. Medulloblastoma is ruled out by location of tumor, age and CD-99 positivity.

CONCLUSION

Small round cell tumors of sinonasal region pose difficulties in diagnosis and management. Thorough knowledge regarding the clinical features, microscopy and immunohistochemistry would help accurate diagnosis and proper management.

REFERENCES

1. Ewing J. Diffuse endothelioma of bone. Proc N Y Pathol Soc 1921;21:17–24.
2. Horowitz ME, Tsokos MG, DeLaney TF. Ewing's sarcoma. CA Cancer JClin 1992;42:300–320.
3. Ramani P, Rampling D, Link M. Immunocytochemical study of 12E7 insmall round-cell tumours of childhood: an assessment of its sensitivity and specificity. Histopathology 1993;23:557–561.
4. Navarro S, Cavazzana AO, Llombart-Bosch A et al. Comparison of Ewing's sarcoma of bone and peripheral neuroepithelioma.An immunocytochemicaland ultrastructural analysis of two primitive neuroectodermalneoplasms. Arch Pathol Lab Med 1994;118:608–615.
5. Dierick AM, Roels H, Langlois M. The immunophenotype of Ewing'ssarcoma.An immunohistochemical analysis.Pathol Res Pract 1993;189:26–32.
6. Shanfield RI. Immunohistochemical analysis of neural markers in peripheralprimitive neuroectodermal tumor (pPNET) without light microscopicevidence of neural differentiation.ApplImmunohistochem Mol Morphol 1997;5:78–86.
7. Gu M, Antonescu CR, Guiter G et al. Cytokeratin immunoreactivity inEwing's sarcoma: prevalence in 50 cases confirmed by molecular diagnosticstudies. Am J SurgPathol 2000; 24:410–416.
8. Aurias A, Rimbaut C, Buffe D et al. Translocation of chromosome 22 inEwing's sarcoma. C R SeancesAcadSci III 1983; 296:1105–1107.
9. Delattre O, Zucman J, Plougastel B et al. Gene fusion with an ETS DNAbindingdomain caused by chromosome translocation in human tumours.Nature 1992;359:162–165.
10. Ambros IM, Ambros PF, Strehl S et al. MIC2 is a specific marker for Ewing's sarcoma and peripheral primitive neuroectodermal tumors. Evidence for a common histogenesis of Ewing's sarcoma and peripheral primitive neuroectodermal tumors from MIC2 expression and specificchromosome aberration. Cancer 1991;67:1886–1893.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 31-12-2015; **Published online**: 14-01-2016