Case Report

Secretory carcinoma in the parotid gland of a pediatric patient. A challenging diagnosis

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Abstract

Secretory carcinoma is a rare, recently identified and recognized neoplasm in major salivary glands. Few cases have been described with only 16 pediatric cases in the literature. We present a case preoperatively identified as a benign parotid lesion whose management was delayed due to the COVID-19 pandemic. Post enucleation of the lesion, histology identified a secretory carcinoma. This led to further and more extensive surgery to ensure complete removal. Clinicians and histopathologists should be aware of secretory carcinoma in their differential, as a high index of suspicion is required to ensure appropriate investigations are performed to obtain the diagnosis. Early identification is important to allow timely appropriate surgery to be performed.

Keywords: Carcinoma, pediatric, parotid, secretory

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INTRODUCTION

Secretory carcinoma (SC) of the salivary glands, formerly known as mammary analogue secretory carcinoma (MASC), is a rare neoplasm, with morphological, immunohistochemical, and molecular features similar to the SC of the breast.[1-3] It was newly recognized in the World Health Organization 2017 classification.[1,3] Pediatric cases of SC are rare with only 16 cases reported in the literature.[4]

Of the cases so far described, most present as a slow growing, fixed, painless nodule that is commonly incidentally identified on examination.[5] Most cases have presented in the parotid gland with a lesion around 1-2 cm in size.[4,6]

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Histologically, microcystic tubular and solid patterns with eosinophilic bubbly secretions were the most common patterns in pediatric patients.[6] Histochemically, secretions stain positive for periodic acid Schiff and are diastase-resistant alongside positive staining for S-100, mammaglobin, vimentin, and cytokeratin-19.[5,7] Molecular detection by fluorescent in-situ hybridization remains the gold standard as a fusion gene, commonly ETV6-NTRK3, t(12;15), (p13;q250), has so far not been reported in any other salivary gland tumour.[6] Although this fusion gene is most commonly reported, other fusion genes including ETV6 have also been reported.[4] The ETV6-NTRK3 fusion gene has been shown to encode a tyrosine kinase shown to promote oncogenesis, by causing increased cell

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proliferation and survival of tumour cells.[2,8-10] Although high grade transformation has been documented in adults, it is yet to have been identified in the pediatric cohort.[6] Current management for pediatric SC is not well known with management ranging from simple excision to neck dissection.[6] SCs with ETV6-NTRK3 fusion gene have been shown to respond to new specific tyrosine kinase inhibitors;[11] hence, recognition of SC in pediatric patients is important to potentially allow targeted therapy in specific clinical circumstances.[4] Preoperative identification of SC from ultrasound-guided fine-needle aspiration is challenging due to overlapping histological and immunohistochemical features with normal salivary gland elements or benign and malignant salivary gland neoplasms.[5,12]

We present here a pediatric case of SC preoperatively believed to be benign and operative management delayed by the COVID-19 pandemic. This case highlights the need for a high index of suspicion for pediatric patients presenting with a salivary gland mass.

CASE HISTORY

A 13-year-old boy was referred by his general practitioner to the ear, nose and throat (ENT) department with a new left infra-auricular mass that had been present for the previous 6 months. The patient reported no associated symptoms such as night sweats or fevers. There was no associated pain or other relevant symptoms. Past medical history includes type 1 insulin-dependent diabetes mellitus and a previous left-sided glue ear which had been treated with a left-sided grommet. On examination, a small, <1 cm, firm mobile left-sided lump overlying the angle of the mandible was palpated. No associated lymphadenopathy was identified.

An ultrasound was performed to further delineate the lesion which showed a 0.9 cm oval-shaped lesion within the superficial lobe of the parotid anterior to the ear. It was suggested this mass likely represented a pleomorphic adenoma. A fine needle aspirate was performed. This showed a highly cellular sample containing cohesive groups, clusters, and sheets of epithelial cells, with scattered similar single cells in background. Occasional cells had oncocytic morphology. There was no significant stromal component. Appearances were suggestive of benign, possibly epithelial-rich pleomorphic adenoma or a monomorphic adenoma. Postultrasound and fine needle aspirate, the patient was listed for a simple enucleation due to its small size and benign appearances and cytology.

Unfortunately, a month post review and consenting for the procedure, the COVID-19 pandemic led to a halt on all non-urgent pediatric operating at our hospital. The patient was reviewed during this time; however, the mass remained stable in size with no concerning features. Postpandemic, the patient was operated almost 2 years post listing for the procedure. There had been no clear change in the size or symptoms of the lesion during this time.

A left parotid extracapsular lumpectomy was performed. A 1.5-cm superficial parotid lump was removed. A facial nerve monitor was used throughout.

Histology [Figures 1-4] showed a rather circumscribed but in places infiltrative epithelial neoplasm in the parotid gland. There were tumour lobules separated by dense and often hyalinized fibrous tissue. The neoplastic cells were moderately pleomorphic, with eosinophilic or clear cytoplasm and vesicular nuclei, with prominent nucleoli. They were arranged in a variety of patterns including solid, micocystic, macrocystic, papillary-cystic, and tubular patterns. The tubules contained periodic acid-Schiff and diastase-resistant eosinophic, colloid-like intraluminal secretions. Mitoses were present but no necrosis or high-grade transformations were noted.

Immunohistochemistry revealed the neoplastic cells were diffusely positive for CK7 and S-100 and negative for p63 and DOG1. The proliferation index with MIB-1 immunostaining was estimated at 15%. Genetic analysis (fluorescent in-situ hybridization) confirmed rearrangement of the ETV6 (12p13) gene. The morphology and immune profile were consistent with a SC. The tumour extended to the limits of the excision and focally showed heat artefact.

Postconfirmation of the histology, the patient was discussed with a tertiary referral center and an magnetic resonance imaging neck with contrast and computed tomography chest with contrast was performed. This showed a suspected small residual tumour within the anterior superficial lobe of the parotid gland but with no other lesions identified. The patient subsequently had a superficial parotidectomy and selective level 2A neck dissection to complete the excision. Postprocedure magnetic resonance imaging showed postsurgical changes but no recurrent disease on the parotid bed or pathological lymph nodes. Histology and immunohistochemistry confirmed no residual malignancy in the parotid gland with no evidence of direct extension or tumour within the scar tissue. In the neck dissection, a single focus within the subcapsular sinus of one of the lymph nodes was histologically suspicious. Immunohistochemistry confirmed this deposit is CK7 and S100 positive and CD68 negative and therefore consistent

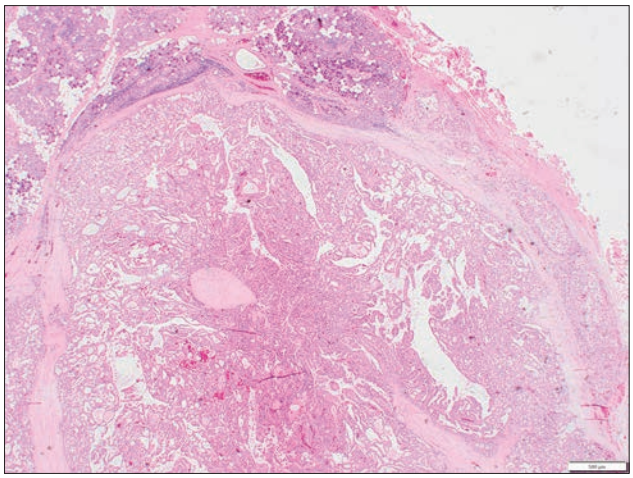

Figure 1: H&E ×20. Neoplasm with infiltrative outline within the parotid gland

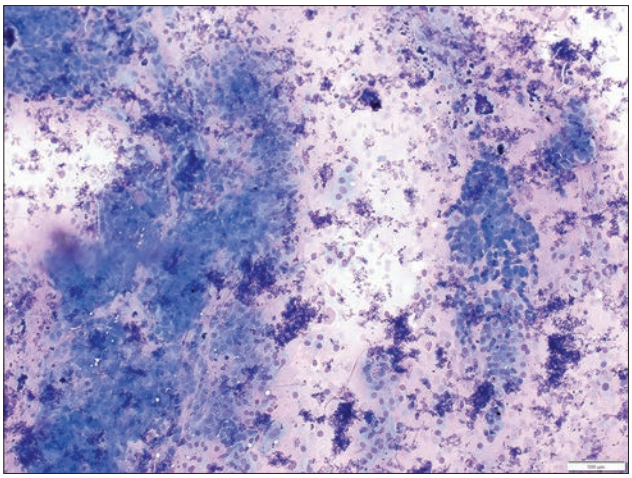

Figure 2: MGG ×200. Cohesive clusters or sheets of epithelial cells with variable eosinophilic, granular to vacuolated cytoplasm, and uniform nuclei with single nucleoli

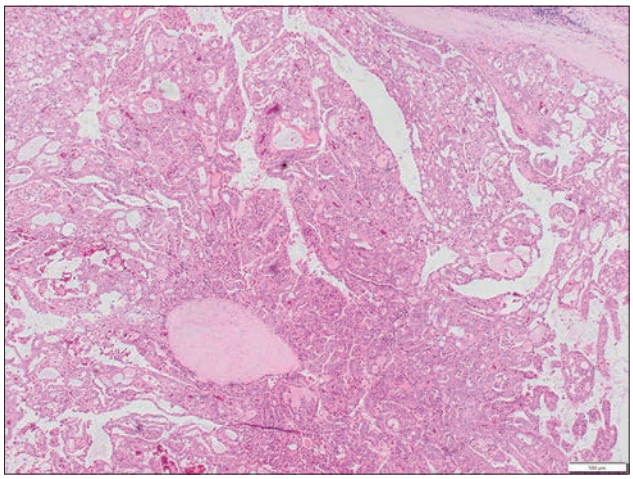

Figure 3: H&E ×40. The neoplasm consists of large cells, with rich eosinophilic or vacuolated cytoplasm and monomorphic round vesicular nuclei, with small but distinctive nucleoli, arranged in a variety of patterns

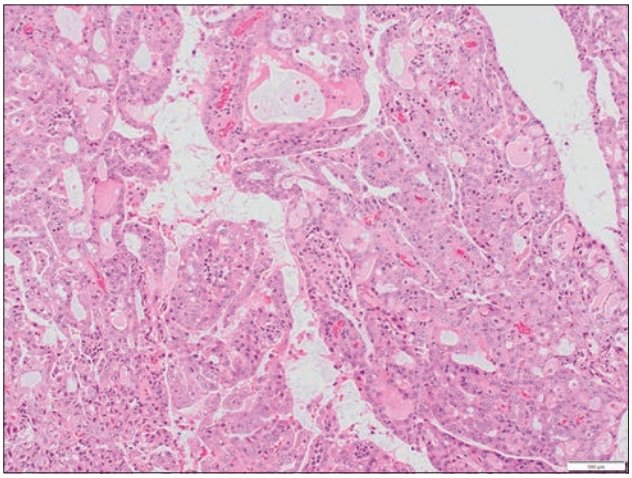

Figure 4: H&E ×100. Neoplastic cells, with eosinophilic or clear cytoplasm and vesicular nuclei, with small but prominent nucleoli

with intranodal deposit of SC. No high-grade features were seen.

DISCUSSION

SC of the salivary gland has been rarely reported in pediatric cases.[4] This case was not identified preoperatively and surgical excision was delayed due to the COVID-19 pandemic. The patient presented with signs and symptoms consistent with a more benign entity and preoperative investigations did not elicit any concerning features. A high index of clinical suspicion would be needed preoperatively to identify the lesion or consider more investigations such as imaging. It is important that all histopathologists and surgeons work closely together to ensure background findings are matched to cellular architecture and cytomorphological features to increase chance of preoperative identification.[12] Cytology is variable and nonspecific and requires a high index of awareness and suspicion and cell block preparation for immunohistochemical stains. A panel of stains including GATA3,[13] p63, DOG1, and S100 is helpful in the differential diagnosis from histological mimics, such as acinic cell carcinoma, intraductal carcinoma, and polymorphous adenocarcinoma. MUC4 appears to be a highly sensitive and specific marker for SC.[14] Clinical and histopathological suspicion of SC can be confirmed with genetic analysis of ETV6 gene.[4,6,12] More studies have been published describing the findings of SC in adult populations;[12] however, more clinical and histopathological presentations in the pediatric cohort are still required to allow more informed clinical decisions. Management of parotid lesions in pediatric cases is challenging due to the balance one must make between being cautious and performing a superficial

parotidectomy with the increased risks this poses, including to the facial nerve, and the risks of incomplete excision and a nonbenign entity during an enucleation such as this case necessitating a more complicated and extensive procedure.

CONCLUSION

We describe a pediatric case of SC that was not preoperatively identified and delayed due to the COVID-19 pandemic. Low clinical suspicion for SC led to incomplete excision leading to a more extensive postoperative procedure. Although a relatively new entity, ENT clinicians and histopathologists should consider SC in patients presenting with a parotid lesion.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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