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Submandibular Gland Small Cell Carcinoma: A Case Report

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Abstract

Introduction: Salivary Gland Small Cell Carcinoma (SmCC) accounts for approximately 2% of all major salivary gland malignancies and less than 1% of all salivary gland tumors. When subcategorized by the affected gland, the parotid gland claims nearly 80% of these diagnoses, making submandibular SmCC a rare entity with only 11 previously reported cases.

Case Presentation: We present our experience with 78 years old male patient with a rapidly enlarging left anterior neck mass. Fine needle aspiration performed of the lesion was consistent with a high grade neuroendocrine tumor. He subsequently underwent gland resection, modified radical neck dissection, and adjuvant radiation therapy. Final immunohistochemical analysis was consistent with submandibular small cell carcinoma.

Discussion: The ideal management strategy for patients diagnosed with submandibular SmCC is currently not well established however it typically involves wide resection with or without radiation and/or chemotherapy. While not previously described, our patient demonstrated symptoms suggestive of a paraneoplastic syndrome at the time of his initial diagnosis. In light of this, salivary gland SmCC should be included on the differential diagnosis for patients presenting with a paraneoplastic syndrome as a harbinger to their underlying disease process. Ongoing studies are crucial for elucidating optimal management strategies for patients diagnosed with this rapidly progressive, rare malignancy.

Keywords: Submandibular gland; Small cell carcinoma; Paraneoplastic syndromes

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Introduction

Salivary Gland Small Cell Carcinoma (SmCC) accounts for approximately 2% of all major salivary gland malignancies and less than 1% of all salivary gland tumors [1]. When subcategorized by the affected gland, the parotid gland claims nearly 80% of these diagnoses, making submandibular SmCC a rare entity with only 11 previously reported cases [2-9]. The objective of this report is to call attention to this aggressive and rare malignancy, add to the current knowledge base, and comment on paraneoplastic syndromes as this may relate to SmCC of salivary gland origin.

Case Presentation

A 78 years old man presented to clinic for evaluation of a painless, left anterior neck mass that had been present for approximately 6 months. Four weeks preceding evaluation, the mass began to rapidly enlarge along with new, mild discomfort. He denied any hoarseness, dysphagia, hemoptysis, or unintentional weight loss. He recently quit smoking with a 30 years pack history. He also relayed a history of difficulty with extubation following a routine procedure 1 year prior to presentation, which was attributed to a profound sensitivity to the paralytic agents used. Physical exam of the neck revealed a 4 cm mass in the anterior left submental and anterior submandibular space, which was firm, mobile, and non tender. No hypoglossal or marginal mandibular nerve weakness was detected. Laryngoscopy was grossly normal. Fine Needle Aspiration (FNA) of the left neck mass was suggestive of a high-grade neuroendocrine carcinoma based on expression of CD56 and chromogranin. PET scan showed an FDG avid left submandibular mass measuring 3.7 cm × 2.4 cm × 3.4 cm with a maximum standard uptake value of 12.7, with central necrosis. No additional hypermetabolic foci were found however there was a bland 8 mm left upper lobe pulmonary nodule. The patient underwent radical excision of the left submandibular gland and a modified radical

Table 1: Details of reported cases of submandibular small cell carcinoma.

Patient	Age	Sex	Size (cm)	Treatment	Local Recurrence	Lymph Node Metastasis	Distant Metastasis	Follow-Up (Months)
1[1]	46	F	10.0	GR, RND, XRT	Yes	Yes	No	DOD (6)
2[1]	85	M	3.8	GR, RND	No	No	Yes	DOD (9)
3[3]	84	M	6.0	None	No	No	Yes	DOD (1)
4[3]	67	F	4.0	GR, XRT	Yes	No	Yes	DOD (51)
5[5]	76	M	Unk	Unk	Unk	Unk	Unk	Unk
6[4]	57	M	Unk	GR, RND, XRT, Chemo	No	Yes	No	NED (72)
7[7]	39	M	2.5	GR, Chemo	No	No	No	NED (12)
8[8]	46	F	Unk	GR, RND, XRT, Chemo	Yes	No	No	Unk
9[2]	70	M	5.0	XRT, Chemo	No	No	Yes	DOD (12)
10[9]	30	M	7.5	GR, XRT, Chemo	No	No	No	NED (6)
11[6]	29	M	10.0	GR, RND, XRT	Yes	Yes	No	DOD (1)
12	78	M	5.5	GR, RND, XRT	Yes	Yes	No	DOD (4)

M: Male; F: Female; GR: Gland Resection; RND: Radical Neck Dissection; XRT: Radiation Therapy; Chemo: Chemotherapy; DOD: Died of Disease; NED: No Evidence of Disease at the time of original article publication

Table 2: Characteristics of immunohistochemical staining.

Patient	Chromogranin	Synaptophysin	Cytokeratin	Neurofilament	NSE*	Leu 7	CD56	CD57	Ki-67
1[1]	+	+		+	+		+	+	
2[1]	+	+		+	+		+	+	
3[3]	+								
4[3]		+			+	+			
5[5]					+	+			
6[4]	+	+			+				
7[7]	+				+				
8[8]	+	+			+				
9[2]	+				+	+			
10[9]	+	+	+				+		+
11[6]	+	+	+		+	+	+		
12	+						+		+

NSE: Neuron Specific Enolase

neck dissection. During surgery, the mass was noted to be adherent to the overlying platysma, digastrics, mylohyoid muscles and the mandibular periosteum. The pathological findings were notable for a nodular lesion measuring 5.5 cm × 5.0 cm × 4.3 cm, weighing 101 grams with cross sections containing focal hemorrhagic/necrotic areas with positive margins. Immunohistochemical (IHC) findings were consistent with SmCC (Figure 1 and 2), positive lymphovascular invasion, perineural invasion and 4 of 21 lymph nodes positive for metastatic disease. The tumor was pathologically staged as TMN IVB (pT3, N2b, Mx). The patient subsequently underwent 33 rounds of adjuvant radiation therapy. Two days following his final treatment, he presented to the hospital with dehydration, altered mental status and hypercalcemia. Work up was consistent with widely metastatic disease; he was made comfort care and passed away shortly thereafter.

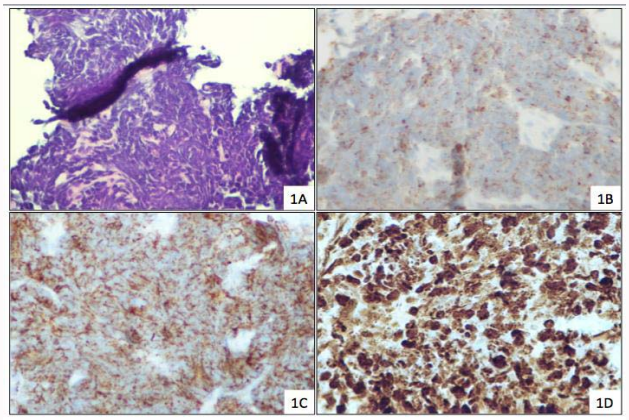

Figure 1: A) Hematoxylin and eosin staining of the cell block of fine needle aspiration of the left neck mass (x40); B) Chromogranin A (x40); C) CD56 (x40); D) Ki-67 (x40).

Discussion

SmCC represents a rare and heterogenous group of malignancies that can be further distinguished histologically as ductal or neuroendocrine types [1,4-6]. Despite these sub classifications, salivary gland SmCC share similar biologically behavior which is typically more favorable than their lung counterparts [1,5]. Histological characteristics include cell diameter of <30 μm with minimal cytoplasm, inconspicuous nucleoli, high mitotic index and fine nuclear chromatin [10]. IHC testing differentiates primary salivary gland SMCC from lesions that have similar histological appearance including metastatic disease, salivary gland tumors with

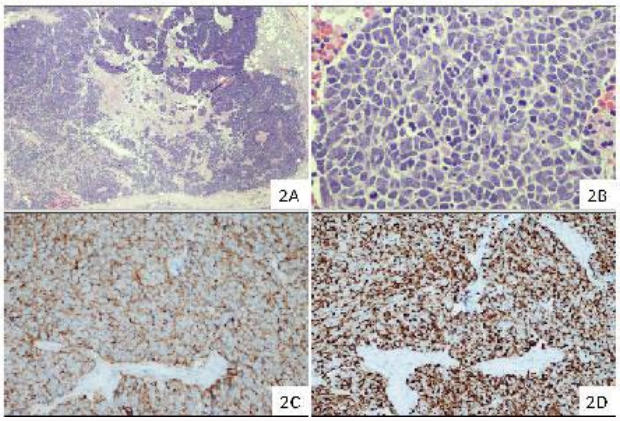

Figure 2: A) Hematoxylin and eosin eosin-stained Small Cell Carcinoma (SSC) of the submandibular gland showing tumor cell sheets and nests with necrosis (x2); B) A high-power view of Small Cell Carcinoma (SSC) of the submandibular gland showing cytomophology of tumor cells with frequent mitotic and apoptotic figures (x20); C) Synaptophysin (x20); D) CK20 (x40).

high-grade transformation, lymphoma, and Ewing's sarcoma [2,6,9]. Positive reactivity on staining to cytokeratin, chromogranin, NSE, synaptophysin, Leu 7, CD 56/57, and/or EMA are all consistent with SmCC while negative testing of additional markers eliminates other possible etiologies [3,10]. Table 1 highlights the 12 known cases of submandibular SmCC. The mean age at diagnosis is 59.7 years old. Previously, the peak incidence of submandibular SmCC occurred during the 5th to 8th decades of life, however more recently Purkayastha et al. [6] and Philip et al. [9] have reported cases implicating a 29 and 30 years old patient respectively [6,9]. Addition of these cases creates a bimodal distribution with peaks occurring during the 4th to 5th and 7th to 9th decades of life. The majority of patients (10/13) demonstrate positive reactivity to chromogranin, synaptophysin, CD56 along with various other characteristic IHC markers including CK20 (Table 2). The mainstay of treatment consists of total gland resection along with radical neck dissection. The majority of patients (7/13) underwent adjuvant radiation therapy however the efficacy of this treatment has yet to be shown clinically significant due to limited population size [1,2,5-7]. The minority of patients received adjuvant chemotherapy however, like radiation therapy, there is no clearly established evidence to support or refute its use within this population [2,4,7-9]. To our knowledge, there are no prior reported cases of submandibular SmCC with symptoms suggestive of an associated Paraneoplastic Syndrome (PS). In our patient's case, a paraneoplastic syndrome was considered as the etiology of his history of profound sensitivity to paralytic agents. Paraneoplastic Syndrome (PS) is disorders characterized by clinical manifestations that occur in association but not as a direct result of malignant tumors [11]. Anomalous immune cross-reactions and/or humoral factors released by malignant tissues are thought to underlie the pathophysiology of many of these disorders [12]. Most often seen in patients with lung primaries, Paraneoplastic Syndrome (PS) can occur in a multitude of malignancies and the precise physiologic derangements that ensue are dictated by the underlying disease process [13]. The signs and symptoms are often detected prior to the definitive diagnosis of an occult malignancy and tend to progress over weeks, months, and years [13]. At a broad glance, Paraneoplastic Syndrome (PS) can be subdivided into those that mainly affect the endocrine, neurologic, dermatologic, rheumatologic, hematologic, or ophthalmic systems [11]. The Paraneoplastic Neurologic Syndromes (PNS), half of all patients will have detectable onconeural antibodies however, the lack of onconeural antibodies does not rule out the diagnosis. Furthermore, the presence of neurologic symptoms doesn't rule in a paraneoplastic syndrome thus making the diagnosis difficult to establish [12,14]. It is currently estimated that 3% to 5% of patients with small cell lung cancers are affected by a Paraneoplastic Neurologic Syndromes (PNS) [11]. Paraneoplastic Syndrome (PS) has not been associated with submandibular SmCC however this may be due in part to its overall rarity. It would be reasonable to include submandibular SmCC on the differential diagnosis for patients who present with paraneoplastic syndromes as a harbinger to their underlying disease process. SmCC of submandibular origin are extremely rare and aggressive tumor that can have a rapidly progressive course. Ongoing studies will be crucial to elucidating optimal management strategies for patients affected by submandibular SmCC.

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References

1. Nagao T, Gaffey TA, Olsen KD, Serizawa H, Lewis J. Small cell carcinoma of the major salivary glands: Clinicopathologic study with emphasis on cytokeratin 20 immuno reactivity and clinical outcome. Am J Surg Pathol. 2004;28(6):762-70.
2. Servato JP, da Silva SJ, de Faria PR, Cardoso SV, Loyola AM. Small cell carcinoma of the salivary gland: A systematic literature review and two case reports. Int J Oral Maxillofac Surg. 2013;42(1):89-98.
3. Gnepp DR, Wick MR. Small cell carcinoma of the major salivary glands. An Immunohistochemical Study. Cancer. 1990;66(1):185-92.
4. Rodriguez JC, Forcelledo MF, Gutierrez LM, Hernandez Vallejo G, Lopez Arranz JS. Small cell undifferentiated carcinoma of the submandibular gland with neuroendocrine features. Ann Otol Rhinol Laryngol. 2004;113(1):55-9.
5. Gnepp DR, Corio RL, Brannon RB. Small Cell Carcinoma of the Major Salivary Glands. Cancer. 1986;53(3):705-14.
6. Purkayastha A, Sharma N, Suhag V, Pandya T. Extremely rare and fulminant case of small cell carcinoma of submandibular salivary gland. Transl Surg. 2016;1(2):44-7.
7. Lin YC, Wu HP, Tzeng JE. Small-cell undifferentiated carcinoma of the submandibular gland: An extremely rare extrapulmonary site. Am J Otolaryngol. 2005;26(1):60-3.
8. Walters DM, Little SC, Hessler RB, Gourin CG. Small cell carcinoma of the submandibular gland: A rare small round blue cell tumor. Am J Otolaryngol. 2007;28(2):118-21.
9. Philip NR, Srinivas T, Naagar R, Aakash, Srinivas V. An extremely rare case of small cell carcinoma in submandibular salivary gland. J Clin Diagn Res. 2017;11(5):ED24-ED5.
10. Ellis GL, Auclair PL. Tumors of the Salivary Glands. AFIP atlas of tumor pathology: Series 4.
11. Kanaji N, Watanabe N, Kita N, Bandoh S, Tadokoro A, Ishii T, et al. Paraneoplastic syndromes associated with lung cancer. World J Clin Oncol. 2014;5(3):197-223.
12. Pelosof LC, Gerber DE. Paraneoplastic syndromes: An approach to diagnosis and treatment. Mayo Clin Proc. 2010;85(9):838-54.
13. Spiro SG, Gould MK, Colice GL. Initial evaluation of the patient with lung cancer: symptoms, signs, laboratory tests, and paraneoplastic syndromes:

ACCP evidence-based clinical practice guidelines (2nd ed). Chest. 2007;132(3):149-60.

14. Honnorat J, Antoine JC. Paraneoplastic neurological syndromes. Orphanet J Rare Dis. 2007;22(2).