

Atypical Chest Pain as a Prelude to Cancer: An Uncommon Presentation of Adenoid Cystic Carcinoma of the Parotid Gland

Alex Zxi Jian Ho, MBBS¹; Ahmad Hafizuddin Johari, MSUR ORL-HNS¹; Khairunisa Ahmad Affandi, MPath²; Wan Ishlah Leman, MSUR ORL-HNS¹

¹Department of Otorhinolaryngology, Head and Neck. Sultan Ahmad Shah Medical Centre @IIUM, Jalan Sultan Haji Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang

²Department of Pathology and Laboratory Medicine. Sultan Ahmad Shah Medical Centre @IIUM, Jalan Sultan Haji Ahmad Shah, Bandar Indera Mahkota, 25200 Kuantan, Pahang

Abstract

Adenoid cystic carcinoma (ACC) of the parotid gland is a rare malignancy characterized by delayed distant metastasis, often presenting as pre-auricular swelling. We report a 47-year-old male who initially presented with unexplained right-sided chest pain, leading to the discovery of a rib lesion and eventual diagnosis of metastatic ACC. Imaging revealed a parotid mass and metastatic involvement of the ribs, confirmed by biopsy. A left subtotal parotidectomy was performed, with histopathological examination confirming ACC. The patient received adjuvant radiotherapy and is stable with no recurrence at the 6-month follow-up. This case underscores the importance of considering head and neck cancers, including ACC, in patients with unexplained chest pain, especially those with a history of salivary gland tumours. Despite ACC's relatively low rate of regional lymph node metastasis, its propensity for distant metastasis, including to uncommon sites such as the ribs, highlights the need for a systematic approach in evaluating atypical presentations. Early detection through self-examination, clinical vigilance, and imaging modalities like PET-CT can significantly improve outcomes. Prolonged surveillance is crucial due to the risk of delayed metastasis. Prompt management in patients with atypical symptoms, such as chest pain, is essential for improving prognosis and patient survival.

Introduction

Adenoid cystic carcinoma (ACC) is an uncommon condition involving minor salivary and submandibular glands. Parotid gland involvement is a rare occurrence with a known incidence of about 2 to 5% (Cantu, 2021). ACC can be histologically classified into three main groups: cribriform, tubular, and solid (da Cruz Perez, de Abreu Alves, Nobuko Nishimoto, de Almeida, & Kowalski, 2006). These classifications are further graded as Grade I (no solid pattern), Grade II (< 30% solid pattern), and Grade III (> 30% solid pattern), with 5-year cumulative survival rates of 39%, 26%, and 5% respectively (Szanto, Luna, Tortoledo, & White, 1984). Tumours with a solid growth component are associated with poorer outcomes compared to those without (da Cruz Perez et al., 2006). Delayed distant metastasis is a well-known feature of parotid gland ACC with reported cases of metastasis to the lung, bone, liver and brain (Cantu, 2021). Gao et al. reported overall 5-, 10-, and 20-year survival rates for patients without distant metastasis to be 85.6%, 67.4% and 50.4% respectively. In contrast, the presence of distant metastasis significantly

decreases survival rates to 69.1%, 45.7%, and 14.3% (Gao et al., 2013). This case represents the first reported instance of parotid ACC with distant metastasis to the ribs.

Case Presentation

A 47-year-old male initially presented with progressive right-sided chest pain persisting for 2 months. Comprehensive investigations were conducted and cardiac etiologies for chest pain were excluded. Incidentally, imaging revealed a lesion over the right 6th rib on chest X-ray and non-contrast Computed Tomography (CT) of the thorax. A subsequent CT-guided biopsy of the lesion revealed features of metastatic adenocarcinoma. A Positron Emission Tomography (PET) scan demonstrated increased fludeoxyglucose-18 (FDG) uptake in both the left intra-parotid node and the prostate gland. Despite these findings, prostate-specific antigen (PSA) levels were within normal limits.

Upon assessment, a left parotid mass measuring approximately 2.0 x 3.0 cm was identified. The mass was firm, non-tender, and exhibited no overlying skin changes. Examination of facial nerve function was unremarkable, and no additional neck swelling was observed. A contrast-enhanced CT (CECT) scan of the face revealed a heterogeneous hypodense lesion within the superficial lobe of the left parotid gland, measuring 1.6 x 2.2 x 2.8 cm, extending

Corresponding Author:
Alex Zxi Jian Ho
alexhozxijian@gmail.com

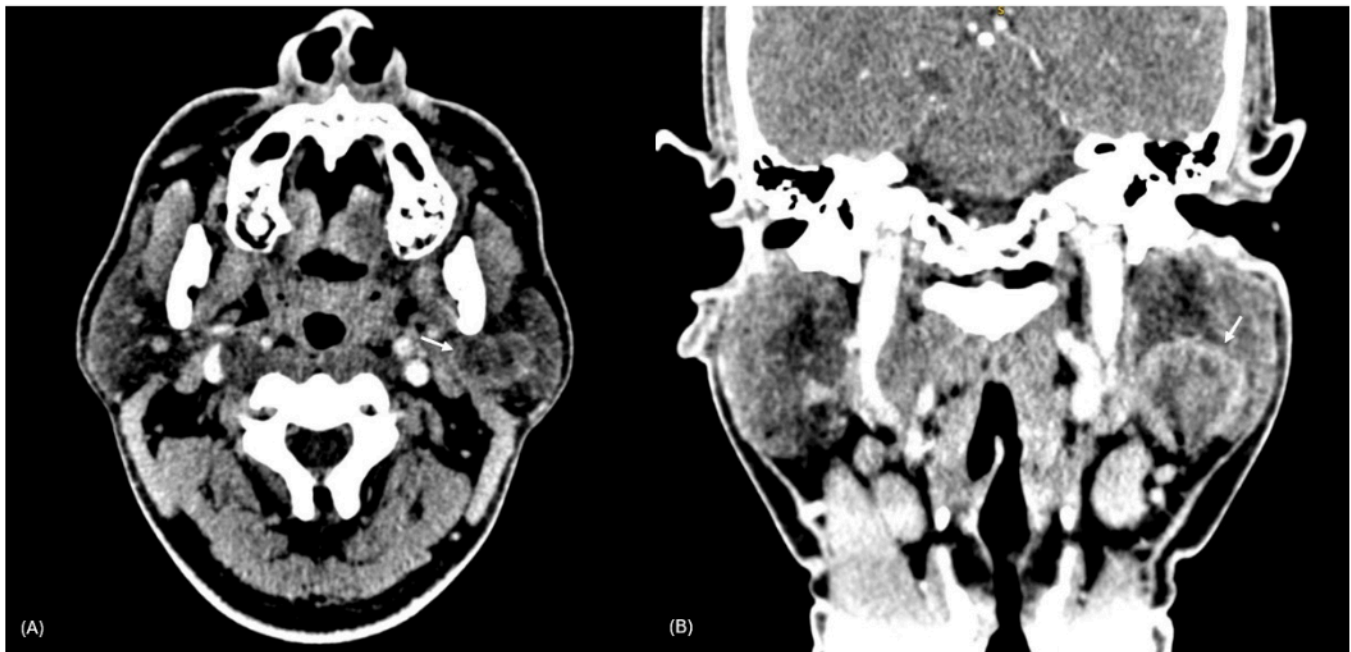


Figure 1. CECT of the Face

A) Axial cut with arrow showing the parotid lesion. (B) Coronal cut with arrow showing the parotid lesion

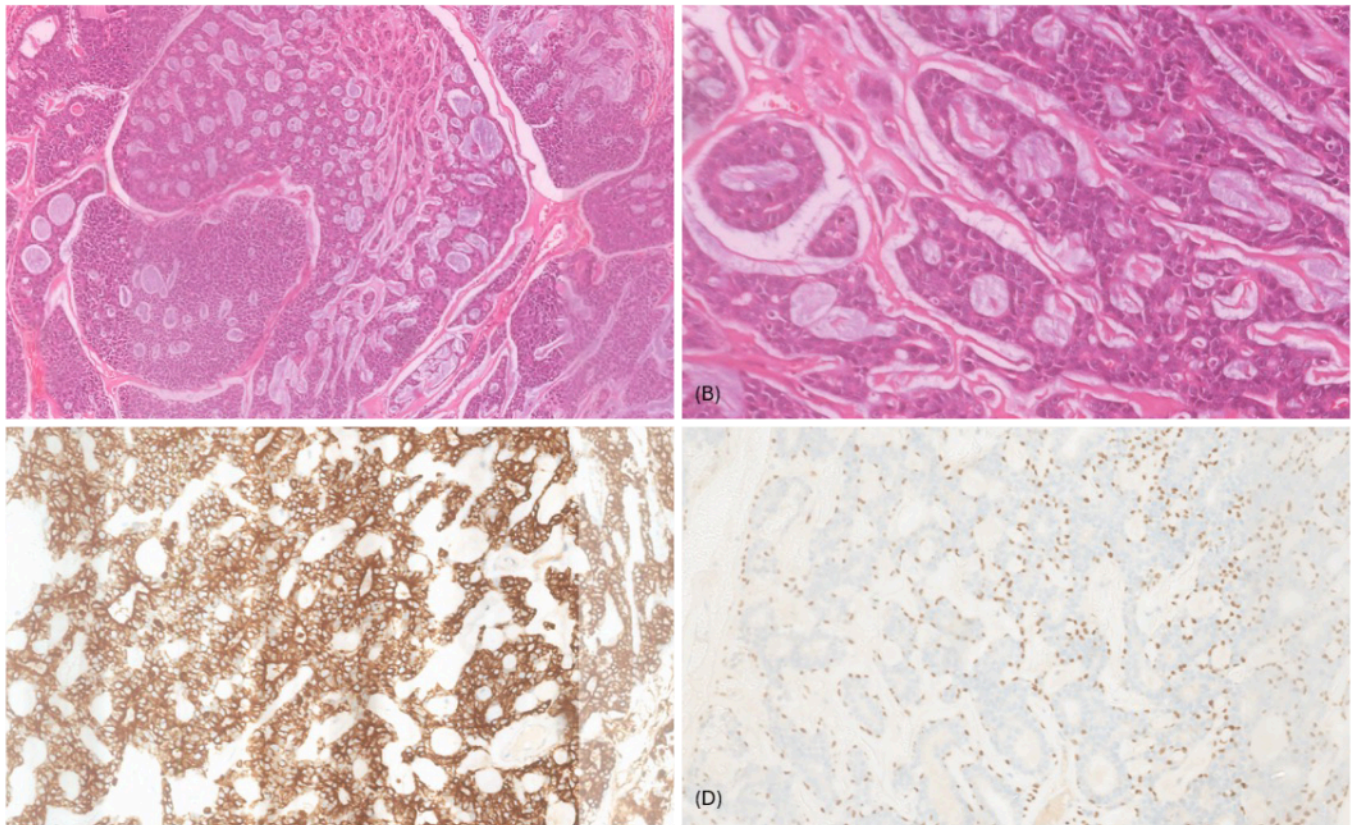


Figure 2. Adenoid Cystic Carcinoma of the parotid

(A) The tumour shows tubular, cribriform and solid growth pattern (H&E, 100x). (B) The tumour is biphasic comprising ductal and myoepithelial cells with basaloid appearance; the cells display mild nuclear pleomorphism, hyperchromatic nuclei, small nucleoli, and scanty cytoplasm (H&E, 400x). Immunohistochemical studies show (C) the ductal cells are positive for CK7; and (D) the myoepithelial cells are positive for p40

into the deep lobe. (Figure 1) Multiple subcentimeter bilateral lymphadenopathies were noted in levels I, II, and III. A biopsy of the left parotid mass confirmed the diagnosis of adenoid cystic carcinoma. Multidisciplinary discussion with the oncology team concluded a diagnosis of left parotid Adenoid Cystic Carcinoma (cT2N0M1) with bone metastasis to the ribs, classifying the condition as Stage IV. Following the diagnosis, a left subtotal parotidectomy was performed.

The histopathological examination confirmed the diagnosis of adenoid cystic carcinoma of the left deep parotid lobe (pT2) (Figure 2), with no evidence of lymphovascular or perineural invasion. The patient was subsequently referred to the oncology team for adjuvant radiotherapy to the ribs. Currently, the patient is doing well, with no signs of recurrence at the six-month follow-up.

Discussion

Parotid gland ACC is a rare neoplasm that typically presents as a pre-auricular swelling, most commonly originating from the superficial lobe (Cantu, 2021). It may also present as a swelling over the lateral oropharyngeal wall. Late-stage symptoms include mild pain and paresthesia (Cantu, 2021). Identified risk factors for ACC include exposure to ionizing radiation, smoking, a history of breast cancer in women, low vitamin C intake, and human papillomavirus (HPV) infection (Cantu, 2021). Despite being characteristically slow growing, ACC may exhibit an aggressive clinical course, early perineural invasion, high rates of local recurrences, and delayed rates of distant metastases (30-40% within 10 years) (Cantu, 2021). Ironically, ACC has a relatively low rate of regional lymph node metastasis (14.2% at presentation and 7% upon follow-up) but a notable propensity for distant metastasis via hematogenous routes (Cantu, 2021).

Delayed distant metastasis is a well-documented feature of parotid gland ACC, with numerous case reports describing metastasis to rare sites. One such example would be a reported case with intracranial metastasis years after loco-regional treatment in Japan (Kazumoto et al., 1998). Another case highlighted intracranial metastasis occurring 15 years post-surgery, underscoring the importance of prolonged surveillance in cases of parotid gland ACC (Atram, Shivkumar, & Gangane, 2022). In Turkey, a patient with parotid gland ACC had lung and bone metastasis, followed by metastases post-surgery to skeletal muscle and skin post-surgery. The patient eventually succumbed to complications from lung metastases (Yurut-Caloglu et al., 2007). Cutaneous metastasis is particularly uncommon, with a notable case reported in Taiwan (Chang, Liao, & Hong, 2003).

To the best of our knowledge, there are three reported cases of bone metastasis in parotid gland ACC in the current literature. Liu et al. described a case of delayed metastasis to the spine three years after complete resection of the diseased parotid gland (Liu et al., 2018) while the other two cases were from Iran, where spine metastasis was noted seven years and nine months post-primary surgery. Instrumentation surgery was recommended for these cases (Safaei, Azimi, & Yazdanian, 2023). This case represents the first reported instance of parotid gland ACC with distant metastasis to the ribs. Typically, patients with parotid gland ACC present initially with infra-auricular swelling. However, in our case, the patient was initially alerted to the condition due to pain from rib metastasis. He did not notice prior parotid swelling, which was only detected upon imaging and clinical assessment. To ensure head and neck cancer metastases

are not overlooked as causes of chest pain, adopting a systematic approach in assessing patients with unexplained symptoms is vital. Clinicians should maintain a high index of suspicion, especially in individuals with a history of salivary gland tumours or prior loco-regional treatments. Incorporating imaging modalities like PET-CT scans can further aid in identifying metastatic disease at atypical sites.

Early detection is crucial to improve outcomes in patients with parotid gland ACC as delayed identification and diagnosis may result in extensive disease and distant metastasis. It is important for patients to perform self-examinations of the parotid glands. Choi et al. proposed a protocol offering step-by-step instructions for self-examination of the parotid gland. The self-assessment involves checking for swelling near the ear, palpating for lumps, assessing jaw discomfort during movement, and observing facial expressions for any weakness (Choi et al., 2021). To improve parotid self-examination and facilitate early detection, patients can periodically photograph the parotid region to monitor for asymmetry or visible changes over time. This approach, combined with regular palpation for lumps, assessment of jaw movement discomfort, and observation of facial expressions, enhances the likelihood of identifying abnormalities earlier and seeking timely medical evaluation, potentially improving the prognosis for individuals affected by this rare and aggressive cancer.

Conclusion

This case highlights the rare occurrence of rib metastasis in parotid gland ACC, emphasizing the importance of considering head and neck cancers in patients with unexplained chest pain. Early identification can be improved by increasing clinician awareness, fostering multidisciplinary collaboration, and implementing routine screening and follow-ups for high-risk patients. Encouraging self-examination, including periodic photographic monitoring, can aid in early detection. It is also important that ACC patients undergo prolonged surveillance due to the potential for delayed and unusual metastases, ultimately improving patient outcomes.

Acknowledgements

We would like to express our sincere appreciation to Sultan Ahmad Shah Medical Centre @IIUM for their invaluable support in allowing us to publish this case report.

Ethics Statement

Informed written consent has been obtained from the patient for case publication and the pictures submission.

Author Contributions

Alex Zxi Jian Ho

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ahmad Hafizzudin Johari

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Khairunisa Ahmad Affandi

Drafting the work or revising it critically for important intellectual content; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Wan Ishlah Leman

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; Final approval of the version to be published; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

References

- Atram MA, Shivkumar VB, Gangane NM. Intracranial remote metastasis from adenoid cystic cancer of parotid gland: Case report and review of literature. *Indian J Otolaryngol Head Neck Surg.* 2022;74(Suppl 3):5949-5953. doi:10.1007/s12070-021-02594-w
- Cantu G. Adenoid cystic carcinoma. An indolent but aggressive tumour. Part A: From aetiopathogenesis to diagnosis. *Acta Otorhinolaryngol Ital.* 2021;41(3):206-214. doi:10.14639/0392-100X-N1379
- Chang CH, Liao YL, Hong HS. Cutaneous metastasis from adenoid cystic carcinoma of the parotid gland. *Dermatol Surg.* 2003;29(7):775-779. doi:10.1046/j.1524-4725.2003.29196.x
- Choi SY, Lee E, Kim E, Chung MK, Son YI, Baek CH, Jeong HS. Clinical outcomes of bulky parotid gland cancers: Need for self-examination and screening program for early diagnosis of parotid tumours. *BMC Cancer.* 2021;21(1):178. doi:10.1186/s12885-021-07902-9
- da Cruz Perez DE, de Abreu Alves F, Nobuko Nishimoto I, de Almeida OP, Kowalski LP. Prognostic factors in head and neck adenoid cystic carcinoma. *Oral Oncol.* 2006;42(2):139-146. doi:10.1016/j.oraloncology.2005.06.024
- Gao M, Hao Y, Huang MX, Ma DQ, Luo HY, Gao Y, et al. Clinicopathological study of distant metastases of salivary adenoid cystic carcinoma. *Int J Oral Maxillofac Surg.* 2013;42(8):923-928. doi:10.1016/j.ijom.2013.04.006
- Kazumoto K, Hayase N, Kurosumi M, Kishi K, Uki J, Takeda F. Multiple brain metastases from adenoid cystic carcinoma of the parotid gland: Case report and review of the literature. *Surg Neurol.* 1998;50(5):475-479. doi:10.1016/s0090-3019(97)00341-8
- Liu SZ, Zhou X, Song A, Huo Z, Zhang J, Wang YP, Liu Y. Spinal metastases from adenoid cystic carcinoma of the parotid gland. *Chin Med J (Engl).* 2018;131(21):2616-2617. doi:10.4103/0366-6999.244125
- Safaei S, Azimi P, Yazdani T. Metastasis of spine from adenoid cystic carcinoma of the parotid gland: Two case reports. *J Med Case Rep.* 2023;17(1):196. doi:10.1186/s13256-023-03926-w
- Szanto PA, Luna MA, Tortoledo ME, White RA. Histologic grading of adenoid cystic carcinoma of the salivary glands. *Cancer.* 1984;54(6):1062-1069. doi:10.1002/1097-0142(19840915)54:6<1062::aid-cnrcr2820540622>3.0.co;2-e
- Yurut-Caloglu V, Caloglu M, Ozyilmaz F, Saynak M, Cosar-Alas R, Karagol H, et al. Lung, bone, skeletal muscles and cutaneous metastases from adenoid cystic carcinoma of the parotid gland: A case report and review of the literature. *Med Oncol.* 2007;24(4):458-462. doi:10.1007/s12032-007-0016-x