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Case study

Desmoplastic small round cell tumor of the submandibular gland—a rare but distinctive primary salivary gland neoplasm

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Summary: Desmoplastic small round cell tumor is a highly aggressive neoplasm that generally involves the peritoneum and pelvis of young patients. Only rare cases occur outside the abdomen. We report a case presenting as a primary submandibular gland tumor in a 24-year-old man. Histologically, although there were irregular tumor islands lying in an abundant desmoplastic stroma, there were also areas comprising large cellular islands with scanty stroma in between, raising the differential diagnosis of various salivary gland carcinomas. The tumor cells were medium sized, with hyperchromatic nuclei and moderate amounts of cytoplasm. The diagnosis of desmoplastic small round cell tumor was confirmed by the presence of a polyphenotypic immunoprofile (positive for cytokeratin, desmin, and neuron-specific enolase) and the characteristic *EWS-WT1* gene fusion. Although rare, desmoplastic small round cell tumor has to be considered in the differential diagnosis of poorly differentiated neoplasms of the salivary gland, especially in young patients.

1. Introduction

Desmoplastic small round cell tumor (DSRCT) is a rare and highly aggressive tumor first characterized by Gerald et al [1] in 1991. It typically affects young patients (mean age, 22 years) with male predilection, who present with widespread intra-abdominal paraserosal masses [2], and the tumors can involve abdominal or genital organs such as the kidney [3], pancreas [2,4], liver[2], spleen [2], ovary [5], cervicovaginal region [6], and testis and paratesticular region [2,7]. Extra-abdominal DSRCT is rare, with cases reported in the brain [2,8], lung [9], pleura [2], nasal cavity and paranasal sinuses [10,11], and soft tissue and bone [10,12]. To our knowledge, only 2 cases have been reported to occur in the salivary gland in the English-language literature [13,14]. We report a case presenting in the submandibular gland, discuss the value of molecular studies in confirming the diagnosis, and summarize the features of DSRCT of the salivary gland.

2. Case report

A previously healthy 24-year-old man presented with a right submandibular mass that had been growing rapidly for 1 month. Computed tomography revealed a well-demarcated

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homogeneous mass measuring 4 cm in the right submandibular gland, without destruction of the surrounding tissues (Fig. 1). Physical examination, abdominal computed tomography, and whole-body positron emission tomography scan revealed no tumor elsewhere. After total submandibulectomy, the patient received chemotherapy and radiotherapy and was well with no evidence of recurrence at 7 months.

3. Materials and methods

3.1. Histochemical and immunohistochemical staining

The tissue was fixed in 10% buffered formalin and processed as usual for paraffin embedding. Paraffin sections were stained with hematoxylin-eosin and mucicarmine. Immunohistochemical staining was performed using the BOND-MAX automated immunostainer (Vision Biosystems, Leica, Australia), with a polymer-based detection system. The antibodies are shown in Table 1. The antigen retrieval method was heat-induced epitope retrieval in EDTA at alkaline pH (pH 8.0).

3.2. Molecular analysis

Dual-colored fluorescence in situ hybridization (FISH) was performed on paraffin section using *EWS* break-apart probe (Vysis; Abbott Molecular, Des Plaines, IL, USA), where splitting of a normally fused red and green signals into separate red and green signals indicates presence of *EWS* gene translocation. The slide was viewed under a Nikon fluorescent microscope using appropriate filters (ECLIPSE E600, Nikon, Tokyo, Japan).

Messenger RNA was extracted from paraffin-embedded tumor tissue. Reverse transcriptase polymerase chain reaction (RT-PCR) was carried out to detect *EWS/WT1* fusion transcripts, using primes as previously described [10]. Appropriate positive and negative controls were included.

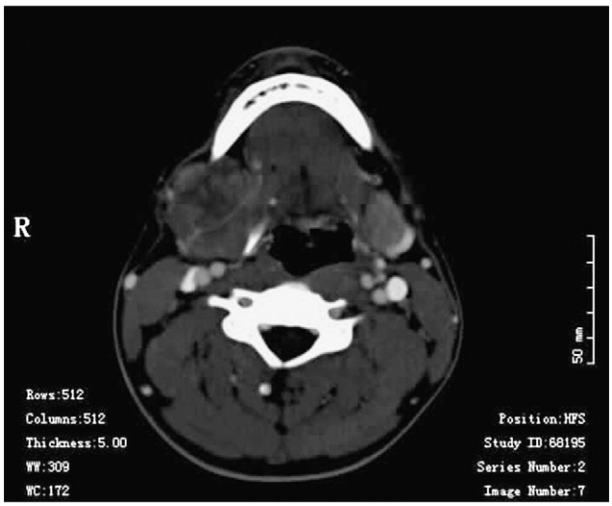

Fig. 1 Computed tomography. A well-demarcated homogeneous mass is seen in the right submandibular gland.

Table 1 Immunohistochemical staining

Antibody	Clone	Source	Dilution	Results
NSE	NSE-P1	Neomarkers, Fremont, CA, USA	1:1500	+
Cytokeratin (CK8/CK18)	CAM5.2	Becton-Dickinson, San Jose, CA, USA	1:50	+
Desmin	D33	Dako, Glostrup, Denmark	1:500	+
p53	DO7	Dako	1:150	+
Ki-67	SP6	Neomarkers	1:200	55%
S-100 protein	Antiserum	Dako	1:4000	−
CD99	O13	Sigent, Dedham, MA, USA	1:1000	−
Myogenin	F5D	Dako	1:800	−
Smooth muscle actin	1A4	Zymed, San Francisco, CA, USA	1:100	−
Synaptophysin	SP11	Neomarkers	1:200	−
Muscle specific actin	HHF-35	Neomarkers	1:100	−

4. Results

4.1. Pathologic findings

Grossly, there was a circumscribed, solid, homogeneous, yellow-gray tumor, measuring 4 cm. Histologically, the tumor was predominantly circumscribed and focally infiltrative, and a peripheral rim of residual salivary gland tissue could be identified (Fig. 2A). It formed sharply demarcated, irregular-shaped, variable-sized nests, cords, and islands in a desmoplastic stroma with variable myxoid or sclerotic change (Fig.2 B). In areas, there were large tumor nests with central coagulative necrosis, separated by scanty stroma (Fig. 2C). The tumor cells were small to medium-sized, with dark round nuclei and scant to moderate amounts of eosinophilic cytoplasm (Fig. 2D). Mitotic figures and apoptotic bodies were readily seen.

4.2. Histochemical and immunohistochemical findings

Mucicarmine stain was negative. The tumor cells were immunoreactive for cytokeratin and neuron-specific enolase (NSE) in a diffuse cytoplasmic pattern (Fig. 2E, F). Although