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Basal cell adenoma in the parapharyngeal space resected via trans-oral approach aided by endoscopy

Case series and a review of the literature

Ting-Ting Wu, MM, Yang-Yang Bao, MM, Shui-Hong Zhou, PhD*, Qin-Ying Wang, MM, Li-Fang Shen, PhD

Abstract

Rationale: Basal cell adenoma (BCA) is a rare benign salivary gland tumor. It is difficult to be completely resected when arising in parapharyngeal space. A contemporary trend is to develop minimally invasive approaches on the premises of safety and complete resection.

Patient concerns: Three patients were referred to our ENT Outpatient Department with the chief complaint of an uncomfortable throat. CT or MRI revealed a unilateral mass in the parapharyngeal space, round or oval in shape, with well-defined borders.

Diagnoses: CT and MRI provided useful information for the preoperative evaluation. The appearance of large-scale cystic components may be an important clue for the diagnosis of BCA. PET/CT images were also available in one case. The final diagnoses were all basal cell adenomas (tubular type) in parapharyngeal space according to the regular histopathological examination after surgery.

Interventions: All three cases were completely resected by a trans-oral approach. The average operative time and estimated blood loss were 86 (range, 61–106) min and 116.7 (range, 50–200) mL, respectively. Endoscopy was used in the largest case to further assess the residual cavity after the complete resection and hemostasis.

Outcomes: Postoperative recovery courses were quick and uneventful, with no neurovascular complication. Patients were discharged on the 3rd–5th day after surgery on an oral diet. One patient reported symptoms of velopharyngeal incompetence, manifested as mild slurred speech and nighttime salivation, for up to 3 months, which recovered spontaneously thereafter. There was no evidence of recurrence in the follow-up period.

Lessons: In our experience, the trans-oral approach appeared to be effective, safe, and less invasive for extirpation of selected basal cell adenomas in the parapharyngeal space. An assistance of endoscopy facilitates the surgery.

Abbreviations: ^{18}FDG PET = ^{18}F-deoxyglucose positron emission tomography, BCA = basal cell adenoma, CK = cytokeratin, CP = calponin, CT = computed tomography, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging, PA = pleomorphic adenoma, PPS = parapharyngeal space, TORS = trans-oral robotic surgery, WT = Warthin tumor.

Keywords: basal cell adenoma, computed tomography, endoscopy, magnetic resonance imaging, parapharyngeal space, trans-oral approach

1. Introduction

Basal cell adenoma (BCA) is a rare benign salivary gland tumor, characterized by isomorphic basaloid cells. The World Health Organization classifies it as a subtype of salivary gland epithelial tumors usually occurring in the parotid gland, but is far less common than pleomorphic adenomas (PAs) and Warthin tumors (WTs), ranking third in benign parotid tumors.[1]

The BCA arising in parapharyngeal space (PPS) is difficult to resect completely, because of the complex and critical anatomical structures peripherally. Classic approaches to reach PPS tumors include trans-cervical, trans-parotid, trans-mandibular, and combinations thereof, but these can cause relatively large injuries and leave obvious facial scars. A contemporary trend is to develop minimally invasive approaches on the premises of safety and complete resection.

2. Methods

We retrospectively collected three cases of BCA occupying the PPS, completely resected by a trans-oral approach. All 3 patients were evaluated and managed in our hospital, and followed up in outpatient department after surgery until December 2017. Surgeries were performed by Dr Zhou (chief attending) and his regular medical team under general anesthesia. Endoscopy was employed in the largest case. Clinical data were collected and analyzed in January 2018.

This study was approved by the local ethics committee (the institutional review board at the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou City, China) (reference number 2017-426), and informed consent was obtained from all patients.

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Department of Otolaryngology, The First Affiliated Hospital, Zhejiang University, Hangzhou City, Zhejiang Province, China.

** Correspondence: Shui-Hong Zhou, Department of Otolaryngology, The First Affiliated Hospital, Zhejiang University, 79# Qingchun Road, Hangzhou City, Zhejiang Province 310003, China (e-mail: 1190051@zju.edu.cn).*

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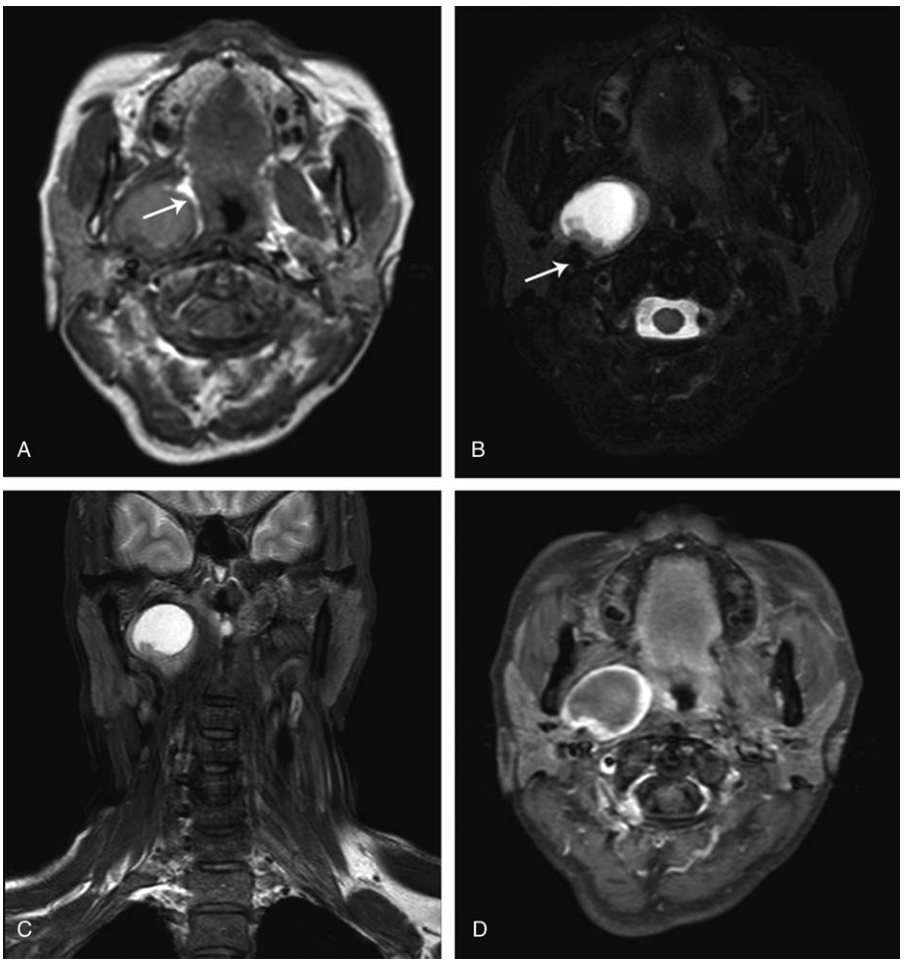

Figure 1. Magnetic resonance imaging (MRI) of case 1 showed a predominantly cystic mass occupying the right parapharyngeal space. The mass was well defined with a diameter of 33 mm. (A) On axial T1-weighted MRIs, the central cystic content showed a homogeneous slightly hyperintense signal versus muscle. The peripheral solid rim showed an isointense signal versus muscle. A fat cap sign was visible at the anterior and medial side of the mass (arrow). (B and C) On axial and coronal T2-weighted images, the central content showed an intensely hyperintense signal and the peripheral rim showed a slightly hyperintense signal, relative to muscle. The structure of the carotid sheath was displaced posteriorly (arrow). (D) On axial enhanced T1-weighted MRIs, the peripheral rim was intensely enhanced after administration of intravenous gadolinium.

3. Results

3.1. Case 1

A 52-year-old Chinese female was referred to our ENT Outpatient Department in January 2017, with the chief complaint of a sore throat after drinking herbal wine. Physical examination revealed a red throat and nontender bulging of the lateral pharyngeal wall at the right side, with no abnormal secretion or ulceration. An extra-oral examination was negative for swelling, tenderness, or lymphadenopathy. Enhanced computed tomography (CT) and a magnetic resonance imaging (MRI) scan revealed a predominantly cystic mass in the right PPS, measuring 33 mm in diameter. This well-defined mass showed peripheral enhancement after administration of intravenous gadolinium (Fig. 1).

The patient underwent a trans-oral tumor resection under general anesthesia with oral tracheal intubation. The standard tonsillectomy position with a Boyle-Davis mouth gag was used routinely (Fig. 2A). After removing the right tonsil, incising the right lateral wall of oropharynx and partial superior pharyngeal constrictor muscles, a shiny mass containing fluid was exposed (Fig. 2B). Intraoperative frozen sections revealed that the tumor originated from epithelial cells of the salivary gland, first suggesting BCA. Then, the tumor was separated carefully; it was found to be attached to the parotid laterally but it was not attached to the internal carotid artery, jugular vein, or any nerve. The duration of surgery was 60 minutes and no neurovascular injury occurred in the process. The amount of bleeding during the operation was ~50 mL. Empiric antibiotics were prescribed routinely to prevent infection after surgery.

The regular postoperative histopathologic examination confirmed the tumor as a BCA (tubular type) with regional brisk growth and capsular invasion. Immunohistochemical examination revealed the tumor was positive for CK (cytokeratin, pan), calponin (CP), CD117, and weakly positive for glial fibrillary acidic protein (GFAP). Positive staining for S-100 was observed in the stroma (Fig. 3).

The patient resumed an oral liquid diet on recovery from general anesthesia and did not require any significant analgesia beyond the first 2 days. The postoperative course was uneventful, and the patient was discharged on the 4th day after surgery with no cranial neuropathy, such as hoarseness, tongue deviation,

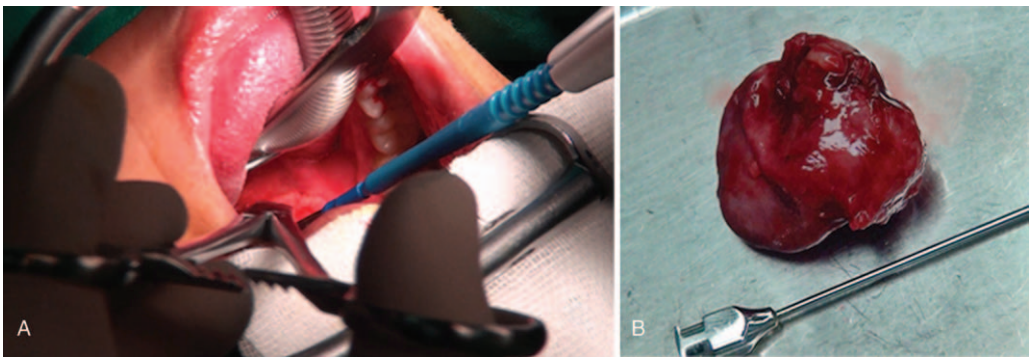

Figure 2. (A) Regular trans-oral approach. The patient was in a standard tonsillectomy position after general anesthesia with oral tracheal intubation. A Boyle-Davis mouth gag was inserted to keep the mouth open, and gauze was used to protect the teeth. (B) A cystic mass measuring 33 mm in diameter was resected completely from case 1.

difficulty in neck rotation, or dysgeusia. There was no recurrence in the follow-up period until December 2017.

3.2. Case 2

A 48-year-old Chinese female presented to our ENT Outpatient Department in April 2016, with a history of intermittent repeated angina in the right oropharynx for 3 months. A physical examination revealed a bulging lateral wall of the oropharynx at the right side, with no abnormal secretion or ulceration. An extra-oral examination was negative for swelling, tenderness, or lymphadenopathy. Subsequent CT and MRI revealed an oval 60 × 40 mm mass in the right PPS (Fig. 4A–E).

Under general anesthesia, the tumor was excised en bloc by a trans-oral approach within 90 minutes (Fig. 5). An endoscope was used to further assess the residual cavity after the complete resection and hemostasis (Fig. 6). The amount of bleeding during the operation was ~200 mL. The tumor was large, measuring 60

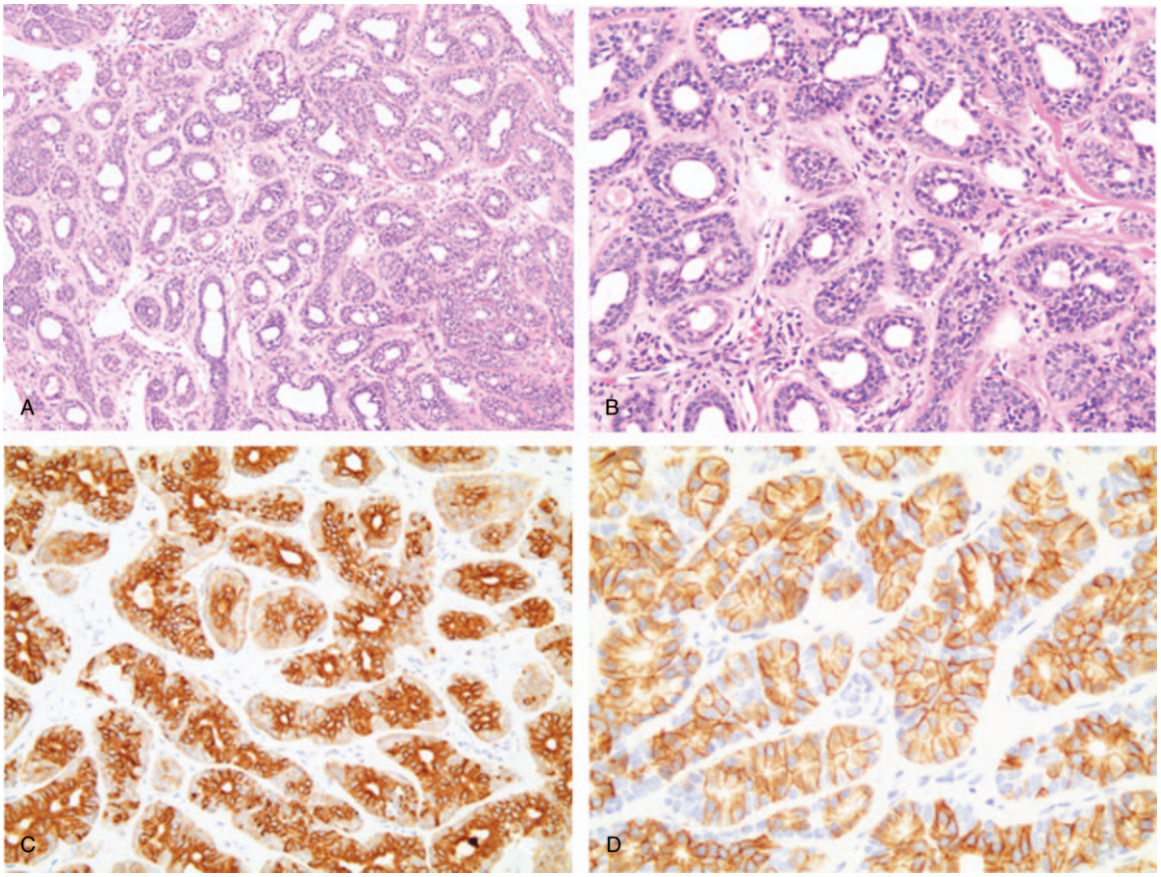

Figure 3. Histologic examination revealed the tumor was a basal cell adenoma of tubular type. (A) Original magnification ×100, hematoxylin and eosin (H&E) staining. (B) Original magnification ×200, H&E staining. (C) The tumor was positive for CK in the immunohistochemical examination. (D) The tumor was positive for CD117 in the immunohistochemical examination.

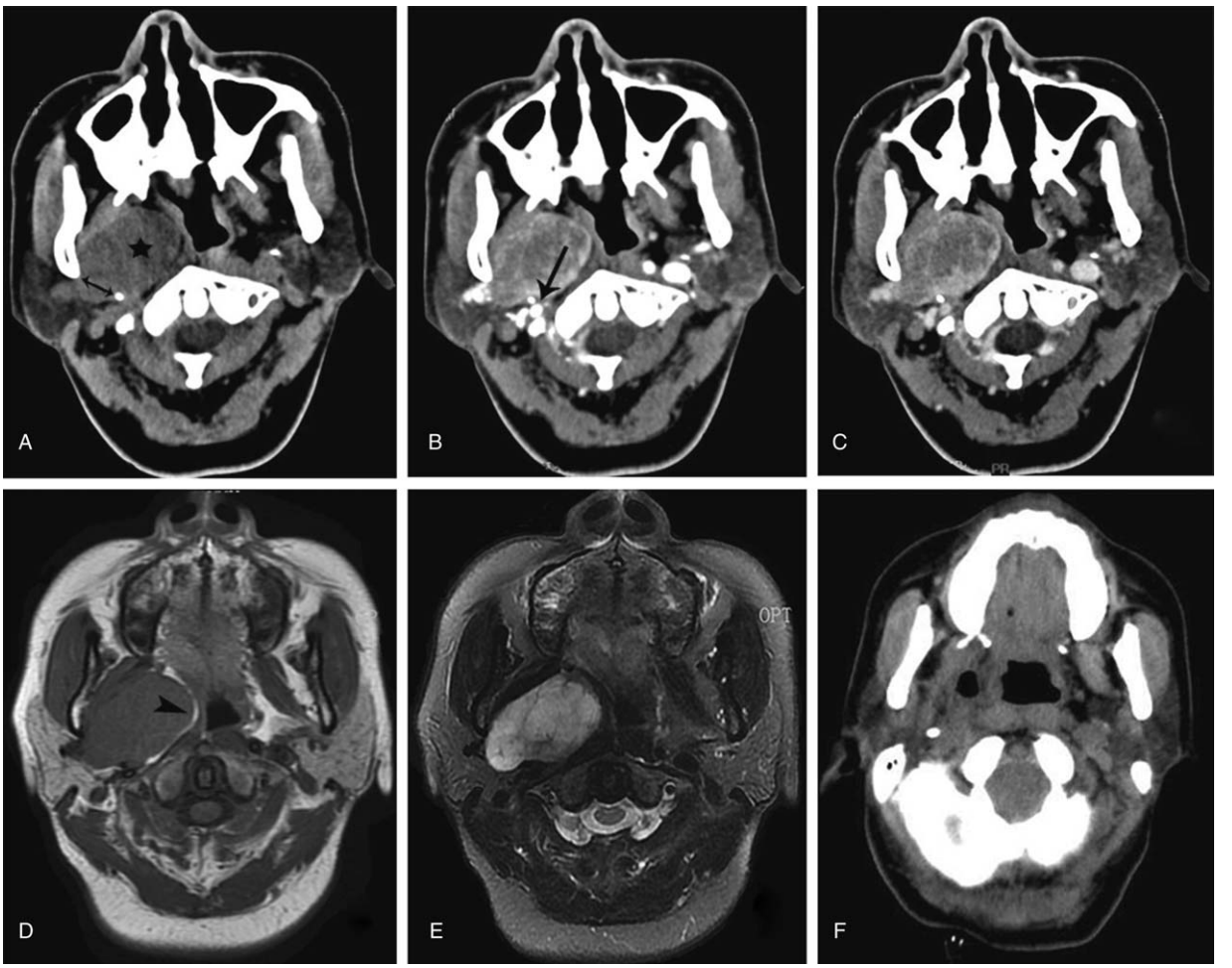

Figure 4. (A) Unenhanced computed tomography (CT) scan showed a well-defined mass measuring 60 × 40 mm in the right parapharyngeal space (PPS) (star). The stylomandibular tunnel (double-headed arrow) was widened due to the tumor. (B) The mass exhibited heterogeneous enhancement at the periphery of tumor in the early phase. The internal carotid artery was displaced laterally and posteriorly (arrow). (C) Enhancement of the mass decreased gradually in the later phase. (D) Noncontrast T1-weighted magnetic resonance imaging (MRI) showed a well-marginated mass, which was isointense relative to muscle. A fat cap sign was visible at the anterior and medial side of the mass (arrowhead). (E) Noncontrast T2-weighted MRIs showed the mass was heterogeneously hyperintense. (F) Follow-up CT scan at 2 weeks after surgery showed a blurry right PPS with no sign of a residual lesion.

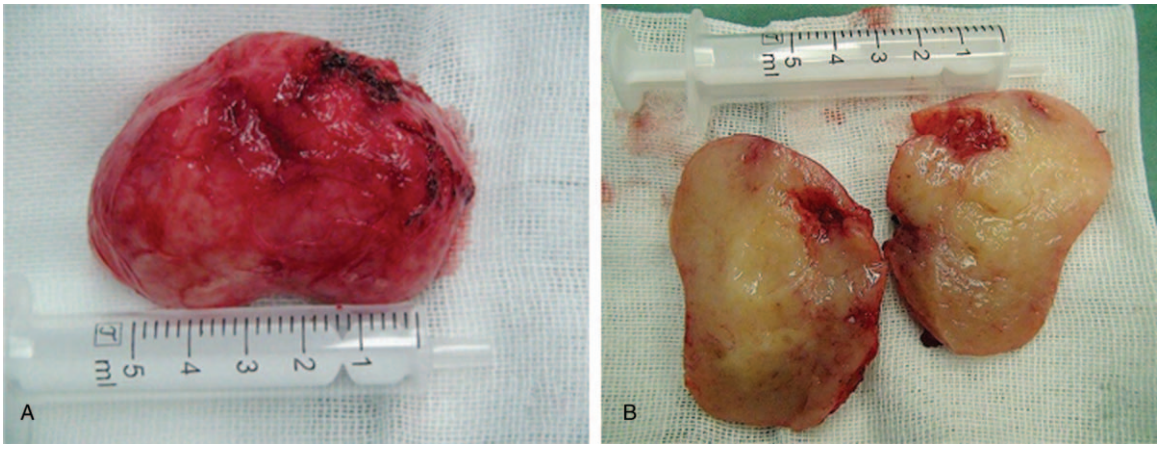

Figure 5. The whole tumor of case 2 after complete resection (A) and its cross-section (B).

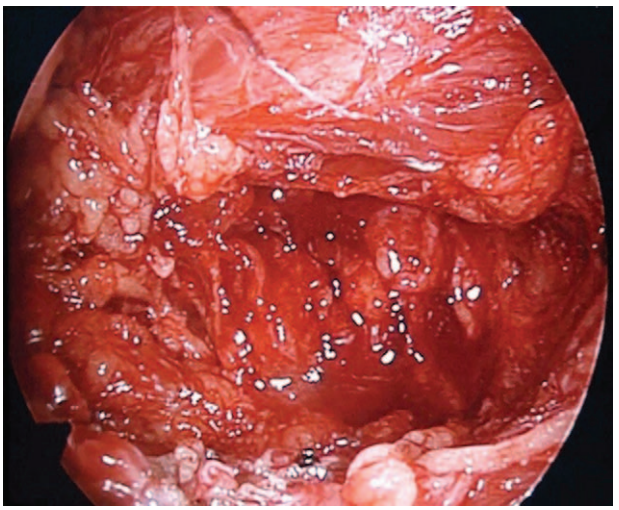

Figure 6. An endoscope was used during the surgery of case 2 to further observe the residual cavity after complete resection and hemostasis.

× 40 × 30 mm and was snugly close to the internal carotid artery and jugular vein. It was coated by an intact capsule, rich in vessels, resulting in easily hemorrhage during surgery. Intraoperative frozen sections revealed the tumor originated from the salivary gland. A regular histopathologic examination demonstrated an encapsulated solid mass, white-gray in color, constituted by 2 layers of tumor cells arranged in a cribriform or tubular pattern. An immunohistochemical examination revealed that the tumor was positive for CK (pan), P63, and negative for SMA, CD43, and GFAP. Focal tumor cells were positive for S-100. Some tumor cells were positive for CP, CD117, and CK18. Weak staining for Ki-67 was observed, and the MIB-1 index was below 10%. The final diagnosis was BCA.

The postoperative course was uneventful, and the patient was discharged on the 5th day after surgery with no complications. A CT scan at 2 weeks after surgery showed a blurry right PPS with no sign of a residual lesion (Fig. 4F). There has been no evidence of recurrence in follow-up until December 2017.

3.3. Case 3

A 41-year-old Chinese female presented to our ENT Outpatient Department in November 2014, with a history of a pharyngeal foreign body sensation for 2 months. Physical examination revealed slight redness of the pharynx, negative for swelling, tenderness, or lymphadenopathy. MRI revealed a round and well-defined mass sized 30 × 20 mm in the right PPS. Due to a history of gastric fundus carcinoid, which had been removed by gastroscopy, the patient was advised to undergo an ^{18}F-deoxyglucose positron emission tomography (^{18}FDG PET)-CT examination to differentiate metastatic lymph node from benign. PET images revealed increased uptake of ^{18}FDG in the right PPS, corresponding well to the mass shape on CT (Fig. 7). No lump or increased uptake in the gastric fundus was observed. No other lymph node, lung, or liver metastasis was evident.

The tumor was excised by a trans-oral approach under general anesthesia within 100 minutes and was found to be an encapsulated cream-colored mass measuring 40 × 30 mm. The amount of bleeding during the operation was ~100 mL. Intraoperative frozen sections revealed the tumor originated from epithelial cells of the salivary gland. A regular histopathologic examination showed the tumor was constituted by 2 layers of basaloid cells arranged in tubular and cribriform patterns. The final diagnosis was BCA in the right PPS.

The postoperative course was uneventful, and the patient was discharged on the 3rd day after surgery with no complications. The patient experienced a comfortable recovery but reported mild slurred pronunciation and nighttime salivation up to 3 months after surgery, which recovered spontaneously thereafter. There has been no evidence of recurrence in follow-up to December 2017.

Table 1 summarizes the clinical and surgical data from the 3 cases.

4. Discussion

The BCA is an uncommon benign epithelial neoplasm of the salivary glands, accounting for ~5% to 7.5% of all salivary gland neoplasms.[2,3] BCAs are composed of relatively isomorphic basaloid epithelial cells, organized with an abundant basal cell layer and distinctive basement membrane-like structure, lacking a myxochondroid stromal component that is usually found in PAs.

Figure 7. Positron emission tomography (PET) images revealed increased uptake of ^{18}F-deoxyglucose in the right parapharyngeal space, corresponding well to the mass shape on computed tomography (CT) and the fusion images.

Table 1

The clinical and surgical information data from the 3 cases have been summarized.

Case no	Sex	Age, y	Tumor side	Surgery date	Surgery time, min	Tumor size, mm	Pathology	Bleeding, mL	Discharged date after surgery
1	F	52	Right	March 8, 2017	61	33	Tubular	50	4th
2	F	48	Right	April 15, 2016	92	60×40	Tubular	200	5th
3	F	41	Right	November 18, 2014	106	40×30	Tubular	100	3th

F = female, min = minute, mL = milliliter, mm = millimeter, y = year.

Grossly, BCA presents as a round or oval mass with a fine fibrous capsule.[4] According to the predominant tumor cell arrangement, BCA has been classified into 4 histologic subtypes: solid, trabecular, tubular, and membranous. All the 3 cases in our report were of the tubular type, featuring bilayered tubular structures consisting predominantly of inner eosinophilic luminal cells and outer cuboidal cells. The most common type reported in previous studies is solid BCA,[3] which exhibits solid proliferation of round or oval tumor cells and cell nests of various sizes, with a palisading row of peripheral tumor cells. In the trabecular type, the tumor cells are arranged in trabecular cords and occasionally form tubular lumens or intercellular canalicular slits within the trabeculae. Membranous BCAs are characterized by palisading of peripheral tumor cells and an excessive hyaline basal membrane.[5]

The PPS resembles an inverted pyramid with its base situated at the skull base and its apex tapered to end at the greater cornua of the hyoid bone. It is bordered medially by the lateral pharyngeal wall and constrictor pharyngis muscles, laterally by the mandibular ramus, anteriorly by infratemporal fossa, and posteriorly by the vertebral column. The stylohyoid ligament divides the PPS into the prestyloid and poststyloid compartments. The prestyloid compartment is the smaller of the 2, containing the deep lobe of the parotid, minor salivary glands, fat, and lymph nodes. The poststyloid compartment contains more critical structures, including the internal carotid artery, internal jugular vein, cranial nerves IX to XII, and the sympathetic trunk. Tumors arising in the PPS are histologically diverse, containing 80% benign tumors and 20% malignancies.[6] The potential space allows tumors to grow to a significant size before causing symptoms. Classification of lesions into prestyloid versus poststyloid origin aids in making the primary diagnosis. The most common tumors in the PPS are of salivary gland origin, typically appearing in the prestyloid compartment, whereas neurogenic tumors are more common in the poststyloid compartment.

The BCAs arising in the PPS tend to be asymptomatic masses and are usually found accidentally. They are considered to be a slowly enlarging, freely mobile, and smooth mass in the oropharynx with medialization of the lateral pharyngeal wall, tonsil, and soft palate. Occasionally, the patient may complain of a foreign body sensation in the throat. An assessment of all cranial nerves is necessary in cases of neural involvement. There is a significant female predilection in BCAs,[3] as in our report (Table 1).

The CT and MRI scans are the first choices in evaluating PPS tumors, presenting benign features, such as unilateral genesis, round or oval in shape, and well-defined borders, as opposed to malignant features, such as invasive growth and indistinct margins. BCAs may be predominantly cystic or solid. The solid component showed intense enhancement after an intravenous contrast injection. A cystic component may denote cystic degeneration or hemorrhage within the tumor.[7] A widened stylomandibular tunnel, and lateral and posterior displacement of the carotid artery, suggest a tumor assigned to the prestyloid compartment.[8] The appearance of a parotid gland pedicle, no visible fat plane preserved between the mass and the parotid gland, and a stratified fat cap located at the anterior and medial side of tumor are all signs indicating that the tumor originated from the parotid gland. Calcification is uncommon.[9]

The CT images of case 2 showed a well-defined lesion, presenting intense enhancement in the early phase, which then decreased gradually in the later phase, consistent with the previous report.[10] PAs show little or no enhancement in an immediate post contrast scan but strong enhancement in a delayed scan.[11] Malignant salivary gland tumors show increased enhancement or a platform in the delayed phase, while most WTs showed decreased attenuation on CT.[12]

The MRIs provide more information for the assessment and differentiation of lesions. Generally, BCAs are isointense, relative to muscle, on T1-weighted images, and hyperintense on T2-weighted images,[13] as shown in case 2. A Japanese study found that nearly half of BCAs have cystic components, and that the cystic ratio of BCAs is significantly higher than that of PAs.[14] A previous pathologic study revealed that 65% of BCAs showed cystic changes to differing degrees,[4] compatible with the imaging observations above. MRIs of our case 1 revealed a cystic mass, which was a clue for the diagnosis of BCA.

The PET/CT images of BCA are rarely reported because of its benign character. Wang et al reported a peculiar BCA located in the left nasal septum, and observed an increased accumulation of ^{18}FDG.[15] Our case 3 underwent an ^{18}FDG PET-CT examination to differentiate a metastatic lymph node from a benign mass, because of her history of gastric fundus carcinoid. Images revealed increased uptake of ^{18}FDG in the right PPS, probably related with the numerous endothelial vascular channels within tumor.[16]

The BCAs and PAs present similar clinical features, such as unusual and occasional recurrence, so it may not be necessary to make an exact differentiation between these 2 histologic types. However, considering the very different treatment planning and prognostic evaluations, it is important to differentiate BCAs from low-grade malignancies, such as basal cell adenocarcinoma, basaloid squamous cell carcinoma, and adenoid cystic carcinoma, which may be subjected to radical tumor resections with lymph node dissection. Thus, if CT/MRIs suggest malignancy, a diagnostic biopsy should be scheduled in the preoperative workup when possible.

The primary treatment for BCAs in the PPS is surgical resection, with the goal of complete removal and functional preservation. The main indications for surgery include relief of mass compressive symptoms and the prevention of malignant transformation. Total parotidectomy is preferred in the membranous type of BCA because it tends to be multicentric, has a

high recurrence rate, and occasionally undergoes malignant transformation.[5] The trans-cervical approach is used routinely in many hospitals, providing sufficient access to the PPS, and is especially suitable for tumors located in a relatively low position or malignancies requiring a wide field for radical resection. However, exposing the superior aspect of PPS is limited with a trans-cervical approach, where a combined mandibulotomy may be required for greater access, thus causing a larger injury and an obvious facial scar.[17] Morbidities such as facial nerve injury, first bite syndrome, and malocclusion increasingly develop. The contemporary trend is to use minimally invasive approaches on the premises of safety and complete resection.

In this report, we describe 3 cases of BCAs in the PPS, all of which were successfully resected by a trans-oral approach. The average operative time was 86 (range, 61–106) minutes. The average estimated blood loss was 116.7 (range, 50–200) mL. Additionally, endoscopy was used in the surgery for case 2 after complete tumor resection and hemostasis, to further assess the surgical cavity and ensure the absence of residual tumor. Postoperative recovery courses were fast and uneventful, except for probably enduring pharyngalgia in the first 2 days. Patients were discharged on the 3rd to 5th day after surgery on an oral diet. One patient (case 3) reported mild slurred speech and nighttime salivation at the first follow-up appointment, which may have been manifestations of velopharyngeal incompetence due to the unhealed wound. The patient was advised to take a wait-and-see strategy. As expected, the symptoms disappeared gradually after 3 months postoperatively.

Goodwin and Chandler first described the trans-oral approach for PPS tumors in 1988, recommending it for relatively small, avascular, extra-oral impalpable, and benign masses.[18] It provides direct access to the PPS and prevents external scars. However, its application has been limited by undesirable comorbidities, such as uncontrollable bleeding, nerve injury, incomplete resection, and increased recurrence rates, up to 25%.[18] With the development of surgical techniques, the trans-oral approach is now increasingly being used for PPS surgeries, providing optimal esthetic outcomes, shortened hospitalized times, and increased patient comfort after the operation. It is our responsibility to tailor surgical planning according to the patient's individual tumor characteristics. The trans-oral approach is safe, convenient, and economical for selected PPS tumors: those bulging significantly toward to the oropharynx, with no trismus or previous radiotherapy-related tissue fibrosis, and no sign of vital structure involvement.[19] The whole surgery is performed in a deep and narrow space that requires surgeons to provide accurate hemostasis and meticulous protection of critical anatomical structures. However, a cervical incision should be considered in case it is required as an adjunctive maneuver. The decision to add a trans-cervical approach is not mainly based on tumor size, but on intraoperative difficulty in visualizing and dissecting the lateral extent of the tumor passing through the stylomandibular tunnel.[20]

Exposure of a large PPS tumor is a challenge, and the typical process of blind/blunt finger dissection increases the risk of tumor spillage and neurovascular injury. Assistance with endoscopy appears to overcome this. With improved illumination and widened visualization, the blind zone behind the tumor can be exposed and vital structures can be managed safely. An angled endoscope enables access to a deeper area and facilitates complete resection.[19] Currently, the trans-oral robotic surgery (TORS) used in the resection of PPS tumors is emerging as a new technique, allowing the use of magnified 3-dimensional visualization and wristed instruments that are convenient for working in narrow corridors. Several institutions have reported their experience with TORS in the removal of PPS tumors, with excellent feasibility and safety.[21] A frequently mentioned drawback of TORS is its lack of haptic feedback. Additionally, TORS requires more skillful practice, involves higher medical costs, is more time consuming, and may be less convenient for patients and hospitals (eg, in China, robotic surgery is only available in several tertiary general hospitals, and patients must pay at least an additional $5000 USD per single use). Thus, further evaluations of efficacy and efficiency regarding TORS are required.

The BCA (except the membranous type) is considered to be a nonrecurrent tumor with a good prognosis after complete resection. The 3 patients described here were followed for 9to 37 months (average 22 months) and no recurrence was observed. The most important causes of recurrence are enucleation with intraoperative spillage and incomplete tumor excision. Malignant transformation in BCA has been reported.[22] Therefore, routine follow-up after surgery is necessary. No distant metastasis has been described.

The limitations of this case series is the small sample size and the short-term follow-up, resulting in uncertain advantages and disadvantages among different approaches for PPS tumors excision. In the future study, a prospective study will be designed to further evaluating the different clinical outcomes among several approaches.

5. Conclusion

The CT and MRI provide useful information for the evaluation of BCA, presenting benign features, such as unilateral genesis, round or oval in shape, and well-defined borders. The appearance of large-scale cystic components may be an important clue for the diagnosis of BCA. We reported 3 cases of BCA and demonstrated that large BCAs of the PPS can be removed by a trans-oral approach safely and completely, with no neurovascular injury or infection. Our practical experience confirmed the trans-oral approach as a feasible, safe, and minimally invasive surgical plan for selected BCAs of the PPS. An assistance of endoscopy facilitates the surgery. The TORS, as a new technique, deserves our attention.

Author contributions

Conceptualization: Ting-ting Wu, Shui-Hong Zhou.
Data curation: Yang-Yang Bao.
Resources: Shui-hong Zhou, Qin-Ying Wang.
Writing – original draft: Ting-ting Wu.
Writing – review & editing: Yang-Yang Bao, Shui-hong Zhou, Qin-Ying Wang, Li-Fang Shen.

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