ABSTRACT

Secretory carcinoma is a recently described salivary gland neoplasm reported in the fourth edition of the World Health Organization classification of head and neck tumors. We report a case of a primary secretory carcinoma arising from the submandibular gland that was completely excised in a 10-year-old. The histomorphologic features and the immunophenotype studies are compatible with secretory carcinoma. Unless proven otherwise by immunohistochemical stains and cytogenetics, secretory carcinoma should be included as a differential in cases of lesion of the major and minor salivary glands that has the primary differential diagnosis of acinic cell carcinoma. This case report aims to contribute to the limited literature about this disease entity and would be one of the few reported cases of the disease in a school-age child.

Key words: secretory carcinoma, submandibular gland mass, ETV6-NTRK3 fusion, school-age child

INTRODUCTION

Secretory carcinoma (SC) (formerly known as Mammary analogue secretory carcinoma) is a salivary gland carcinoma that is frequently misdiagnosed as acinic cell carcinoma but is now known to be a distinct entity that is identical to SC of the breast, showing morphologic, immunohistochemical, and genetic similarities between the two entities. This entity was reported by Skalova et al., taking advantage of the fact that mammary SC is associated with the t(12;15) (p13;q25) translocation leading to the ETV6-NTRK3 gene fusion.2,3 It was seen to occur predominantly (76%) in the parotid, minor salivary glands of the oral cavity and submandibular gland. It has also been described in the nasal cavity, skin, and thyroid gland. It is more common in adults, with reported cases ranging from 5 to 87 years old, and it is slightly predominant in males (M/F ratio: 1.4:1).4 Presented here is a 10-year-old male with a rapidly growing left submandibular mass having histopathologic features compatible with SC. The diagnosis of SC is sparsely reported among children and has not been documented in a pediatric patient in any Philippine database, hence this case report serves as an addition to the growing body of literature and adds to the rare entities diagnosed in childhood.

CASE

This is a case of a 10-year-old male who developed an enlarged left submandibular mass. Consulting in another institution, the parents were advised that their child must undergo excision biopsy. The patient was subsequently diagnosed to have acinic cell carcinoma (ACC). This case was brought to our pediatric center as a slide review. Based on the histomorphologic features, we formulated a differential diagnosis which include lesions with thyroid lineage that encompass ectopic thyroid (ET) and metastatic well-differentiated thyroid carcinoma, ACC, adenoid cystic carcinoma (AdCC) and SC. The microscopic findings on the hematoxylin and eosin-stained slides of representative sections of the lesion presented diagnostic overlaps among the differentials. Immunohistochemistry studies show a
positive immunoexpression to GATA3 and Mammaglobin (Figure 1), but negative staining to thyroglobulin, TTF1, DOG1 and CD117 antibodies (Figure 2) (Table 1). Molecular cytogenetic testing for ETV6-NTKR3 is suggested and a final pathologic report of SC was made thereafter.

**DISCUSSION**

It is reported that SC accounts for <0.3% of all salivary gland tumors and SC makes up 4.5% of malignant salivary gland disease processes. In the most recent update, there have been a total of 248 SC cases reported in the literature, and about 24% of these cases arose in minor salivary glands between 2010 and 2017.13,14 Two patients with oral cavity-originated SC were reported and was subjected to a pooled analysis of previously reported SC cases. It is highly likely that many cases of SC are previously diagnosed as ACC owing to their similar histological findings. The treatment strategy for minor salivary gland-originated SC is similar to ACC; however, SC is an indolent salivary gland malignancy, although 25% of cases are reported to have lymph node metastasis but distant metastases are rare. Thus, clinical stage and high-grade transformation are the main adverse prognostic factors in which establishing an accurate histopathologic diagnosis, confirming the ETV6-NTRK3 fusion gene by genetic analysis is important both for diagnostic and prognostic purposes.15-17 Currently, the guidelines for surgical treatment, chemoradiation, and follow up of these cases have not been standardized due to the small number of cases.18

*ET: Ectopic Thyroid, ACC: Acinic Cell Carcinoma, AdCC: Adenoid Cystic Carcinoma and SC: Secretory Carcinoma.

**Figure 1.** (A) Low power view showing varisized lobules composed of tumor cells with eosinophilic, vacuolated cytoplasm (H&E, 100x). (B) High power view showing a vesicular nuclei and conspicuous nucleoli. The lobules contain eosinophilic intraluminal material (H&E, 400x). (C) Focal nuclear immunoreactivity to GATA3 (400x). (D) Strong, diffuse membranous to cytoplasmic immunoreactivity to Mammaglobin (400x).

**Figure 2.** Approach to arriving at our diagnosis.
SC is a recently described salivary gland carcinoma frequently misdiagnosed as ACC but is now known to be a different entity analogous to the SC of the breast that is also associated with the t(12;15)(p13;q25) translocation leading to the ETV6–NTRK3 gene fusion. Morphologically, the cases representing this disease entity are characterized by the presence of microcystic and glandular spaces with abundant eosinophilic secretion that is positive for PAS, mucicarmine, MUC1, MUC4, and mammaglobin. The cells have an apocrine appearance with vacuolated, eosinophilic cytoplasm and uniform vesicular nuclei with small nucleoli. Like mammary SC of the breast, the cells are positive for cytokeratin, S-100 protein, BRST-2, and mammaglobin, but are negative for androgen receptor, p63, and DOG-1. They are low-grade carcinomas that recur in approximately 30% of cases but only rarely metastasize or result in death. Rare examples with high-grade transformation (dedifferentiation) have been described and behave more aggressively.19 In the case presented, it microscopically shows varisized lobules composed of tumor cells with eosinophilic, vacuolated cytoplasm, vesicular nuclei, and conspicuous nucleoli. The lobules contain eosinophilic intraluminal material (Figure 1A) (Figure 1B). Immunohistochemically, SC will have 100% diffuse, nuclear immunoreactivity to GATA3 and like its counterpart in the breast, SC express mammaglobin at levels that can be easily detected by routine immunohistochemistry that would establish mammaglobin as a diagnostic tool for confirming SC.20,21

It must be taken to account that considerable overlaps also exist among the immunohistochemical profiles of the differential diagnoses, and that this should be a caveat in the interpretation of individual immunohistochemical stains. In typical cases, morphology in combination with these markers are sufficient to diagnose SC. Further investigations via molecular study for SC is characterized by the ETV6–NTRK3 fusion gene, with its most common translocation partner being the NTRK3 gene.22

CONCLUSION

We encountered a case of SC arising from the left submandibular gland from a 10-year-old, male child. Patient underwent complete excision of the mass and is currently asymptomatic. The diagnosis is based on the clinical presentation and morphologic features supported by the immunoreactivity of the tumor cells to GATA3 and Mammaglobin (Figure 1) and negative immunostaining for Thyroglobulin, TTF1, DOG1, and CD117. To the best of our knowledge, this is one of the limited cases, especially given the patient’s age, to report this approach to a diagnosis (Figure 2) of SC.

ETHICAL CONSIDERATION

Patient consent was obtained before submission of the manuscript.

STATEMENT OF AUTHORSHIP

The authors certified fulfillment of ICMJE authorship criteria.

AUTHOR DISCLOSURE

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REFERENCES


