

Extraskkeletal Ewing Sarcoma of the Parotid Gland: A Case report.

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ABSTRACT

We report a case of Extraskkeletal Ewing sarcoma of the parotid gland from the Royal Medical Services. The aim of reporting this case is to describe a rare mesenchymal tumor of the parotid gland with emphasis on the value of utilizing immunohistochemical stains in confirming the diagnosis.

Keywords: Ewing sarcoma, Immunohistochemical stain, Mesenchymal tumors, Parotid gland
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Introduction

The majority of salivary gland tumors are of epithelial origin .The mesenchymal tumors comprise only 1.5-3%.(1, 2, 3) Extraskkeletal Ewing sarcoma/primitive neuroectodermal tumors (EES/PNET) rarely occur in the head and neck region with only five cases reported in a series of 118 patients including the parotid gland. (4, 5) EES/PNET occurs usually in adolescents and young adults between the ages of 10 and 30 years. The disease follows an aggressive course with a high recurrence rate in addition to distant metastasis.

The imaging studies are useful in determining the tumor size, extent of invasion, and relation to the underlying bone. Histologically EES/PNET is composed of uniform small round to oval cells containing cytoplasmic glycogen and sometimes arranged around central space filled with fibrillar extension of the cells (Homer-Wright rosettes). Immunohistochemical stains and genetic studies are useful to exclude other small round cell tumors as well as other sarcomas.

Case Report

A Forty- six year old male presented with 6 weeks history of left preauricular swelling, rapidly increasing in size and causing dysphagia.

The examination revealed a 5x5cm fixed left parotid mass compressing the facial nerve and causing facial nerve weakness. The patient had enlarged cervical lymph nodes of variable size .Neck MRI with IV contrast showed an irregular heterogeneous enhancing lesion about 8x7x4 cm involving the superficial and deep lobes of the left parotid gland. The mass showed hypointenseT1-weighted and HyperintenseT2-weighted features. (Figure1A, 1B and 1C). No Definite bony destruction was seen.

Radiological differential diagnosis included mucoepidermoid carcinoma versus adenoid cystic carcinoma.

Chest CT revealed no lung consolidation, nodule, pleural effusion, mediastinal or hilar lymphadenopathy .Brain MRI without IV contrast was negative for any definite enhancing masses.

FNA was performed many times and showed sheets, clusters and single forms of atypical cells with pleomorphic atypical nuclei having coarse granular chromatin. Apoptosis and necrosis were seen. (Figure 2A and 2 B)The final cytological diagnosis was reported as malignant. Excision was recommended for further subtyping .Tissue biopsy revealed a malignant round cell tumor. The cells had round to oval hyperchromatic nuclei and scant eosinophilic cytoplasm. Mitotic figures and apoptotic bodies were present as well as foci of necrosis. (Figure3A and 3B) Immunohistochemical stains performed on tissue biopsy revealed the following results:

The tumor cells were strongly immunoreactive for Vimentin, CD99 and

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BCL-2. Figure (4A, 4B and 4C) They were negative for pan-cytokeratin (CK), CK14, MNF116, LCA, CD34, CD43, MPO, CD30,

CD68, CD23, CD21, S100, Desmin and Synaptophysin.

No cytogenetic study was performed. The histopathological diagnosis was Extraskelatal Ewing sarcoma/Primitive neuroectodermal tumor (EES/PNET)

The patient received neoadjuvant chemotherapy and underwent Left parotidectomy.

The left parotidectomy specimen revealed a creamy colored tumor measuring 7cm in maximum dimension. The microscopic findings revealed a malignant round blue cell tumor consistent with PNET/Ewing sarcoma infiltrating the salivary gland tissue, the surrounding skeletal muscles, adipose tissue and the received parapharyngeal tissue. The excision was incomplete. None of the seven included lymph nodes showed metastatic tumor. The included bone from the mandible was free of tumor as well.

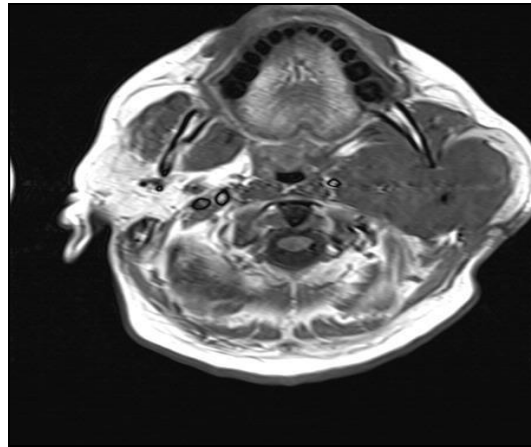
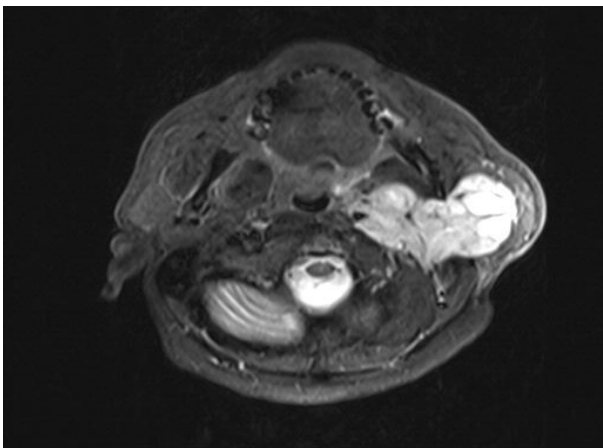


Fig 1a

Fig1b

Fig1(A,B):Head and Neck MRI showing a well defined lobular shaped soft tissue lesion measuring about 8x7x4 cm seen at the angle of left mandible mostly arising from left parotid gland which appears hypo intense in T1(Figures1A) and hyper intense in T2 (Figure1B)

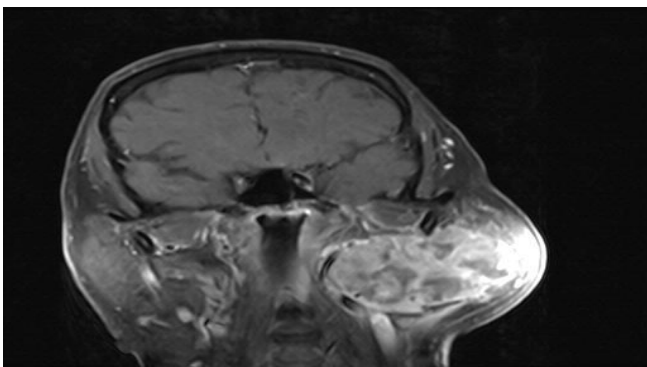


Fig 1C: Multiple internal septations and heterogeneous enhancement in post contrast images.

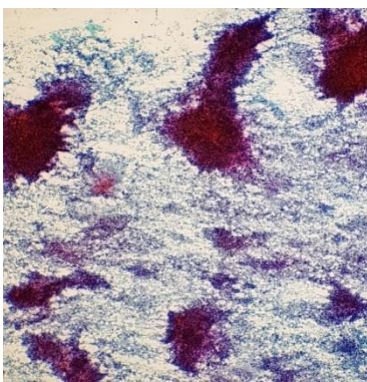


Fig2A

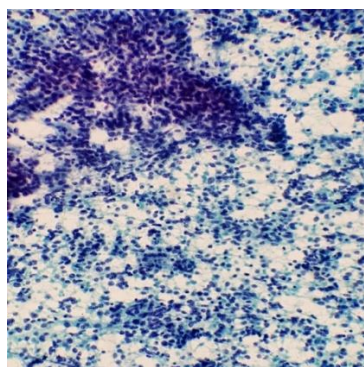


Fig 2B

Fig 2(A and B): FNA showing highly cellular smears of small round tumor cells (/Pap stain, 10X A and B) .

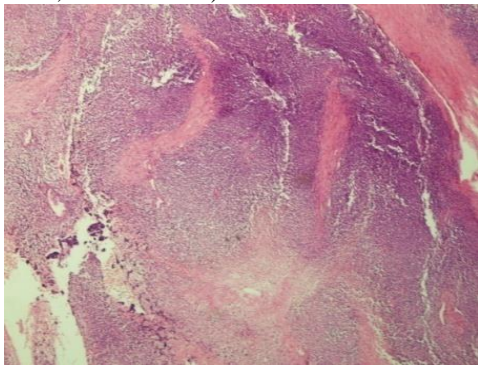


Fig 3A

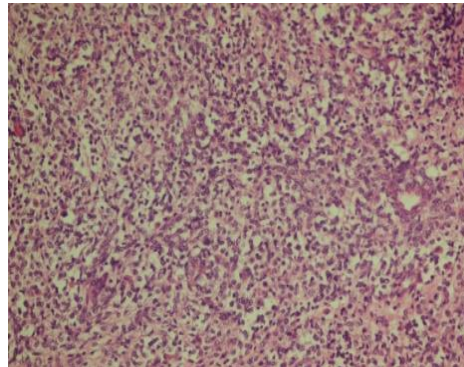


Fig 3B

Fig 3(A and B): H&E stained sections showing cellular tumor of small round cells with high mitosis and foci of necrosis. ((20X) and (40X) view)

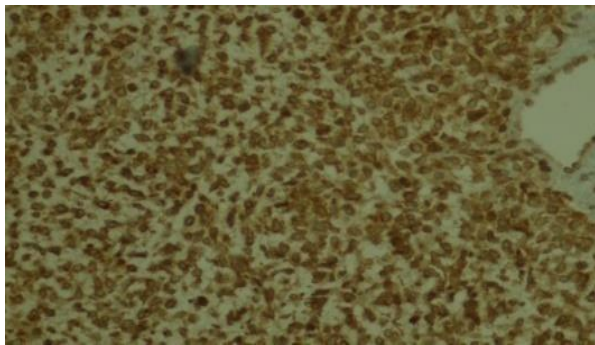


Fig4A: BCL-2 immunostain showing Diffuse immunoreactivity in the tumor cells.

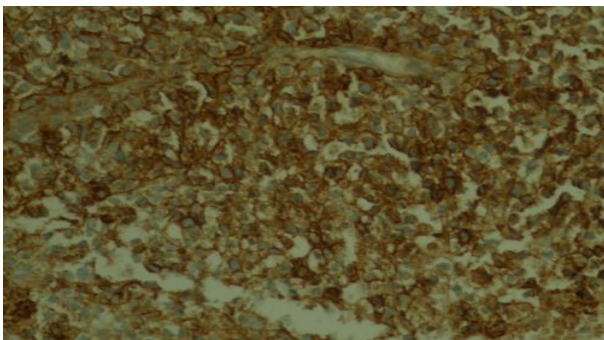


Fig 4B: CD99 immunostain showing diffuse immunoreactivity in the tumor cells.

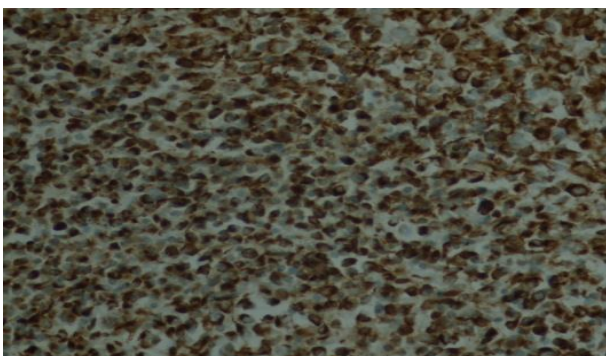


Fig 4C: Vimentin immunostain showing diffuse immunoreactivity in the tumor cells.

Discussion

Salivary gland tumors are rare and account for 3-6% of all neoplasms of the head and neck.⁽⁶⁾ Tumors mostly involve the parotid gland in 42.9-90%, the submandibular glands in 8-19.5% and only around 14-22% of tumors affect the minor salivary glands, mainly presenting in the palate.⁽⁷⁾

The mesenchymal tumors arising in the salivary gland tumors are rare. About 82% of these tumors involve the parotid glands with Rhabdomyosarcoma being most common tumor found.⁽²⁾

Extraskelatal Ewing sarcoma/Primitive neuroectodermal tumors (EES/PNET) arising in salivary gland in general are uncommon. They are aggressive round cell tumors usually presenting in the second decade of life with equal sex incidence in contrast to 10 years average age of skeletal Ewing sarcoma and 2:1 male to female ratio. EES/PNET arising in the parotid (as in our case) usually manifests as rapidly growing painful or painless mass compressing the facial nerve and causing facial nerve palsy. In high resolution CT they present as irregular mass with heterogeneity and hypodensity and with contrast enhancement, they show heterogeneous enhancement with necrotic and cystic areas. Linear enhancement occurs in 72% of tumors.⁽⁴⁾ In MRI, the tumor is isointense to muscle on T1-weighted images, while hyperintense on T2-weighted images.⁽⁹⁾

EES/PNET microscopically are indistinguishable from skeletal Ewing sarcoma; both are composed of uniform small round or oval cells containing cytoplasmic glycogen and sometimes arranged around central space filled with fibrillar extension of the cells (Homer-Wright rosettes).

Electron microscopy reveals cytoplasmic neurosecretory granules with microtubules and microfilaments in addition, short dendritic processes lie between cells in peripheral primitive neuroectodermal tumors (pPNETs) which are absent in Ewing sarcoma.^(9,10)

Histological features cannot differentiate Ewing sarcoma/PNET from other round cell tumors such as malignant lymphoma, poorly differentiated salivary gland tumors, rhabdomyosarcoma, neuroblastoma and Merckel cell carcinoma in addition to other sarcomas such as synovial sarcoma and undifferentiated pleomorphic sarcoma.^(11,12) Immunohistochemical stains are useful to exclude these differential diagnoses. CD99/MIC2 is expressed in approximately 97% of EWS/PNET, however it is also positive in acute lymphoblastic lymphoma / leukemia, alveolar rhabdomyosarcoma and granulocytic sarcoma.⁽¹³⁾ Antibody against FLI1, a nuclear stain, has been shown to be specific for EWS/PNET in the presence of CD99 positivity.⁽¹⁴⁾ The tumor cells may also express neuron-specific enolase (NSE), Synaptophysin, and S-100 protein depending on the degree of neuroectodermal differentiation.⁽¹⁴⁾ Genetic studies are also important in reaching the definite diagnosis. Approximately 90% of the tumors harbor the (11;22)(q24;q12) translocation and the remaining 10% of EWS/PNET tumors have t(21;22)(q22;q12) a translocation between EWS and another member of the ETS family, which produces an EWS-ERG fusion.⁽¹⁵⁾ PNET are highly aggressive tumors. These tumors mostly metastasize to lung, bone and bone marrow.⁽¹⁰⁾ Micrometastatic disease is demonstrated in the bone marrow by using reverse transcription polymerase chain reaction (RT-PCR) technology in up to 30% of patients who are thought to have a localized disease.⁽¹⁰⁾ These tumors mostly metastasize to lung, bone and bone marrow.⁽¹⁰⁾ In a large series of 54 patients, the rate of metastases ranges from 20–31% survival rate is less than 25%.⁽⁹⁾ Surgical excision with tumor-free margins combined with chemotherapy and radiation are the treatment of choice for PNET/EWS tumors, however complete resection of head and neck PNET/EWS can be difficult due to involvement of vital structures. The most important prognostic factors in Ewing family tumors (EFTs) include the stage, primary tumor site and size, patient age, and response to therapy.⁽¹⁴⁾ The prognosis is poor with overall 5-year and 10 year survival rates of primary sarcomas of parotid glands were 42% and 20%, respectively.⁽²⁾

Conclusion

EES/PNET are rare in the head and neck region. They are highly aggressive round cell tumors and can be differentiated from other similar round cell tumors by using immunohistochemical stains and cytogenetic analysis. Despite its rarity it should be included in the differential diagnosis of small round cell tumors of the parotid gland.

References

1. Sandhu MS, Kalra N, Singh DP, Radotra BD, Jain M, Suri S. Case report: Extraskelatal Ewing's sarcoma of the parotid gland. *Indian Journal of Radiology and Imaging*. 2000 Oct 1;10(4):227.

2. **Cockerill CC, Daram S, El-Naggar AK, Hanna EY, Weber RS, Kupferman ME.** Primary sarcomas of the salivary glands: case series and literature review. *Head & neck.* 2013 Nov 1;35(11):1551-7.
3. **Wajstaub S, Deb P, Chorneyko KA.** Undifferentiated sarcoma of the parotid gland with osseous metaplasia. *Archives of pathology & laboratory medicine.* 2002 Jul;126(7):849-52.
4. **Agir H, Brasch HD, Tan ST.** Extra-skeletal Ewing's sarcoma of the submandibular gland. *Journal of Plastic, Reconstructive & Aesthetic Surgery.* 2007 Dec 1;60(12):1345-8.
5. **Soule EH, Newton Jr W, Moon TE, Tefft M.** Extraskelatal Ewing's sarcoma. A preliminary review of 26 cases encountered in the inter group rhabdomyosarcoma study. *Cancer.* 1978 Jul;42(1):259-64.
6. **Bansal AK, Bindal R, Kapoor C, Vaidya S, Singh HP.** Current concepts in diagnosis of unusual salivary gland tumors. *Dental research journal.* 2012 Dec;9(Suppl 1):S9.
7. **Eveson JW, Cawson RA.** Salivary gland tumours. A review of 2410 cases with particular reference to histological types, site, age and sex distribution. *The Journal of pathology.* 1985 May;146(1):51-8.
8. **Xiao H, Bao F, Tan H, Wang B, Liu W, Gao J, et al.** CT and clinical findings of peripheral primitive neuroectodermal tumour in children. *The British journal of radiology.* 2016 Feb 23;89(1060):20140450.
9. **Ghosh A, Saha S, Pal S, Saha PV, Chattopadhyay S.** Peripheral primitive neuroectodermal tumor of head-neck region: our experience. *Indian Journal of Otolaryngology and Head & Neck Surgery.* 2009 Sep 1;61(3):235-9.
10. **Stafford EM, Honrado CP, Moscatello AL, Wilson YL, Weissbrod PA.** Primitive neuroectodermal tumors. Available at: emedicine.medscape.com/article/855644-overview. Accessed May. 2010;5.
11. **Agrawal G, Gupta A, Chaudhary V, Mazhar H and Tiwari S.** Undifferentiated Pleomorphic Sarcoma of Submandibular Gland- A Rare Case Report. *J Sarcoma Res.* 2017; 1(1): 1003
12. **Kota Nagappa D, Krishnamurthy J.** FNAC of Extra-Skeletal Ewing's Sarcoma of the Parotid Gland. *Iranian Journal of Pathology.* 2011 Sep 1;6(4):208-11.
13. **Jayakumar S, Power D.** Ewing's sarcoma/PNET: A histopathological review. *Internet J Orthop Surg.* 2006;3:1-9.
14. **Desai SS, Jambhekar NA.** Pathology of Ewing's sarcoma/PNET: Current opinion and emerging concepts. *Indian journal of orthopaedics.* 2010 Oct; 44(4):363.
15. **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 Cytopathology: Interdisciplinary International Journal of the American Cancer Society.* 2007 Jun 25; 111(3):192-9.