CASE REPORT

Microcystic/Reticular Schwannoma Arising in the Submandibular Gland: A Rare Benign Entity that Mimics More Common Salivary Gland Carcinomas

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Received: 1 September 2015 / Accepted: 24 November 2015 / Published online: 30 November 2015
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Abstract Microcystic/reticular schwannoma is a recently described variant of schwannoma with a predilection for the gastrointestinal tract, rarely involving the head/neck region. This is the first reported case involving the submandibular gland. We present a case in a 34 year old man with 4.5 cm submandibular mass. Fine needle aspiration suggested a spindle cell lesion. Frozen section evaluation raised the possibility of mucoepidermoid carcinoma. Resection showed a well circumscribed mass with a mucoid appearance. Histologic findings include a lobular architecture with fibrous septa, a lympho-plasmacytic infiltrate, and scattered lymphoid aggregates at the periphery. There are two distinct histologic patterns with solid areas of spindle cells and areas of spindle/ovoid cells with a microcystic pattern in a myxoid background. The

tumor has a pushing border, with extension into adipose and adjacent parenchyma, without cytologic atypia or necrosis. Immunohistochemical stains are positive for S-100 and CD34, and negative for calponin, mammoglobin, ALK1, p63, ER, GFAP, SMA, desmin, cytokeratin 7, cytokeratin AE1/AE3, and C-Kit. Mucicarmin stain is negative. Recognition of this benign unusual variant of schwannoma is paramount for appropriate conservative treatment due to the morphologic and immunohistochemical overlap with primary salivary gland carcinomas.

Keywords Schwannoma · Microcystic schwannoma · Reticular schwannoma · Submandibular gland · Salivary gland

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Background

Schwannomas are benign neoplasms of the nerve sheath that are typically composed of well differentiated Schwann cells. Approximately 90 % occur sporadically, while 10 % occur synchronously, both in association with neurofibromatosis syndromes and without [1]. Histologically, classic schwannomas are characterized by two distinct patterns, showing cellular areas of spindle cells with nuclear palisading (Antoni A) and hypocellular, myxoid areas (Antoni B) [2]. However, many histologic forms exist, including ancient, cellular, epithelioid, hybrid type, melanotic, plexiform, and psammomatous variants [3–12]. A rare morphologic variant known as microcystic/reticular schwannoma was recently described in a 10 patient series in 2008 [13]. Since the initial case series, at least 16 more cases (including the present case) have been reported.

A review of the current literature demonstrates that microcystic/reticular schwannoma shows a predilection for

the gastrointestinal tract (sixteen of the twenty six reported cases) with a slight female predominance (fifteen of the twenty six cases). The mean age of presentation is 58 years, with a median age of 62 (Fig. 1).

While there is some variability in the histopathology of the tumor depending on the location, common features include predominant microcystic and reticular spaces filled with myxoid material. The tumor is composed of spindle cells with ovoid nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm, set in a myxoid background. Occasional foci of classical schwannoma patterns (Antoni A and Antoni B areas) can be present. Focal lymphoid aggregates are common when the tumor arises in the soft tissue, but is

rare in those arising in the gastrointestinal tract. Nuclear atypia, necrosis, and mitotic activity are rare to absent.

Despite this distinct appearance, thus far these lesions appear to behave in the same way as a classic schwannoma, and no recurrences have been reported in the literature after excision. Although there are no reports of malignant transformation, there is one case report of a malignant epithelioid peripheral nerve sheath tumor with a similar microcystic/reticular pattern. This case, however, demonstrated mild to moderate atypia at the time of diagnosis, and had a more varied appearance with multifocal hypercellular areas. Furthermore, this malignant neoplasm measured 10×10 cm, much larger than the average size of microcystic/reticular schwannomas [13–27].

Fig. 1 Number of reported cases of microcystic/reticular schwannoma by location and age

Clinical History

A 34-year-old male presented to the head and neck surgery clinic with complaint of slowly enlarging left neck mass over 6 months with associated pain. Review of systems revealed no dysphagia, B-symptoms, odynophagia, trismus or facial nerve weakness. Physical examination demonstrated a large, mobile 2-cm mass within the substance of the left submandibular gland without any overlying skin changes. Left lateral tongue sensation and facial and hypoglossal nerve function was intact. Ultrasound and computed tomography (CT) revealed a lobulated mass extending posterolaterally from the normal-appearing left submandibular gland with extension into the parapharyngeal space, and an enlarged but normal-appearing left level IIA lymph node. Fine needle aspiration of the mass was read as spindle cell lesion with myxoid material present, favoring a benign salivary gland neoplasm.

Excision of the left submandibular gland with selective neck dissection involving levels IA and IIA was performed. Intra-operatively, the mass was noted to be mobile and did not involve the superficial fascial layers or fat. Frozen section analysis of the primary lesion was read as mucin producing neoplasm, with a differential diagnosis favoring mucoepidermoid carcinoma (intermediate grade).

An enlarged level IIA lymph node was encountered and sent to pathology. Frozen section analysis of lymph node specimens returned negative for carcinoma. Given these findings, a comprehensive neck dissection was deferred.

Pathology

Gross and Histologic Features

Grossly, the lesion was a well circumscribed, unencapsulated mass measuring $4.5 \times 3 \times 1.9$ cm, arising from the

superior portion of the attached submandibular gland. The lesion had a soft, tan, gelatinous cut surface.

Microscopic examination shows a multinodular tumor separated by fibrous septa with a lymphoplasmacytic infiltrate, and scattered lymphoid aggregates surrounding the nodules (Fig. 2a). The tumor is well circumscribed, unencapsulated, and has a distinct pushing border between the surrounding submandibular gland parenchyma. However, there are focal areas with a more irregular border, showing tumor cells present in both surrounding fat and adjacent salivary gland parenchyma (Fig. 2b, c).

The lesion has two distinct histologic patterns. Some areas show a solid proliferation of spindle to ovoid cells, with slight focal nuclear palisading. Other areas show a

pattern of anastomosing and intersecting spindle cells in a lace-like network, giving a reticular pattern of round to oval microcysts ranging from 15 to 200 microns in diameter, filled with acellular myxoid stroma. The tumor has uniformly bland appearing cytology; no evidence of cytologic atypia or necrosis is present in the tumor (Fig. 2d, e). Focal microcalcifications are present in the lesion.

Ancillary Studies

Special stain for mucicarmin is negative. The tumor is diffusely immunoreactive for S-100 (Fig. 2f) and CD34. There is focal immunoreactivity for EMA at the periphery of the nodules, highlighting perineurial cells. The tumor is

Fig. 2 **a** Multinodular tumor separated by fibrous septa with a lymphoplasmacytic infiltrate and scattered lymphoid aggregates surrounding the nodules. **b** Tumor with a pushing border into adjacent submandibular gland. **c** Focal microscopic presence in

surrounding fat. **d** Areas with proliferation of bland appearing spindle to ovoid cells. **e** Areas of spindle to ovoid cells with a microcystic/reticular pattern, set in a myxoid background. **f** Tumor cells with diffuse positive immunoreactivity for S-100 protein

not immunoreactive for Pan cytokeratin AE1/AE3, cytokeratin 7, calponin, p63, C-Kit, mammoglobin, ALK protein, ER, GFAP, desmin, or SMA.

Discussion

Mesenchymal neoplasms are rare in salivary glands, representing only about 2–5 % of salivary gland tumors [28]. Furthermore, only 10 % of salivary gland soft tissue tumors arise in the submandibular gland [29]. Schwannomas, in particular, are rare in the submandibular gland, with only ten reported cases, most of which have been the classic type [30–39]. Given the rarity of schwannomas in this location, and the unusual histology of this variant, which often lacks the classic verocay body organization, one may initially overlook the true diagnosis.

The histologic appearance of this neoplasm—with its distinct cell populations, prominent myxoid background, and pushing border with focal presence in surrounding tissue—poses a diagnostic dilemma. This is particularly true in the salivary gland, where primary salivary gland tumors can present with highly variable histopathology. Despite the lack of overt cytologic atypia, the presence of tumor cells in adjacent tissues—due to its mesenchymal nature—can also be erroneously suggestive of an invasive process. Therefore, a broad differential diagnosis exists, including primary epithelial and myoepithelial tumors of the salivary gland, both benign and malignant.

Malignant epithelial tumors in the differential are ones with cystic growth, including mucoepidermoid carcinoma, mucinous adenocarcinoma, and salivary duct carcinoma. However, these entities typically display more frank cellular atypia or true invasion of adjacent tissues, unlike a schwannoma. In addition, they are all immunoreactive for pancytokeratin AE1/AE3 and not for S-100. All of these entities will also have true mucin on PAS or mucicarmine stain.

Other malignant epithelial tumors include adenoid cystic carcinoma, cystadenocarcinoma, low grade cribriform cystadenocarcinoma, polymorphous low grade adenocarcinoma (PLGA), and mammary analogue secretory carcinoma. These are of particular interests, because like schwannoma they can also be immunoreactive for S-100, however they are all immunoreactive to select cytokeratins, unlike schwannoma. Adenoid cystic carcinoma will also be immunoreactive for myoepithelial markers, and occasionally C-Kit. Cystadenocarcinoma usually exhibits a more infiltrative growth pattern, and it produces true mucin. Low-grade cribriform cystadenoma will be immunoreactive to myoepithelial markers surrounding the cystic space, demonstrating its intraductal growth. PLGA, despite its patchy S-100 positivity, is immunoreactive to cytokeratins.

Mammary analogue secretory carcinoma should also be immunoreactive to mammoglobin, and some produce true mucin.

Benign neoplasms in the differential include mucinous myoepithelioma and cystadenoma.

The rare and recently-described mucinous myoepithelioma is typically composed of spindle, plasmacytoid, or epithelioid cells with a myxoid or hyalinized stroma. In addition, mucinous myoepithelioma can variably stain positive for S-100. However, the tumor cells in mucinous myoepithelioma are immunohistochemically positive for cytokeratins and myoepithelial cell markers, such as calponin and p63, and they produce true mucin, which can be highlighted by mucicarmine and PAS-diacetate staining [40]. Cystadenoma will have cystic spaces but lacks the proliferation of spindle cells seen in this schwannoma. Histologically there is only minor overlap, however immunohistochemistry would be confirmatory, as cystadenoma will be immunoreactive for cytokeratins and not for S-100.

The diagnosis of this uncommon lesion is difficult on histologic features alone, and ancillary studies are indispensable in making the diagnosis. However, recognition of this entity is paramount, as the literature demonstrates that despite its predilection for the GI tract, it can occur at virtually any site in the body. Given its variable appearance, it can mimic many other more common primary neoplasms, and the correct diagnosis of this benign entity is essential to avoid confusion with carcinomas with similar histologic morphology.

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