Can pituitary adenoma stimulate an adenoid cystic carcinoma in the oral cavity: An intriguing case with literature review

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Abstract

Adenoid cystic carcinoma (ADCC) is a pathology affecting exocrine glands originating primarily from the minor salivary glands. Although rare in incidence, but there are cases of seeding of cells of adenoid cystic carcinoma into intracranial sites via different routes. We report of an intriguing case of remote metastasis of an intracranial tumor in the pituitary diagnosed as pituitary adenoma which spread to the oral cavity as ADCC. According to our perspective, it is the first reported case of seeding of cells from intracranial pituitary adenoma to intra-oral site manifesting as ADCC.

Keywords: Adenoid cystic carcinoma, metastasis, oral cancer, pituitary adenoma

Introduction

Adenoid cystic carcinoma (ADCC) is a tumor or pathology affecting mainly the minor salivary glands, the major salivary glands, lacrimal gland, bronchus, breast, and intestinal and genital tracts.\(^1,2\) It is characteristically slow growing but often invades the cranial base directly with rates of cranial base invasion between 4% and 22%.\(^3\) However, intracranial remote metastasis from ADCC of the salivary gland is quite rare,\(^4\) but it has been reported in the literature.\(^5\) Pituitary adenomas are the third most common all primary intracranial tumors. However, primary pituitary adenomas metastases into extracranial sites are very rare. We report a rare incidence of remote metastasis of an intracranial tumor in the pituitary to the oral cavity. According to our perspective, it is the first reported case of seeding of cells from cephalad to caudad direction.

Case Report

A 69-year-old male patient reported to our department with the chief complaint of growth in the right lower back tooth region associated with difficulty in chewing food from that side since 6 months. The patient also complained of pain in the same region since 6 months. The swelling was initially small in size and gradually increased to reach the present size. The pain was moderate, intermittent, localized, aggravated on chewing food and subsided on its own medical history revealed pituitary macroadenoma [Figure 1]. It was diagnosed...
4 years back in a neurosurgical center patient had visited due to systemic symptoms. The tumor was surgically treated by pituitary decompression via endonasal transsphenoidal approach 4 years back and the patient was asymptomatic after the surgery [Figure 2]. On intraoral examination a well-defined erythematous swelling with ill-defined borders measuring about 2 cm × 3 cm in size was seen on the right lower posterior buccal mucosa involving the retromolar area and pterygomandibular raphe extending into the soft palate [Figure 3]. On palpation, the swelling was firm in consistency and tender. In light of the patient's history, and clinical examination, a provisional diagnosis of salivary gland neoplasm was given. The lesion was excised in toto and sent for histopathological examination, the excision site was sutured using the buccal pad of fat which healed uneventfully on follow-up [Figure 4]. The patient is under follow-up every 3 months, and there has been no recurrence of tumor intraorally, also there are no systemic symptoms to prove recurrence of intracranial tumors over a period of 2 years.

Histopathological examination of the excised specimen revealed stratified squamous epithelium and partially encapsulated mass comprising of hypercellular areas. Cells are arranged in small nests, cords, islands with tubular, and cribriform patterns. The prominently solid pattern was seen. Lobules of minor salivary glands were seen at the periphery. Perineural invasion was also seen [Figure 5]. The overall histopathological features were diagnostic of ADCC. The specimen was further subjected to immunofluorescence study in which pituitary tumor transforming gene (PTTG) was seen [Figure 6].

**Discussion**

ADCC is a malignant salivary gland tumor which was first described by Billroth in 1859 as cylindroma, due to its cribriform appearance formed by the tumor cells with cylindrical pseudolumina or pseudospaces.[6,7] The term “ADCC” was introduced by Ewing (Foote and Frazell) in 1954. ADCC has a rare incidence of <1% of all malignancies of head and neck. It represents 5-10% of all salivary gland neoplasms.[8] Intraorally 50% of ADCCs occur on the palate. The area of the greater palatine foramen is more commonly involved in the palate. The other less common sites of involvement are a lower lip, buccal mucosa, the floor of the mouth retromolar area, tonsillar pillar area, sublingual gland.[8] The nose and paranasal sinuses are also affected by ADCCs.[9]

Generally tumors are classified according to the histologic pattern that predominates. Szanto et al. graded ADCC as cribriform or tubular (Grade I), <30% solid (Grade II) or >30% solid (Grade III).[10] Cribriform is the most common and solid is the least common. It is seen that mostly ADCCs do not occur in “pure” cribriform, tubular or solid types but are rather mixed. It is common to have more than one histopathologic pattern
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Metastasis to oral cavity

Pituitary adenoma is the most common type of pituitary disorder. They are benign neoplasms that account for 10-15% of all intracranial masses. Usually detected during the autopsy and radiologic studies indicate that the majority of these tumors are incidentalomas without clinical significance.

The World Health Organization classified pituitary tumors (2000) into the three grades: Benign, intermediate or atypical, and malignant. Pituitary adenomas are also categorized based on primary cell origin and type of hormone secreted by these cells. Tumors are also categorized based on size as microadenomas - tumors that are <10 mm in size and are located totally within the sella turcica, macroadenomas in turn are large tumors (>10 mm), totally intrasellar but are often associated with extrasellar extension. Such tumors usually extend inferiorly into the sphenoid sinus, but mostly go superiorly into the suprasellar space (due to lower resistance) which puts pressure on the optic apparatus, or extends into the cavernous sinuses on either side.

ADCC is characteristically slow growing but often invades the cranial base directly with rates of cranial base invasion between 4% and 22%. However, intracranial remote metastasis from ADCC of the salivary gland is quite rare. According to Shotton et al., cranial base invasion occurs along three routes: The eustachian tube, the mandibular and maxillary nerves, and the internal carotid artery. There are four metastatic pathways to the pituitary gland; (1) Direct blood-borne metastasis to the posterior lobe with subsequent expansion, (2) blood-borne metastasis to the pituitary stalk with growth into the anterior and posterior pituitary lobes, (3) blood-borne metastasis to the clivus, dorsum sellae, or cavernous sinuses, which then spreads into the pituitary gland, and (4) leptomeningeal spread with involvement of the pituitary capsule.

The tumor cells can spread to different distant parts which usually involve the liver, lymph nodes, bone, and lung and unusual places, such as heart, pancreas, eye, ear, ovary, and myometrium. In our case, it has spread to the oral cavity. The spread pathway of tumor cells from pituitary has not been determined but has been proposed to be varied, including cerebrospinal fluid circulation and lymphatic or hematogenous metastasis to extracranial sites. The seeding of tumor cells can be attributed to the biological properties of tumors, such as invasion or to the surgical procedures used. According to the existing literature, the metastases of pituitary tumors generally occur after surgery to extracranial sites, especially after craniotomy. Tanaka et al. reported the development of metastases after surgery performed for primary pituitary tumors in 21 (70%) of 30 cases. It was felt that surgery may precipitate post-operative metastasis of pituitary adenomas. According to neurosurgeon’s, this can be due to several reasons. First, neurosurgery, especially in craniotomy, there can be a rupture of the tumor capsule as well as damage to the normal arachnoid membrane, leading to the spread of tumor cells along the subarachnoid space. Second, the vasculature around the tumor are encroached, which may lead to hematogenous spread. Third, tumor cells can also disseminate by the surgical

Figure 5: Histopathology shows cells are arranged in small nests, cords, islands with tubular, and cribiform patterns

Figure 6: Immunofluoresence study shows pituitary tumor transforming gene emitting blue color

in a single neoplasm and all three patterns can be observed in the majority of tumors. The main reason for histologic typing is to assess the prognostic difference between histologic types. In terms of prognosis tubular pattern (well differentiated) is observed to have the best prognosis compared to the cribriform pattern (moderately differentiated) and solid pattern (poorly differentiated). Perineural invasion is characteristic of these tumors and occurs in up to 60% of cases. It was also seen in our case in the histopathology report.

Furthermore, expression of PTTG has been reported to be seen in high rates in pituitary adenomas. This gene also has been implicated in the invasiveness of the tumor. It has also been reported with ADCC. Our case also showed expression of PTTG. It raised suspicion that the adenoid cystic carcinoma is not an independent entity but may be due to the seeding of the cells of pituitary adenoma to the oral cavity. It prompted us to search the available literature for this cephalad to caudad spread.
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instruments or flush water. It is seen that the most patients who reported with post-operative metastases of pituitary tumors underwent craniotomies before 2000. After 2000, the endonasal transsphenoidal surgical technique is done in more than 90% of pituitary tumor surgeries. The endonasal transsphenoidal approach rarely causes a massive cerebrospinal fluid leakage or tumor cell dissemination to the subarachnoid space, and, as a result, the possibility of surgery associated post-operative tumor metastasis in the subarachnoid space is reduced,[16] but still chances are there as is seen in our case.

Conclusion

Usually, the oral lesion is the first and only symptom of disease which might be growing silently elsewhere in the body. A prompt diagnosis of such lesions warrants a holistic approach toward the systemic investigation. Tumors such as the present case can be easily confused with primary salivary gland neoplasm compelling the surgeon to focus attention to it while the systemic cause gets neglected leading to catastrophic consequences. So though rare, metastasis from intracranial pituitary tumors must be considered in the differential diagnosis of ADCC.

References