Ewing's sarcoma of the trachea in an adolescent girl

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Primitive neuroectodermal tumors (PNET) are aggressive neoplasms of neuroectodermal origin. Although they are known to arise in a host of locations, involvement of the trachea has rarely been reported. We describe an adolescent girl who presented with stridor and was diagnosed with PNET of the trachea. She is in remission following treatment with combination chemotherapy and local radiotherapy.

Primitive neuroectodermal tumors (PNET) are a heterogeneous group of highly malignant neoplasms of neuroectodermal origin. Largely a disease of children and adolescents, PNETs have been diagnosed across all age groups. Most often, PNETs arise in the chest wall, paravertebral region, retroperitoneum, and extremities. PNET of the trachea is exceedingly rare, with only a few reported cases (1–3). Here we report the case of a 14-year-old girl who presented with stridor and was eventually diagnosed with PNET of the trachea.

CASE PRESENTATION

A 14-year-old girl presented to us with a 6-month history of dry cough and dyspnea. She also gave a history of significant weight loss and dysphagia for solids for the past 2 months. On examination, she had an Eastern Cooperative Oncology Group performance status of 1, and chest examination revealed bilateral rhonchi. Computed tomography of the thorax showed a well-enhancing homogenous mass of $16 \times 20 \times 15$ mm arising from the anterior and left lateral wall of the trachea with intraluminal extension causing airway narrowing, and it was seen extending to the left paratracheal region *(Figure 1)*. A fiber optic bronchoscope–assisted biopsy was done. Histopathology showed a neoplasm composed of sheets of atypical small round cells beneath the respiratory epithelium. The tumor cells were positive for MIC2 membrane staining and for pan cytokeratin (AE1/AE3). Other markers like desmin, myogenin, and synaptophysin were negative. The morphological and immunohistochemical profile was consistent with the diagnosis of PNET *(Figure 2)*. Staging evaluation including computed tomography scan of the abdomen, Technetium^{99} bone scan, and bone marrow biopsy were normal.

The patient was started on chemotherapy with vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide (VAC/IE). At 12 weeks of chemotherapy, she received intensity-modulated radiation therapy to the primary site at a dose of 55 Gy given over 30 fractions. She has completed 1 year of chemotherapy and is presently on follow-up.

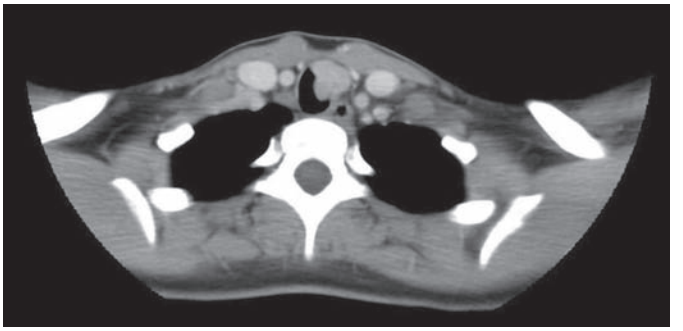

Figure 1. CT of the thorax showing a moderately enhancing soft tissue lesion involving the left anterolateral wall of the trachea at the T3 vertebral level causing luminal narrowing.

DISCUSSION

PNETs are aggressive small round cell tumors of neural crest lineage, coming within the ambit of the Ewing's sarcoma family of tumors (ESFT). The median age at diagnosis is 19.5 years, and 30% of patients present with metastatic disease. Compared with patients with skeletal ESFT, patients with extraskeletal ESFTs are more likely to be older and female and to have tumors in axial locations (4). Clinical features are often site specific, with swelling and pain being the most common presentations.

There have been very few reported cases of tracheal PNETs. One case described a young male presenting with stridor and hemoptysis caused by a PNET arising in the distal trachea. After initiating chemotherapy with the VAC/IE regimen, the tumor was resected and adjuvant radiation with 50.4 Gy over 28 fractions was administered, followed by completion of the planned chemotherapy (1). In another case of tracheal PNET

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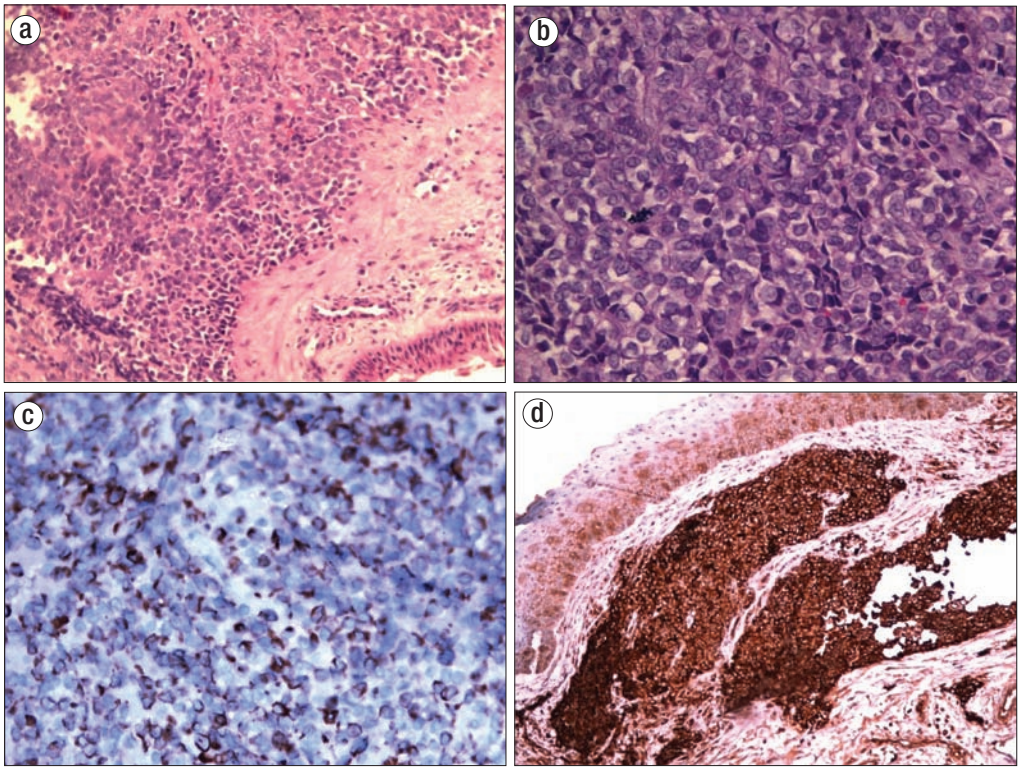

Figure 2. Biopsy sections. Sheets of small round cells (hematoxylin and eosin) at **(a)** 200× and **(b)** 400×. **(c)** Paranuclear dot and cytoplasmic staining with pan cytokeratin (AE1/AE3). **(d)** Strong membranous staining with CD99.

in an elderly man presenting with respiratory obstruction, the patient was treated only with resection and radiotherapy in view of his comorbidities. He had a relapse at distant sites 3 months after completing treatment (2). A 63-year-old woman with a tumor on a pedicle in the trachea, causing obstruction, was treated with surgery alone and was disease free at 14-month follow-up (3).

Differentiating ESFT from other small round cell tumors is important, given the difference in therapy. The close differential diagnoses are neuroblastoma, rhabdomyosarcoma, lymphoma, and small cell osteosarcoma. Folpe et al, in their analysis of 56 cases of genetically confirmed ESFT, noted that CD99 was positive in all cases (5). Currently, the demonstration of a chromosomal translocation between Ewing Sarcoma Breakpoint Region 1 gene and members of the E26 transformation-specific gene family is the gold standard for the diagnosis of ESFT. The t(11; 22) (q24; q12), which fuses Ewing Sarcoma Breakpoint Region 1 to Friend Leukemia Integration 1 gene, is the most common, being present in 85% to 90% of cases (6). In our patient, both MIC2 and pan cytokeratin were positive, and neurogenic and myogenic markers were negative. This helped exclude close differentials like rhabdomyosarcoma, neuroblastoma, and lymphoma and pointed towards a diagnosis of PNET.

The landmark first North American Intergroup Ewing's Sarcoma study established vincristine, actinomycin D, cyclophosphamide, and doxorubicin as the most active agents in the systemic therapy of ESFT (7). Incorporation of ifosfamide and etoposide to this backbone was demonstrated to further improve survival in nonmetastatic ESFT (8). At present, the 5-year overall survival and disease-free survival rates in nonmetastatic ESFT in adults are 52% and 34%, respectively (9).

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