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Sinonasal teratocarcinosarcoma with yolk sac elements: a neoplasm of somatic or germ cell origin?

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Abstract Sinonasal teratocarcinosarcoma is an uncommon, aggressive, morphologically heterogenous tumor composed of cells derived from the 3 somatic layers. A histogenetic origin from a multipotential adult somatic stem cell with divergent differentiation has been favored over a germ cell origin. This assumption has been based on the lack of germ cell elements and, until recently, the absence of demonstrable amplification of 12p. We report a case that exhibited foci of yolk sac elements with papillary structures and intracytoplasmic periodic acid-Schiff–positive, diastase-resistant, α-fetoprotein–positive, hyaline globules. An expanded area of undifferentiated cells, likely precursor cells, in the basal layer of the overlying mucosal epithelium transitions into and merges with the immature epithelial, neuroepithelial, and mesenchymal components. These previously unreported histomorphological features support the hypothesis that this tumor is a teratomatous tumor arising from pluripotent embryonic stem cells in the basal layer of the sinonasal epithelium. That notion is further supported by fluorescence in situ hybridization cytogenetic analysis, which showed a distinct subpopulation of the tumor cells with an extra copy of chromosome 12p13.

Keywords: Sinonasal teratocarcinosarcoma; Yolk sac; Germ cell origin

1. Introduction

Sinonasal teratocarcinosarcoma (SNTCS) is an uncommon highly aggressive malignant tumor that is morphologically heterogeneous and composed of cells of different somatic layers, ectodermal, mesenchymal, and endodermal, with varying degrees of malignant differentiation [1-4]. The origin of this tumor remains controversial, although histogenesis from a multipotential adult somatic stem cell with divergent differentiation has been suggested. This assumption has been based on the lack of germ cell elements such as yolk sac elements, germinoma, embryonal carcinoma, or choriocarcinoma, and recently, on the absence of demonstrable amplification of 12p, usually isochromosome 12p (i12p) often associated with tumors of germ cell origin [5].

The ectodermal and endodermal components have variably included squamous, immature neuroepithelium, and glandular elements with or without mucin secretions. The mesenchymal components have included smooth muscle, chondromatous, and rhabdomyoblastic areas with primitive and sarcomatous features. However, in most reported series, no germinoma, embryonal carcinoma, choriocarcinoma, or yolk sac elements have been demonstrated, hence, the assumption that SNTCS is a tumor that arises from multipotential (adult) somatic stem cells. Based on these findings and the lack of i12p, this tumor has been considered unlikely to be of germ cell origin, even though 2 case reports have immunohistochemically documented the presence of few α-fetoprotein (AFP)–positive cells [2,6]. However, a recent report that documented the finding of trisomy 12 in a case of SNTCS with a subclone of cells showing loss of 1p [6] supports the possibility that the tumor is of pluripotential embryonic stem/germ cell origin.

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We present a case report of SNTCS with foci of yolk sac elements, AFP-positive hyaline granules, and area of proliferating undifferentiated basal layer cells of the respiratory epithelium transitioning into primitive clusters of tumor cells and merging with areas of epithelial, neuroepithelial, and mesenchymal elements. Fluorescence in situ hybridization (FISH) cytogenetics for chromosome 12p amplification was also studied.

2. Clinical history

The patient is a 51-year-old woman who presented with proptosis and an enlarging nasal mass protruding from her right nasal vestibule, which she noticed 4 to 5 months before presentation. Her history was significant for progressive right-sided blurry vision, nasal airway obstruction, anosmia, and intermittent rhinorrhea.

On examination, her right eye was proptotic with restriction of medial gaze, and a tan-colored firm mass was seen extruding from the right nasal cavity. Computed tomography images revealed a large nasal mass involving the entire right nasal cavity, displacing the septum laterally and extending into the cribriform area of the skull base and anterior cranial fossa displacing the right orbital contents and medial rectus muscles. The mass measures approximately 56 × 41 mm, involves the frontal and sphenoid sinuses, and erodes the medial wall of the left maxillary sinus. Examination under anesthesia revealed a hemorrhagic solid brown mass with extensive necrosis filling the entire nasal cavity; only the inferior turbinate was identifiable. An initial incisional biopsy of the mass was done, and the patient subsequently underwent a craniofacial resection and postoperative radiotherapy.

3. Pathologic findings

The surgical resection specimen consists of grossly irregular, fragmented hemorrhagic, friable necrotic mass. Microscopic examination showed that most of the viable and diagnostic tissue was present in the initial biopsy specimen and consists of variable epithelial, neuroepithelial, and mesenchymal elements as well as undifferentiated, primitive cellular component. Numerous nests of benign squamous clusters with cytoplasmic vacuolation reminiscent of fetal oral squamous mucosa were identified (Fig. 1A). Collars of primitive myxoid mesenchyme, fibrocollagenous stroma, and sarcomatous stromal cells surround some islands of squamous epithelium. Epithelial glandular differentiation with acinar, tubular, and ductal structures is demonstrated with mucin present in some of the glandular epithelium (Fig. 1B). These are strongly positive with cytokeratin, AE1/AE3, with predominant CK7 staining and focal CK20 positivity. A range of benign to malignant mesenchymal areas is seen with focal fibrous area, hyalinized osteoid-like tissue, chondromyxoid foci, and undifferentiated sarcomatous areas with skeletal muscle differentiation, positive with desmin (Fig. 1C, D). The primitive undifferentiated areas (Fig. 1E) also stained positive with neuron-specific enolase, synaptophysin, and chromogranin. Primitive neural areas with background neurofibrillary matrix and glial cells were present (Fig. 1F); focus of immature neuroepithelium with poorly formed tubular structures was also noted, and it stained strongly positive with CD56 and synaptophysin.

An area of malignant papillary structures reminiscent of yolk sac elements was identified, with central vascular core and outer layer of epithelium. Intracytoplasmic periodic acid-Schiff–positive, diastase-resistant hyaline globules, which were also AFP positive, were present within some of the epithelial cells (Fig. 2A-D). Placental alkaline phosphatase, human chorionic gonadotropin, and CD30 immunohistochemical stains were negative. Focally positive S100 dendritic cells are present, scattered in the squamous islands. CD99 shows strong cytoplasmic dotlike pattern and membrane cytoplasmic staining in spindle cell and epithelial areas, respectively.

An expanded area composed of undifferentiated clusters of cells was seen in the basal layer of the overlying respiratory epithelium. These basal cellular clusters were morphologically similar to the undifferentiated components of the tumor and merge with the immature neural fibrillary tissue and primitive undifferentiated cells in the underlying stroma (Fig. 3A and B).

4. Fluorescence in situ hybridization

Fluorescence in situ hybridization was done for evaluation of chromosome 12, particularly the presence of an isochromosome (i12p). Fluorescence in situ hybridization analysis using a locus-specific probe for the short arm of chromosome 12 (12p13/ETV6) is predominantly normal for copy number of chromosome 12 and 12p13. However, a subpopulation in the tissue shows an extra copy of 12p13 in approximately 9% of the cells evaluated (87/967). Despite the suboptimal nature of the tissue sections for FISH analysis, 3 copies of 12p are distinct in this subpopulation of cells. Using a pericentromeric probe for chromosome 12, the copy number of chromosome 12 is abnormal in approximately 7% of cells (35/482).

5. Discussion

Sinonasal teratocarcinosarcoma is a rare highly aggressive tumor with heterogeneous architectural patterns and is also composed of derivatives of the different 3 germ cell layers, that is, ectoderm, mesoderm, and endoderm. The tumor often manifests both benign and malignant components with the carcinomatous component being predominantly adenocarcinoma and squamous cell carcinoma. In view of the multiplicity of structures and pleomorphism