

Ewing's sarcoma of larynx: Report of a rare case with review of literature

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Citation

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Abstract

Primitive neuroectodermal tumors (PNETs) are a group of highly malignant tumors composed of small round cells of neuroectodermal origin that affect soft tissue and bone. Most peripheral primitive neuroectodermal tumors (pPNETs) manifest in the thoracopulmonary region (Askin tumor), pelvis, abdomen, and extremities and reveal a paucity of cases in the head and neck. The treatment of these is also not well defined. Here, we present a case report with aim of organ preservation.

INTRODUCTION

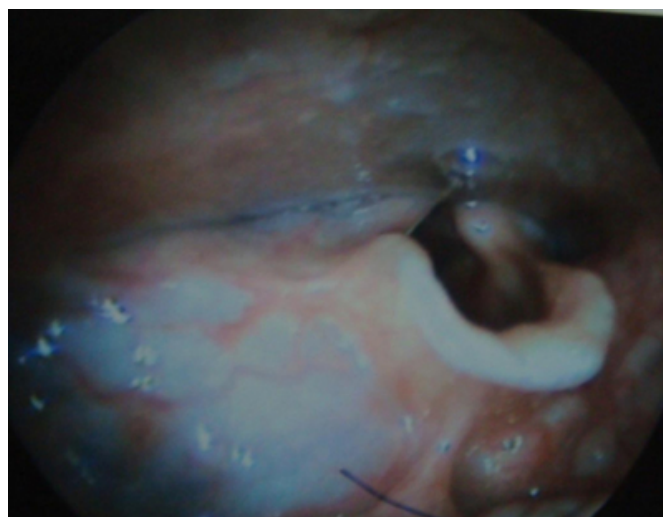
Primitive neuroectodermal tumors (PNETs) are a group of highly malignant tumors composed of small round cells of neuroectodermal origin that affect soft tissue and bone. Here we present a case study of malignant peripheral primitive neuroectodermal tumor (p PNET) presenting in larynx in a young 27-year-old female. The mode of presentation and management of this case with a review of literature is discussed in brief here.

CASE REPORT

A 27-year-old female presented with progressively increasing hoarseness for 3 months. She also had difficulty in swallowing for one month. On flexible nasopharyngoscopy a smooth globular mass was seen in right vallecula and pyriform sinus pushing epiglottis towards the left side. (fig.1) CT scan showed a moderately large soft tissue mass in right pyriform sinus with involvement of right paralaryngeal space and ipsilateral vocal cord, highly suggestive of neoplastic process.

Figure 1

Figure 1 - tumor at presentation



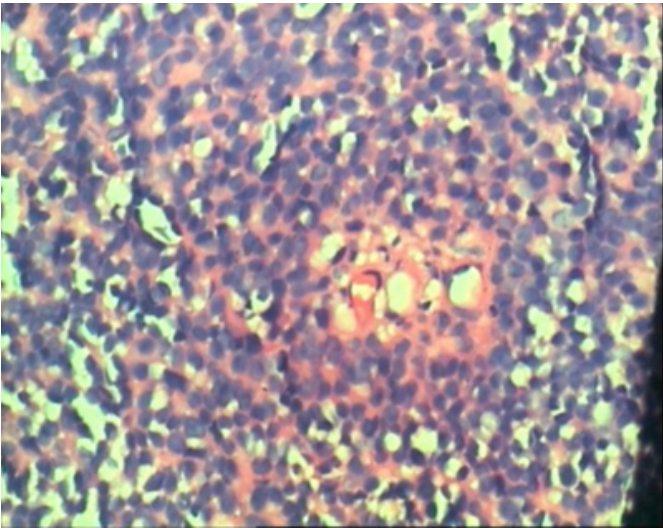
Direct laryngoscopy was performed which showed a tumor in right vallecular region pushing epiglottis, aryepiglottic fold into midline. The tumor was smooth, globular & firm. Capsule over the tumor was dissected and biopsy from deeper tissues was taken.

Histopathological examination revealed tumour within the submucosa arranged as sheets, nests, and ill formed acini with short cords. The small neoplastic cells exhibited enlarged pleomorphic and hyperchromatic nuclei with a coarse granular to stippled chromatin pattern (fig.2). Immunohistochemistry revealed malignant round cell tumour infiltrating fibrous tissue. It was strongly positive for mic-2 and negative for chromogranin, synaptophysin, CK &

p63. Bone marrow biopsy was done which showed normocellular bone marrow. Ultrasonogram of abdomen & pelvis was reported normal.

Figure 2

Figure 2 - microscopic picture (H & E)



On positron emission scan there was evidence of metabolically active disease (primary) at vallecula on the right side with metastasis to the right upper deep cervical lymph node.

Patient was started on chemotherapy EFT (Ewing's family of tumors) 2001 PROTOCOL for 8 cycles (Table 1) over a period of 3 months and, after one month she was started on radiotherapy. During radiotherapy course the patient was given injection vincristine (2 mg i.v bolus) weekly. Radiotherapy was given 50.4 Gy/28 fractions over 43 day’s period. Patient was given one more cycle of chemotherapy after one week of completion of radiation with Ifosfamide, Vincristine, Etoposide & Mesna, following which she was given 8 bolus doses of injection vincristine at a weekly interval. The primary growth disappeared along with cervical lymph node completely (fig. 3) at the end of the therapy. Repeat CT scan was performed after completion of therapy, showing disappearance of the tumor and no lymphadenopathy. Patient is disease free for 6 months post completion of all treatment & is under regular follow-up and serial endoscopic evaluation at monthly intervals.

Figure 3

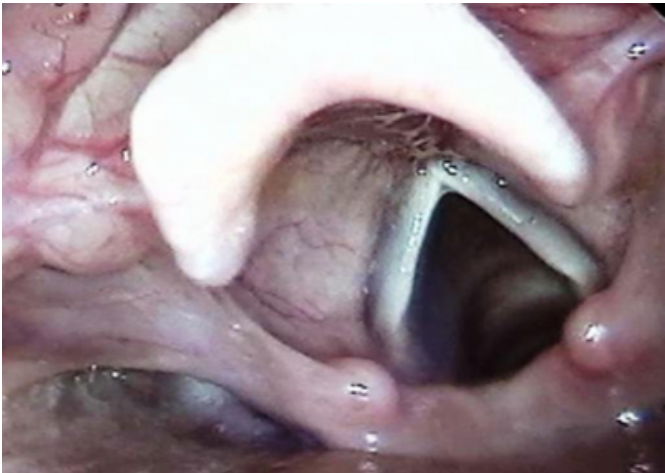
Table1. Ewing’s Family of Tumor EFT-2001 Protocol

WEEK	0	1	2	3	4	5	6	7	8
	V	V	V	V	V	V	V	V	V
	I			I			A		A
	E			E			C		C
CYCLE	1			2			3		4

Using Vincristine(V), Ifosfamide(I) and Etoposide(E)

Figure 4

Figure 3 – post treatment : tumor mass disappeared completely



DISCUSSION

Primitive Neuroectodermal Tumors are a group of highly malignant tumors composed of small round cells of neuroectodermal origin.

Batsakis et al (1996) divided the PNET family of tumors into the following 3 groups based on the tissue of origin.¹

CNS PNETs - Tumors derived from the central nervous system

Neuroblastoma - Tumors derived from the autonomic nervous system

Peripheral PNETs (pPNETs) - Tumors derived from tissues outside the central and autonomic nervous system.

pPNETs are also classified as part of the Ewing family of tumors (EFTs). PNETs and EFTs are often referred to interchangeably in the literature. Ewing sarcoma, however, is more common in bone, while PNETs are more common in soft tissues. Immunohistochemical and cytogenetic studies suggest that all these tumors have a common origin. Stout

first described PNETs in 1918, and these tumors were thought to arise directly from nerves.² Based on molecular cytogenetic analysis, both Ewing's sarcoma and pPNETs are known to share the same reciprocal translocations, most commonly between chromosomes 11 and 22. Further advances in immunohistochemical analyses have helped further distinguishing PNETs and Ewing's sarcoma from other small, round, poorly differentiated tumors, including rhabdomyosarcoma, neuroblastoma, and lymphoma. PNETs often exhibit aggressive clinical behavior, with worse outcomes than other small, round cell tumors. Most peripheral primitive neuroectodermal tumors (pPNETs) manifest in the thoracopulmonary region (Askin tumor), pelvis, abdomen, and extremities. In a large series of 26 cases, Jones and McGill reported 11 of 26 patients with disease in the head and neck.³ Most other large published series, however, reveal a paucity of cases in the head and neck.^{4,5,6} Of the published cases involving the head and neck, the sites of presentation are diverse, including, but not limited to, the paranasal sinuses, jugular foramen, oral cavity, nasal cavity, neck, skull, lingual nerve, parotid gland, larynx, retropharyngeal space, masseter, temporal area, pterygomaxillary space, and orbit.

On light microscopy, PNETs appear as a monotonous collection of small, round, darkly stained cells. However, PNETs cannot be distinguished from other tumors with small round cells based on histological studies alone. Other tumors with a similar appearance on light microscopy include rhabdomyosarcoma, neuroblastoma, and non-Hodgkin lymphoma.

Cytogenetic analyses of PNETs reveal the close relationship among tumors in the Ewing family of tumors (EFTs). Approximately 95% of all EFTs include a translocation that involves the EWS gene on chromosome 22 band q12 and other chromosomes, most commonly chromosome 11. The expression of the MIC2 gene produces an antigen, MIC2, which consistently identifies both Ewing's sarcoma and PNETs.

Obtaining a complete resection of disease with negative margins is of paramount importance in surgically treating

primitive neuroectodermal tumors (PNETs) in the head and neck. In some cases, however, the aggressive nature and diffuse spread of these tumors preclude complete surgical excision. Chemotherapy and radiation are necessary adjuncts in the treatment of primitive neuroectodermal tumors (PNETs).

Current recommendations include neoadjuvant chemotherapy with surgical excision or radiotherapy followed by adjuvant chemotherapy. The most significant prognostic factor is the presence or absence of metastatic disease, with the former group of patients having a dismal long term prognosis. Despite advances in chemotherapy and radiotherapy regimens, cure rate in patients with metastatic disease remains dismal (20%). Significant advances in the neoadjuvant and adjuvant chemotherapeutic regimens, as well as improved facility in diagnosing these tumors through cytogenetic and immunohistochemical analysis, should improve long-term disease-free survival.

ABBREVIATIONS

PNET - Primitive neuroectodermal tumor

EFT - Ewing family of tumors

pPNET - peripheral primitive neuroectodermal tumors

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