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Case Report

Intracranial extension of parotid adenoid cystic carcinoma presenting as trigeminal neuralgia: A case report ☆,☆☆

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ABSTRACT

Being rare malignancies, parotid gland adenocarcinomas are most significantly represented by the ACC subtype due to their aggressive nature and propensity for PNI. We present a case of a 56-year-old male with right-sided trigeminal neuralgia and facial palsy, diagnosed with ACC of the parotid gland with intracranial extension. Tumor progression occurred with brain, lung, and liver metastases, so he was placed on palliative care despite chemotherapy. This case underscores the diagnostic and management challenges associated with ACC with PNI.

Introduction

Parotid gland adenocarcinomas are rare malignancies, comprising only 2.9% of salivary gland tumors and a small fraction of head and neck cancers [1]. Among these, adenoid cystic carcinoma (ACC) is a significant subtype, accounting for 17% of malignant salivary gland tumors and 26% of malignant parotid gland tumors [2,3]. Despite its slow growth, ACC is distinguished by its aggressive behavior, particularly its propensity for perineural invasion (PNI). PNI involves the infiltration of tumor cells into nerve sheaths, a process that contributes to tumor progression and metastasis. Clinically, this can manifest as perineural spread (PNS), characterized by tumor exten-

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sion along nerve pathways, often with intracranial involvement [4]. Both PNI and PNS are associated with poor prognostic outcomes, including higher rates of recurrence, distant metastasis, and reduced survival [4].

We present a case of a 56-year-old male with right-sided trigeminal neuralgia and facial palsy, later diagnosed with adenoid cystic carcinoma of the parotid gland with intracranial extension. Despite initial chemotherapy, the tumor progressed with brain, lung, and liver metastases, requiring palliative care and gemcitabine-based treatment.

Case presentation

A 56-year-old male with an unremarkable past medical and surgical history presented with a 1-month history of right-sided trigeminal neuralgia and facial palsy. He reported persistent facial pain and weakness, which progressively worsened. On examination, there was marked weakness of the right facial muscles, consistent with facial nerve dysfunction. The physical examination revealed no palpable masses in the parotid region, but tenderness was noted on the right side of the face. There were no other significant findings in his past medical or surgical history, and his family history was noncontributory.

An initial computed tomography (CT) scan of the brain was followed by magnetic resonance imaging (MRI). The CT scan showed enlargement of the right parotid gland with an associated intracranial soft tissue-dense lesion in the right temporal region (shown in Fig. 1). MRI revealed a malignant lesion in the right parotid gland with evidence of mandibular nerve involvement extending through the foramen ovale (shown in Fig. 2). A core biopsy of the lesion was performed, revealing a moderately differentiated adenocarcinoma with lymphovascular invasion.

Following the biopsy, the patient underwent a comprehensive diagnostic workup, including detailed imaging studies and laboratory tests. Further evaluation with a whole-body CT scan revealed no evidence of metastasis at that stage. Immunohistochemical analysis of the biopsy confirmed the diagnosis of adenoid cystic carcinoma, a subtype of parotid gland adenocarcinoma. Given the tumor's location and extent, a multidisciplinary team was consulted to develop a management plan, which included chemotherapy with carboplatin and paclitaxel for multiple cycles.

After 5 months, follow-up imaging, including CT and MRI, was performed after completing 4 cycles of chemotherapy. These scans showed enlargement of the previously noted intracranial extension of the right parotid tumor in the right temporal region, with newly developed perifocal vasogenic edema (shown in Fig. 3). Chest and abdominal CT scans were ordered after the patient started complaining of dyspnea and wheezing. The CT scan revealed new metastases to the brain, lungs, and liver (shown in Fig. 4). He was started on gemcitabine-based chemotherapy and supportive care, including PEG tube placement for nutritional support and fentanyl patches for pain management. Regular follow-up imaging and clinical assessments were planned to monitor treatment response and manage symptoms.

Discussion

The parotid gland, the largest salivary gland in the human body, is located anterior and inferior to each ear. As an exocrine gland, it secretes saliva into the oral cavity through Stensen's duct, which opens near the second upper molar tooth [1,2].

Salivary gland cancers are rare, comprising 0.3% of all cancers and about 6% of head and neck cancers in the United States [3]. Among salivary gland tumors, the parotid gland is the most frequent site of origin. A study analyzing 683 salivary gland tumor cases identified adenocarcinoma in only 20 cases (2.9%), emphasizing its rarity [4]. Conversely, a 2022 study involving 5739 salivary gland tumor cases revealed that 35% were malignant, with mucoepidermoid carcinoma being the most common subtype (26%), followed by adenoid cystic carcinoma (17%) and polymorphous adenocarcinoma (12%) [5]. Specifically, adenoid cystic carcinoma accounted for 26% of all malignant parotid gland tumors. Insights from an Icelandic study involving 678 patients further revealed that 3.7% of all parotid gland tumors were adenoid cystic carcinoma [6]. These findings highlight the rarity of adenocarcinoma subtypes in the parotid gland, emphasizing the importance of accurate histological differentiation for proper diagnosis and management.

Perineural invasion (PNI) is frequently observed in head and neck tumors due to the dense network of nerve fibers in the region [7]. It is not exclusive to these malignancies, as it also occurs in pancreatic, colonic, and prostate cancers. PNI

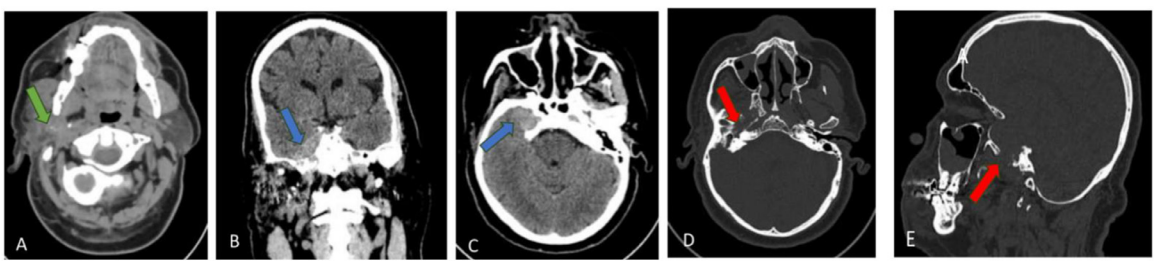

Fig. 1 – Initial brain CT without contrast in multi planes presented in mediastinum (A) brain (B,C) and bone (D,E); (A) Enlargement of right parotid gland lesion with extension to the superficial lobe (green arrow), (B & C) Intracranial soft tissue dense lesion at the right temporal region(blue arrow), (D & E) Bone destruction at right greater wing of sphenoid (red arrow).

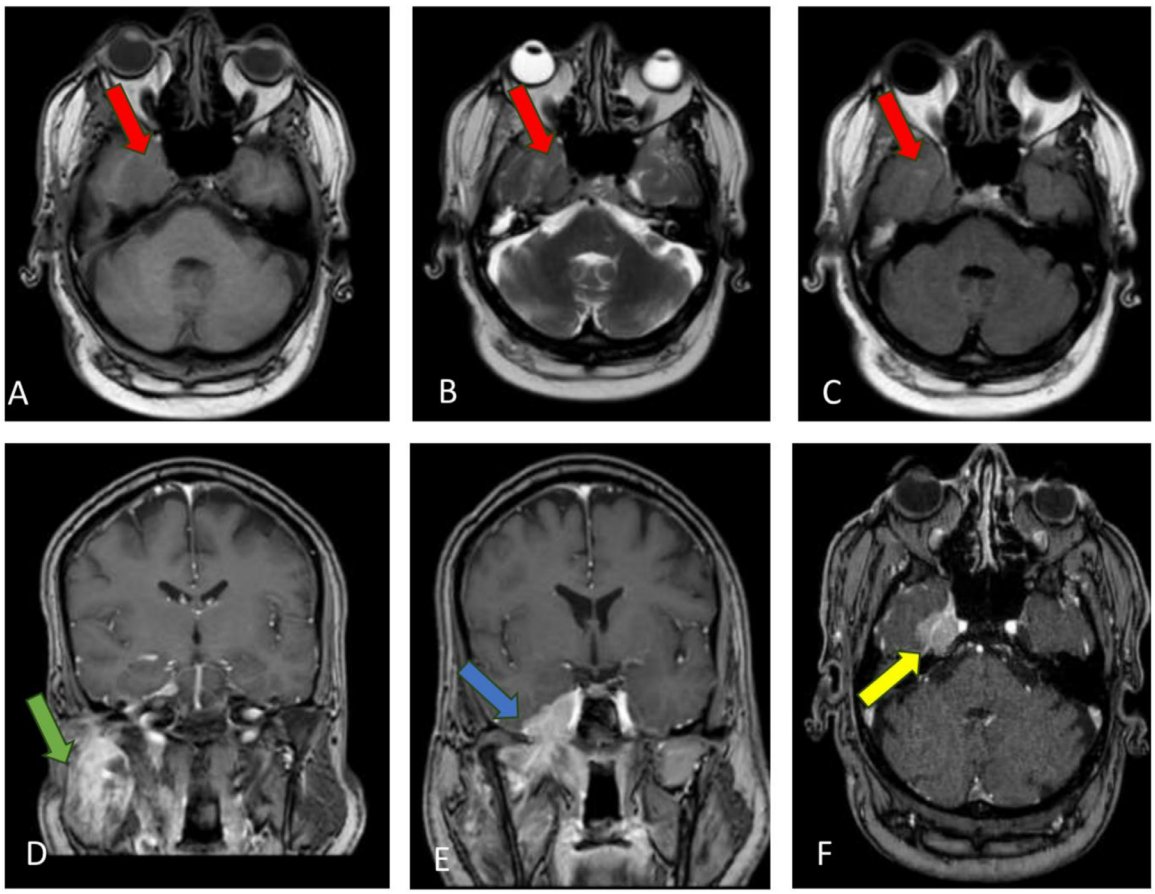

Fig. 2 – Brain MRI with and without IV contrast; (A) T1-wighted image in axial plane showed isointense lesion at the right temporal region (red arrow), (B & C) T2-wighted and FLAIR images in axial plane showed isointense lesion (red arrow), (D) T1 with IV contrast in coronal plane, showed avid enhancing lesion at the right parotid gland (green arrow), (E) T1 with IV contrast in coronal plane; showed intercranial extension of right parotid gland lesion along the mandibular nerve throw the Foramen Ovale (blue arrow), (F) T1 with IV contrast in axial plane: showed right temporal region extra axial enhancing solid mass representing intracranial extension of right parotid tumor (yellow arrow).

refers to tumor cell presence within the nerve sheath, distinct from perineural spread (PNS)—a clinical and radiological manifestation of tumor extension along nerve pathways [8,9]. PNI strongly correlates with poor prognosis, including increased recurrence rates, metastasis, and reduced survival [8]. Muscular denervation secondary to nerve involvement may present differently depending on the stage. In the acute and subacute stages, edema is observed, while chronic stages are marked by fatty replacement and muscular atrophy [10].

The pathogenesis of PNI involves key molecular pathways, including the phosphoinositide 3-kinase (PI3K)/Akt pathway, which regulates cellular survival and growth; the mitogen-activated protein kinase (MAPK) pathway, critical for proliferation and differentiation; and the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway, crucial for immune regulation and tumor progression [11]. Additionally, neurotrophic factors such as nerve growth factor (NGF), glial cell line-derived neurotrophic factor (GDNF), and brain-derived neurotrophic factor (BDNF) play pivotal roles by facilitating tumor migration along nerves through permissive microenvironments [11]. Understanding these mechanisms is essential for improving cancer diagnostics and therapeutic strategies.

On imaging, adenoid cystic carcinoma (ACC) of the parotid gland typically appears as a well-defined or ill-defined mass. Lesions often demonstrate diffuse infiltration into surrounding structures [12]. Perineural spread is a hallmark feature of ACC. On MRI, this may present as enlargement and/or enhancement of affected nerves, erosion or enlargement of foramina (e.g., skull base foramina), or obliteration of perineural fat layers [13]. CT imaging complements MRI by providing a detailed evaluation of bone invasion and changes in the skull base foramina, such as erosion or enlargement. However, CT is less sensitive than MRI for detecting perineural spread [14]. Tumor spread along retrograde perineural pathways should be carefully investigated. Intracranial involvement is characterized by soft-tissue replacement of cerebrospinal fluid in Meckel's cave and convexity of the lateral cavernous sinus wall. While MRI sensitivity for detecting perineural spread along the skull base is high (95%-100%), it decreases to 63% when mapping the full extent of the disease [10].

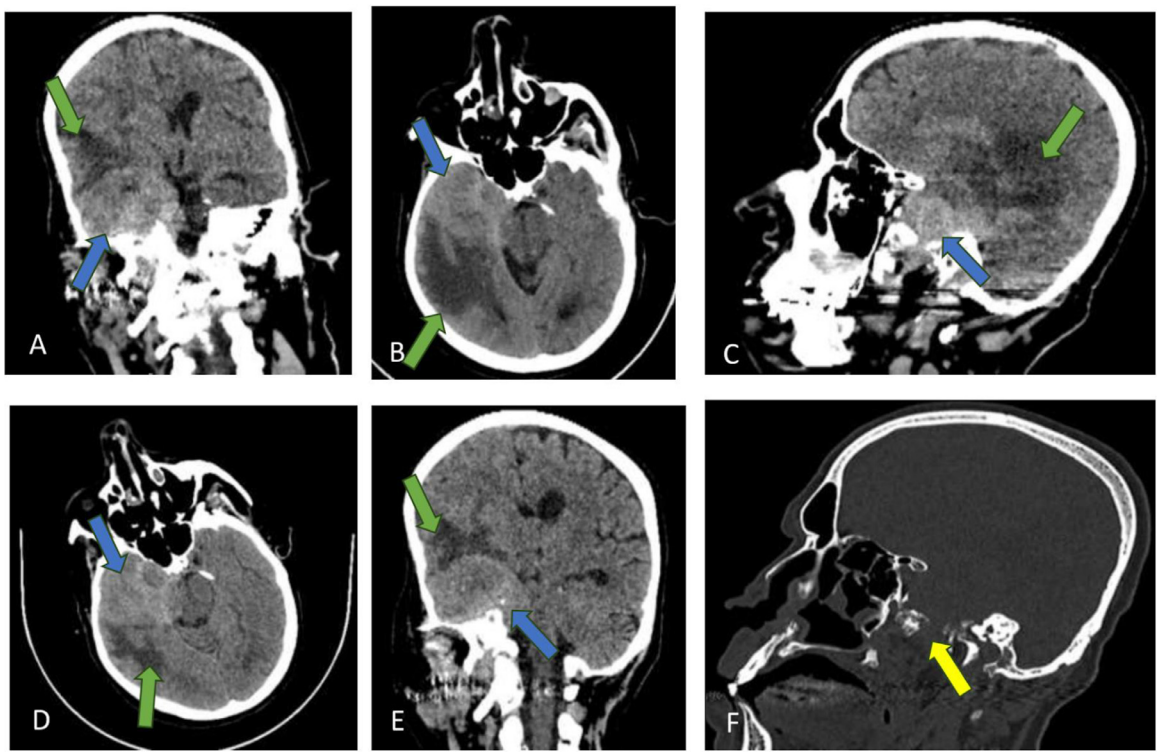

Fig. 3 – Follow up brain CT without contrast after 5 months in multi planes presented in brain (A-E) and bone (F); (A-E) Showed enlargement of previously noted intracranial extension of right parotid tumor at the right temporal region (blue arrow) with newly developed perifocal vasogenic edema (green arrow). (F) Bone destruction at right greater wing of sphenoid (yellow arrow).

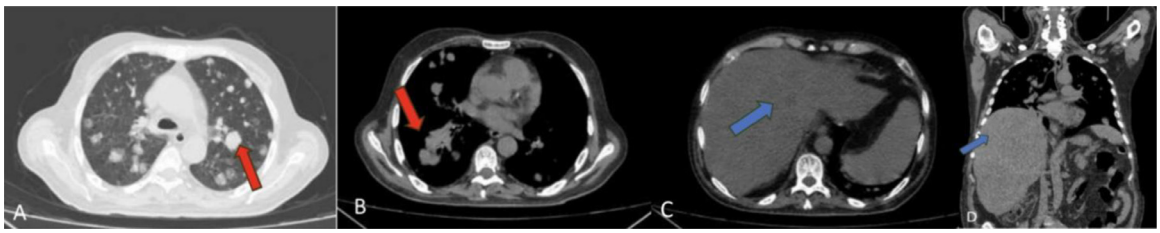

Fig. 4 – Chest CT without IV contrast after months from first presentation; displayed in axial plane, lung (A) and mediastinum (B & C) windows and in coronal plane in mediastinum window (D); (A and B) multiple scattered lung nodules at both lung fields representing secondary deposits-metastasis (red arrow), (C and D) The visualized upper cuts for the abdomen showed enlarged liver with irregular contour occupied by multiple hypodense lesions; representing hepatic metastasis (blue arrow).

Parotid gland adenocarcinoma with intracranial perineural spread can be challenging to diagnose because its symptoms overlap with those of various neurological conditions involving nerve dysfunction. This overlap often leads to misdiagnoses, delaying appropriate treatment. One potential misdiagnosis is trigeminal neuralgia, as patients with perineural spread may experience facial pain along the distribution of the trigeminal nerve [15]. Similarly, Bell's palsy, characterized by unilateral facial weakness, can be another common misdiagnosis [15]. In some cases, symptoms may resemble those of chronic sinusitis or otitis media, with patients reporting referred pain, headaches, or ear-related issues. Tumors involving cranial nerves V or VII can lead to such presentations, often delaying diagnosis until the disease has reached an advanced stage. Additionally, persistent temporal or facial pain might suggest temporal arteritis (giant cell arteritis), especially in older adults. This vascular condition can be misdiagnosed when the underlying cause is perineural tumor invasion [15]. Given these possibilities, clinicians should remain alert for red flags, such as progressive symptoms, multiple cranial nerve involvement, or resistance to conventional treatments, and pursue advanced imaging and biopsy when malignancy is suspected.

Superficial parotidectomy is the most commonly performed surgical procedure for treating benign lesions in the superficial lobe of the parotid gland. In some specialized cen-

ters, this technique is also used for managing T1/T2 low-grade malignancies. However, in most centers, all parotid cancers are addressed with either conservative or radical parotidectomy [16]. For T3/T4 and high-grade primary parotid gland tumors with lymph node metastases, adjuvant radiation therapy should be administered to both the primary tumor site and the neck. Given that the local recurrence rate for T1/T2 primary parotid carcinomas ranges from 7% to 15%, postoperative radiation therapy is recommended not only for primary malignant parotid tumors with unfavorable prognostic factors but also for T2N0 carcinomas and certain T1 tumors [17].

The prognosis of parotid gland adenocarcinoma with intracranial perineural spread (PNS) is generally poor, as perineural invasion (PNI) is a hallmark of aggressive tumor behavior and is strongly correlated with unfavorable outcomes. Although the 5-year survival rate for ACC patients is relatively high compared to other epithelial malignancies, the recurrence rate remains alarmingly high, largely due to the microscopic spread of tumor cells along nerve sheaths [18]. Even with successful tumor removal, the risk of late-onset distant metastasis remains the leading cause of mortality, demonstrating the need for meticulous surgical margins and cautious postoperative monitoring [18].

Conclusion

This case is a representation of the aggressiveness of adenoid cystic carcinoma of the parotid gland with respect to its perineural spread and intracranial and distant metastases. Advanced imaging and histological diagnosis are crucial for early intervention. Despite aggressive treatment, the prognosis remains poor in advanced cases, highlighting the need for a multidisciplinary approach, meticulous surgical management, and vigilant follow-up to improve outcomes.

Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Patient consent

Written informed consent was obtained from the patient himself for his anonymized information to be published in this article.

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