CASE REPORT

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ENDODERMAL SINUS TUMOR OF THE PARANASAL SINUSES

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Abstract: Background. We report a rare case of endodermal sinus tumor (EST) of the paranasal sinus in a 59-year-old man with a 6-week history of nasal obstruction.

Methods and Results. High-resolution MRI showed a right nasoethmoid mass with obstructive changes in the sphenoid, frontal, and right maxillary sinuses and orbital and intracranial extension. Histologic analysis showed 2 distinct histologic features: poorly differentiated carcinoma and EST. Immunohistochemical studies showed strong keratin staining in both components and restricted positivity of alpha-fetoprotein in the endodermal sinus-like component. The patient underwent 3 cycles of neoadjuvant chemotherapy consisting of ifosfamide, paclitaxel, and cisplatin, which resulted in significant regression of the tumor, but after the fourth cycle, the mass showed a slight increase in size. The tumor was excised with clear margins through an anterior craniofacial approach to the skull base. Histologic examination of the resected specimen showed extensive fibrosis with residual areas of viable tumor composed mainly of the poorly differentiated component with only residual microscopic foci of EST. Adjuvant postoperative intensity-modulated radiation therapy was administered. At 1-year follow-up, the patient was tumor free, with normal alpha-fetoprotein levels.

Conclusion. Because of the rarity of this entity, no standardized treatment protocol has been defined. The involvement of the anterior skull base in our case necessitated a radical craniofacial resection, despite a partial response to chemotherapy.

Keywords: skull base; germ cell tumor; craniofacial resection; paranasal sinuses; endodermal sinus tumor

Endodermal sinus tumor (EST) is an uncommon malignant germ cell tumor that originates mainly from the gonads, and only 20% are encountered in extragonadal sites. Other terminologies used to describe EST are yolk sac tumor, teratocarcinoma, and germ cell tumor. EST at extragonadal sites is rare and may be difficult to recognize. Of the extragonadal sites, the sacrococcygeal region, vagina, retroperitoneum, liver, head and neck region, central nervous system, and mediastinum have been documented.1 Of the various head and neck sites, EST is found most frequently in the neck.2 EST arising in the sinonasal region is a rare occurrence, with only 8 such examples reported in the English-language literature. This tumor is well known to secrete basic fetal markers such as alpha-fetoprotein and human chorionic gonadotrophin and is highly chemosensitive. The present case of paranasal sinus involvement is the ninth reported case and the second one with the intracranial extension involving the anterior skull base. A review of all
reported cases of EST is presented to highlight the clinical presentation, management, and outcome of this rare neoplasm.

CASE REPORT

The patient was a 59-year-old man with a 6-week history of nasal obstruction who was seen with a sinonasal mass. High-resolution MRI showed malignant-appearing right nasoethmoid mass with obstructive changes in the sphenoid, frontal, and right maxillary sinuses as well as orbital and intracranial extension (Figure 1A). Endonasal biopsy was performed, and initial histopathological examination of the tumor at a different facility rendered a diagnosis of poorly differentiated carcinoma with sarcomatoid features. Reevaluations at our institution revealed 2 distinct histologic features: (1) poorly differentiated carcinoma composed of solid sheets of cohesive malignant epithelial cells; and (2) EST (yolk sac tumor) (Figures 2A and 2B). The latter was composed of lace-like tumor cords with pseudoglandular and the characteristic “Schiller Duval” bodies. Subsequent immunohistochemical studies showed strong keratin
staining in both components and restricted positivity of α-fetoprotein in the endodermal sinus-like component (Figures 2C and 2D). Human chorionic gonadotropin immunostaining was performed and showed negative staining in both tumor components. The patient received 3 cycles of neo-adjuvant chemotherapy consisting of ifosfamide, paclitaxel, and cisplatin. Significant regression of both the tumor mass and the levels of α-fetoprotein were seen (Figure 3), and the patient reported significant improvement of his symptoms. Imaging obtained after induction chemotherapy showed significant reduction of tumor size, particularly intracranially (Figure 1B). However, 1 month after completing his fourth chemotherapy cycle, the levels of α-fetoprotein started to rise again, and the tumor mass showed slight increase in size (Figures 1C and 3). The systemic workup did not reveal any distant metastasis. Surgical resection was recommended.

Complete tumor excision was performed through anterior craniofacial approach to the skull base. The extracranial approach included a right lateral rhinotomy, medial maxillectomy, anterior and posterior ethmoidectomy, bilateral sphenoidotomy, partial septectomy, medial orbitectomy, and right dacrocystorhinostomy. The intracranial approach included a bifrontal craniotomy and resection of cribriform plate and fovea ethmoidalis. The margins of resection were found to be free of the tumor. Histologic examination of the resected specimen showed extensive fibrosis with residual areas of viable tumor composed mainly of the poorly differentiated component with only residual microscopic foci of EST. Postoperatively, the patient had excellent recovery, and his α-fetoprotein levels dropped from a preoperative level of 75 units to only 8 units after surgery (Figure 1D). Adjuvant postoperative radiation therapy was administered using intensity modulated radiation therapy. On the patient’s 1 year follow-up visit, he was tumor free and his α-fetoprotein levels remain normal (Figure 3).

DISCUSSION

Germ cell malignancies are a heterogeneous group of neoplasms that include germinoma, malignant teratoma, embryonal carcinoma, EST, and cholangiocarcinoma. Germ cell tumors arising in the head and neck constitute approximately 5% of all gonadal and extragonadal germ cell tumors in children. Only a small percentage of these are yolk sac tumors, and their occurrence in the paranasal sinus region is extremely rare, especially in adults. Of the 8 previously reported cases of EST involving the paranasal sinus, 7 have been in children. Our case is the second in an adult. Although head and neck ESTs have in general shown a predilection for children and female sex, we have found a male predominance in EST involving the paranasal sinuses (Table 1).

Four distinct histopathologic types of EST have been described, namely, pseudopapillary, reticular, polyvesicular vitelline, and solid. Pseudopapillary pattern is the classical pattern associated with the characteristic “Schiller Duval” bodies (arrays of a single row of tumor cells about a blood vessel that in turn being surrounded by a cystic space), although several patterns may exist in various areas within a single tumor. Despite this polymorphic histopathologic appearance, EST consistently shows positive immune reactivity to cytokeratin antibodies on immunohistochemistry. Although not characteristic, certain chromosomal abnormalities (particularly chromosomes 1, 3, and 6) have been described in EST. ESTs are thought to arise either from primordial germ cells that have migrated improperly during embryonic development, or from undifferentiated pluripotent embryonic or extraembryonic cells that have escaped the influence of primary developmental factors. Friedman suggested that germ cells are present in apparently ectopic sites in all humans. The notion that ESTs develop by malignant transformation of primordial germ cells is not supported by cases in
which malignant tumors occur in the absence of teratomatous elements, especially in the gastrointestinal tract, kidney, and urinary bladder. Furthermore, since animal experiments have induced EST in the absence of primordial germ cell, it is argued that somatic cells can be induced to differentiate into structures resembling fetal yolk sac. Also, in a series of teratocarcinosarcomas of the nasal cavity and paranasal sinuses, the pathologic descriptions suggested that these tumors apparently exhibit a spectrum of somatic tissue differentiation. In our case report, histopathologic examination of the resection specimen after induction chemotherapy revealed the residual tumor to be mainly poorly differentiated carcinoma, suggesting that the germ cell component was more responsive to induction chemotherapy. Similar findings were suggested by Manivel et al.

Extragonadal germ cell tumors of head and neck in general and the sinonasal region in particular have a poor prognosis because they are usually unresectable at diagnosis. EST tends to recur locally and is usually associated with a high incidence of metastasis to lung, liver, regional lymph nodes, and bone at the time of diagnosis. Although alpha-fetoprotein is a characteristic marker for EST, it is also elevated in adult patients with hepatocellular and pancreatic carcinomas. In patients with EST, serum alpha-fetoprotein levels may be used as a prognostic marker predicting recurrence, residual disease, and metastatic disease.

The treatment strategy of EST depends on the site and stage of the tumor. Surgical excision is the treatment of choice for patients with localized or adjacent tumors, and induction or adjuvant chemotherapeutic responses are beneficial in surgically inaccessible regions. Radiotherapy may be beneficial in surgically inaccessible regions while those with residual disease may require salvage chemotherapy. Patients with advanced or disseminated disease may benefit from systemic chemotherapy. Aziz suggested that aggressive chemotherapy is indicated in recurrent cases. Prognosis has improved considerably with the development of advanced cases. Prognosis has improved considerably with the development of advanced cases. Although alpha-fetoprotein is a characteristic marker for EST, it is usually elevated in adult patients with hepatocellular and pancreatic carcinomas. In patients with EST, serum alpha-fetoprotein levels may be used as a prognostic marker predicting recurrence, residual disease, and metastatic disease.

Table 1. Reported cases of endodermal sinus tumor in paranasal sinus.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Ref.</th>
<th>Age, y</th>
<th>Sex</th>
<th>Anatomic sites</th>
<th>Histopathology</th>
<th>Lab</th>
<th>Mets</th>
<th>Treatment</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>3</td>
<td>F</td>
<td>Nasal cavity, MS, PPF, Orb, Ethm, Crib-plate</td>
<td>EST</td>
<td>AFP, Ctk</td>
<td>CT (4 cycles)</td>
<td>CR, Survival = 10 mo (DOD)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>4; D = 2 mo</td>
<td>M</td>
<td>Nasal cavity, MS, Orb</td>
<td>EST</td>
<td>AFP</td>
<td>CT + RT (46 Gy)</td>
<td>CR, Survival = 17 y (alive NED)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>1.5; D = 5 mo</td>
<td>M</td>
<td>Nasal cavity, MS, palate, Nasopharynx</td>
<td>Terratoma with prominent EST</td>
<td>AFP</td>
<td>Surg. Debulk + CT (1 cycle)</td>
<td>Alive but LF</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>2.5</td>
<td>M</td>
<td>MS, palate, oral cavity,</td>
<td>Undifferentiated germ cell tumor</td>
<td>AFP</td>
<td>CT (4 cycles)</td>
<td>CR, Survival = 3 y (alive NED)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8</td>
<td>3</td>
<td>F</td>
<td>PNS, nasopharynx</td>
<td>EST (mature teratoma excised in neonatal period)</td>
<td>AFP</td>
<td>Surgery, CT, RT</td>
<td>PR Survival = 1.5 y (DOD)</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>4</td>
<td>M</td>
<td>MS, Nasal cavity, cheek</td>
<td>EST</td>
<td>–</td>
<td>CT + RT (45 Gy)</td>
<td>CR, Survival = 5.7 y (NED)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>10</td>
<td>43</td>
<td>M</td>
<td>MS, Ethm, Frontal sinus, Orb, MS</td>
<td>EST with transitional cell (cylindric) carcinoma</td>
<td>–</td>
<td>Lung Surgery (+CFR) + CT + RT (66 Gy)</td>
<td>PR, Survival = 1.5 y (Putm. mets)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>10 mo</td>
<td>F</td>
<td>MS, Ethm, Orb, SB, BPF, ITF, RT, TMJ, MCC, palate, nasopharynx</td>
<td>EST</td>
<td>–</td>
<td>Nil</td>
<td>Survival = 1 mo (DOD)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: D, duration; PNS, paranasal sinus; MS, maxillary sinus; PPF, pterygopalatine fossa; ITF, infratemporal fossa; BPF, base of pituitary fossa; SB, sphenoid bone; TMJ, temporomandibular joint; Ethm, ethmoids; Crib-plate, cribiform plate; MCC, middle cranial cavity; AFP, alpha-fetoprotein; Ctk, cytokeratin; CR, complete remission; CT, chemotherapy; RT, radiotherapy; LF, lost to follow-up; DOD, dead of disease; NED, no evidence of disease; CFR, craniofacial resection; Pulm. mets, pulmonary metastasis.
and hence better suited for advanced disease.21 Because of rarity of this entity, a standardized treatment protocol has not yet been defined. Hence, the response to the treatment of germ cell tumors in general has been quite variable considering their polymorphic histology, multiple locations, variable biology, and different stages and ages of presentation. Despite partial response to chemotherapy, involvement of the anterior skull base in the current case necessitated a radical craniofacial resection. Only 1 other adult case with involvement of the skull base was previously reported (no. 7 in Table 1).

A study of potential prognostic factors in multivariate analysis has shown that only the extent of disease is an important variable associated with the final outcome of germ cell tumors.22 Surprisingly, Aziz reported that metastasis to lymph nodes is not related to prognosis.21 However, the presence and size of residual tumors after surgery were closely related to prognosis. It is noteworthy that both cases (ours and case no. 7) with anterior skull base involvement revealed an association of a carcinomatous element. Whether such “hybrid” histology is more prone to occur in adults with skull base involvement or predisposes to a worse outcome remains unknown.

REFERENCES