

Bone Metastasis as Initial Presentation of an Aggressive Adenoid Cystic Carcinoma of Mandible: Case Report

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1. Abstract

Adenoid cystic carcinoma (ACC) is a slowly growing malignant neoplasm with possible widespread distant metastasis. The diagnosis requires thorough clinical, radiological and histopathologic examination. Here, we report a case of a 40-year-old male who presented back pain, paresthesia, dysphagia and swelling around the left mandibular region. He was referred to our rheumatology department to explore a multiple vertebral and iliac involvement revealed by initial imaging including computed tomography (CT) and magnetic resonance imaging (MRI). His physical examination showed a 3×2 cm hard fixed and mass in the left mandibular region and a right facial palsy. In laboratory tests, he had severe hypercalcemia, treated with intensive hydration, diuretics, corticosteroids and bisphosphonates but the serum calcium level normalized only after dialysis. Radiologically, an infiltrative left para pharyngeal tissue mass was detected. It has an endocranial extension. Biopsy of the bone lesion was performed, and the findings indicated a cribriform pattern of ACC. The diagnosis of metastatic ACC was made but the tumor was deemed unresectable. A palliative treatment by chemotherapy and radiotherapy was indicated but the patient died one month later. Thus, the aim of the present case report is to describe an unusual case of ACC of the mandible revealed by bone metastasis.

2. Introduction

Adenoid cystic carcinoma (ACC) is a malignant tumor that may affect either the major or minor salivary glands of the oral cavity [1].

It occurs most often in minor salivary glands and the submandibular gland, and less frequently in the sublingual and parotid glands. Other rare locations include lacrimal and ceruminous glands as well as other sites in the head and neck, including the nasal and paranasal sinuses, trachea and larynx [2]. Although it presents a widespread age distribution, peak incidence occurs predominantly among women, between the 5th and 6th decades of life [3]. ACC is a relentlessly growing tumor characterized by perineural invasion and multiple local recurrences. Regional lymph node metastases are rare. In sharp contrast, hematogenous metastasis is common, especially to lung, bone and liver [4]. This tumor remains, an extremely difficult disease to treat and that is why it was described by Conley and Dingman as “one of the most biologically destructive and unpredictable tumors of the head and neck” [5]. We report a case of adenoid cystic carcinoma of the submandibular gland revealed by bone metastasis in a 40-year-old man.

3. Case Presentation

A 40-year-old male complained of back pain for about three months. The pain had gradually increased in intensity, with a loss of ambulatory capacity and general weakness. Initial imaging (including CT and MRI) showed multiple vertebral and iliac involvement and the patient was referred to our rheumatology department for exploration (Figure 1). Medical history revealed that he was suffering from pain, paresthesia, dysphagia and swelling around the left mandibular region and had visited a local dental clinic for the same complains, nine months ago. He also reported alcohol

consumption and cigarette smoking. The physical examination revealed a 3×2 cm hard and fixed mass in the left mandibular region, but contrary to our expectations, a right facial palsy (Figure 2). The overlying skin was intact, and no ulceration was noted. Neither motor nor sensory deficit was observed but there was a mild limitation in the hip flexion and extension range of motion in the right hip joint. Initial laboratory investigations revealed white blood cells count of 13270/ml, hemoglobin level of 10,5 gr/dl and platelets count of 193300/ml. The erythrocyte sedimentation rate was high (65 mm) and the C-reactive protein level was high (41mg/ml). Serum calcium was increased at 4.66 mmol/L (2.2–2.6 mmol/L) and the creatinine at 320 μM/L. Serum parathormone was low (6ug/ml). Urgent treatment of this malignant hypercalcemia was started, combining intensive hydration, diuretics, corticosteroids and bisphosphonates. Our patient didn't respond initially to any of these treatments and a good control of this hypercalcemia was obtained after dialysis. Then, the patient was referred to the otorhinolaryngology department to explore the right facial palsy and to search for the primary neoplasm. On examination, it was confirmed a grade V right facial palsy (Facial grading of House and Brackman) with a smooth bulge involving the left side of soft palate. The tonsil was pushed medially. The swelling was firm, mobile and covered with intact mucosa. Cranio-facial CT and MRI showed a 6 * 4.5 * 4 cm left para pharyngeal tissue mass infil-

trating the pre-stylian, infra temporal fossa, the pterygoid muscles and the temporal muscle with discreet deviation of the oropharyngeal pathway to the right. it invades the ramus and the horizontal branch of the left mandible with rupture of the vestibular and lingual cortex (figure 3). The tumor invades the base of the skull with endocranial extension. No cervical lymphadenopathy was noted. Endocranial extension was noted with the invasion of the tent of the cerebellum on the left side, a lateral infiltration of the cerebral trunk, the pre-pontic and pre-peduncular cisterns. A core biopsy of the bone lesion was carried out and histopathologic analysis showed an invasive tumor, made by solid nests and cribriform areas. A clump of basaloid epithelial cells containing a fluid similar to mucus in the lumen was found out. This cribriform pattern of the lesion gave the entire structure a typical "swiss cheese" appearance. Atypical tumor cells were detected and immunohistochemical study revealed that tumor cells are diffusely positive C-kit (CD117). Based on the above features, the diagnosis of ACC of possible salivary gland origin was given (Figure 4). Based on the overall clinical, radiographic, and histologic findings, a diagnosis of metastatic ACC was made. The tumor was deemed unresectable, therefore palliative treatment by chemotherapy and radiotherapy was indicated. Unfortunately, none of these treatments was given and the patient died one month later.



Figure 1: CT scan axial section showing lesion involving the right iliac crest

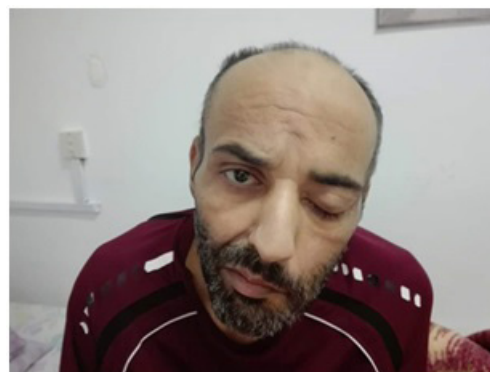


Figure 2: Grade V right facial palsy with severe facial dysfunction; no forehead motion, eyelid closure issues, inability to smile, mid-facial asymmetries, poor oral function and lower lip asymmetry.

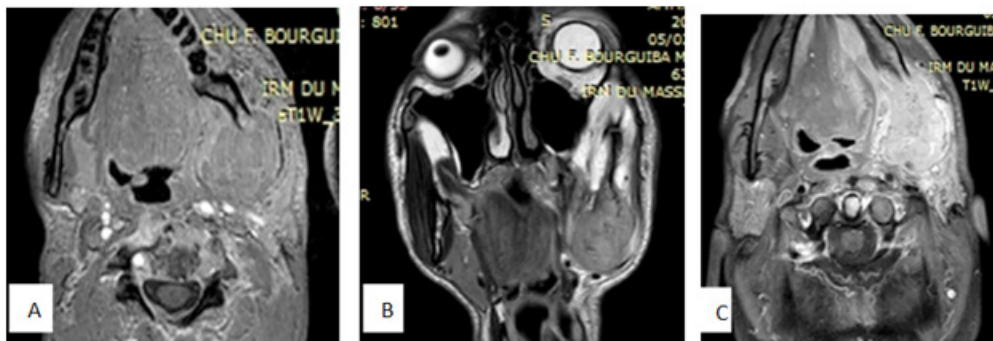


Figure 3: Magnetic resonance images. (A) Axial T1 image showed a mass with hypo signal T1. (B) Coronal T2 image showed a discreet hyper signal T2 of the lesion. (C) axial injected T1 image showed an enhancing after injection. The mass invades the ramus and the horizontal branch of the left mandible with rupture of the vestibular and lingual cortex and extension to the masseter muscle. The tumor invades the pre-stylian space; the infra temporal fossa; the pterygoid muscles and the temporal muscle with discreet deviation of the oropharyngeal pathway to the right.

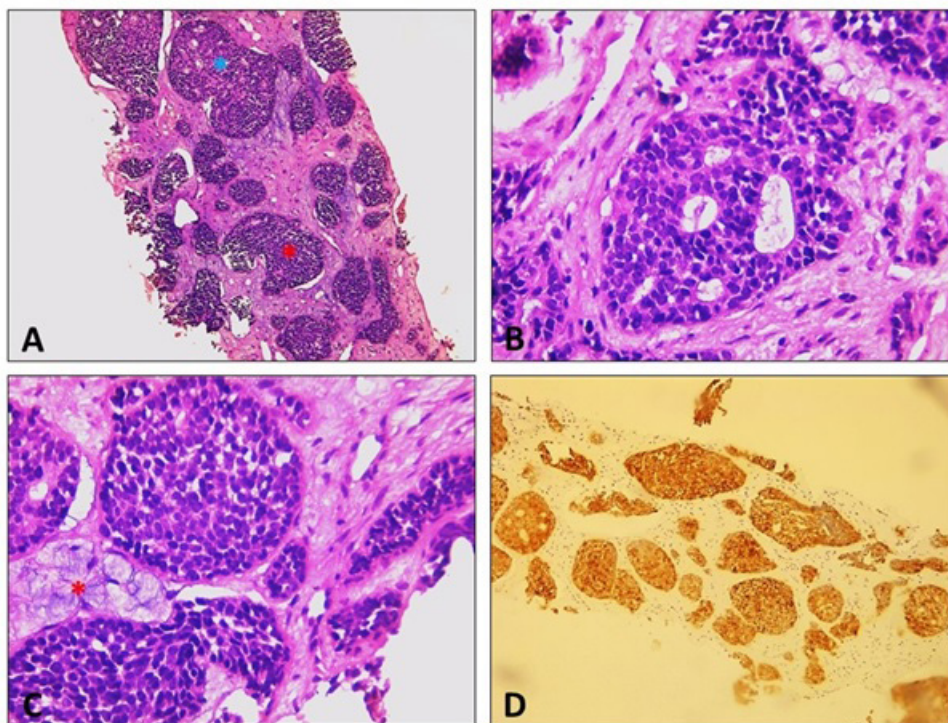


Figure 4: A: Core biopsy of the bone lesion showing an invasive tumor, made by solid nests (red asterisk) and cribriform areas (blue asterisk) (hematoxylin & eosin x 40). B: Cribriform structures have hyaline or basophilic material within the luminal spaces (hematoxylin & eosin x 400). C: Solid pattern is composed of sheets of basaloid cells with mild atypia and rare mitoses. The stroma surrounding tumor nests is often desmoplastic and rarely paucicellular and myxoid (red asterisk) (hematoxylin & eosin x 400). D: Immunohistochemistry showing diffuse and strong positivity of tumor cells for C-kit (CD117).

4. Discussion

Adenoid cystic carcinoma is an uncommon tumor of salivary gland origin. The first term used to describe the histological finding was « cylindroma » by Billroth in 1859 and it was later renamed by Foote and Frazell in 1953 as « adenoid cystic carcinoma » [6]. Although ACC can occur in all age groups with a peak incidence age between the fourth and sixth decades, with no gender predilection [7]. It usually presents as slowly growing firm unilocular mass in the gland and the duration of the lesion, prior to initial presentation, may vary from less than 1 week to several years [8]. Despite its slowly growing, this tumor is highly invasive with a high recur-

rence rate. Pain and swelling of the jaw are the most frequent clinical presentations [6,9,10]. Paresthesia, muscle weakness, tooth mobility and trismus are an uncommon finding. Although the most common initial presentation is unclear. The posterior body and the angle of the mandible were most commonly occurred [11]. The occurrence of bone metastasis usually corresponds to rapid tumor dissemination and death of the patient, such as illustrate our case, whereas lung metastases demonstrate a less aggressive clinical course [12].

Although the pathogenesis of ACC remains unclear and the tumor can be difficult to assess clinically, so a diagnostic criterion

was proposed and established: radiographic evidence of osteolysis, presence of intact cortical plates, absence of a primary tumor within the major or minor salivary glands, and histological confirmation of the typical architectural and morphological features of ACC [13,14]. However, CT and MR imaging remains useful in surgical planning, especially to delineate the extent, local invasion, and perineural spread of the tumor. The lesions are generally poorly defined and have infiltrative margins [15]. Histologically, there are three variants of the ACC: cribriform, tubular and solid. The cribriform variant is the most classic, which is characterized by islands of basaloid epithelial cells that contain multiple cylindrical, cyst-like spaces resembling swiss cheese [16]. The tubular pattern is characterized by glandular spaces of elongated tubules lined by epithelial cells and surrounded by single or multiple layers of basaloid cells. The solid pattern is composed of solid epithelial islands with central areas of necrosis; the cells are small, basophilic and hyperchromatic with a densely granulated nucleus [17]. A well-established analysis of histopathological findings is necessary to confirm the final diagnosis of ACC. Furthermore, many other settings could influence the prognosis of this tumor such as the perineural invasion and lymph node metastasis [18]. Immunohistochemical (IHC) study show positive expression of myoepithelial cells for S100, p40 and cytokeratins (CKs), while ductal cells express strongly CK 7 [16]. ACC shows usually strong and diffuse positivity for c-KIT (CD117) in tumor cells in the solid pattern, all cells surrounding cyst-like spaces in the cribriform pattern, and luminal cells in the tubular pattern [19]. The treatment of ACC is influenced by location of the tumor, stage at diagnosis and the histologic grade [20]. The treatment of choice is radical surgical resection, ensuring free margins, and postoperative radiotherapy [21]. Mendenhall et al, compared radiotherapy alone to radiotherapy combined with surgery and concluded that combination treatment is preferable [22]. Unfortunately, local recurrences occur despite combined treatment with surgery and radiotherapy. The 5 to 10-year recurrence rates range from 30% to 75% [23]. Several chemotherapy studies have been performed over the years. The results show consistently low response rates to cytotoxic chemotherapy for metastatic disease [24]. In patients with adverse prognostic factors, some studies showed that concurrent chemoradiotherapy, especially with platinum-based chemotherapy seems to be effective in improving locoregional control [25]. In a few cases, temporary partial disease response or stabilization may be achieved. The current consensus is that chemotherapy should be reserved for patients with symptomatic metastases or rapidly progressing disease who are not candidates for other treatment modalities [24]. Due to the ineffectiveness of cytotoxic chemotherapy in advanced ACC, several ongoing trials are testing agents that inhibit fibroblast growth factor receptor signaling or other signaling pathways. Novel treatments based on the recently sequenced tumor genome are under development [26,27].

5. Conclusion

Due to the exceedingly rare occurrence of ACC and its extremely slow growth pattern, the diagnostic remains a challenge to every clinician. However, this tumor has usually fatal outcome especially when the diagnosis is made due to the appearance of metastasis. The present case illustrate that salivary gland tumors should be considered as origin of bone metastasis which is uncommon. Long-term follow-up is imposed to rule out regional and distant metastases in patients with intraosseous ACC.

References

1. Mader C, Gay WD. Intraoral adenoid cystic carcinoma. *J Am Dent Assoc.* 1979; 99(2): 212-214.
2. Hiyama T, Kuno H, Sekiya K, Oda S, Kobayashi T. Imaging of Malignant Minor Salivary Gland Tumors of the Head and Neck. *Radiographics.* 2021; 41(1): 175-191.
3. Waldron CA, el-Mofty SK, Gnepp DR. Tumors of the intraoral minor salivary glands: a demographic and histologic study of 426 cases. *Oral Surg Oral Med Oral Pathol.* 1988; 66(3): 323-333.
4. Kokemueller H, Eckardt A, Brachvogel P, Hausamen JE. Adenoid cystic carcinoma of the head and neck--a 20 years' experience. *Int J Oral Maxillofac Surg.* 2004; 33(1): 25-31.
5. Conley J, Dingman DL. Adenoid cystic carcinoma in the head and neck (cylindroma). *Arch Otolaryngol.* 1974; 100(2): 81-90.
6. Al-Sukhun J, Lindqvist C, Hietanen J, Leivo I, Penttila H. Central adenoid cystic carcinoma of the mandible: case report and literature review of 16 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2006; 101(3): 304-308.
7. Hu HY, Liu YY, Wang H, Jiang M. Primary Intraosseous Adenoid Cystic Carcinoma of the Mandible: A Comprehensive Review with Analysis of 2 Additional Cases. *J Oral Maxillofac Surg.* 2017; 75(8): 1685-1701.
8. Johnson PA, Millar BG, Leopard PJ. Intraosseous adenoid cystic carcinoma of the mandible. *British Journal of Oral and Maxillofacial Surgery.* 1989; 27(6): 501-505.
9. Brookstone MS, Huvos AG. Central salivary gland tumors of the maxilla and mandible: A clinicopathologic study of 11 cases with an analysis of the literature. *Journal of Oral and Maxillofacial Surgery.* 1992; 50(3): 229-236.
10. Martinez-Madrigal F, Pineda-Daboin K, Casiraghi O, Luna MA. Salivary gland tumors of the mandible. *Ann Diagn Pathol.* 2000; 4(6): 347-353.
11. Capodiferro S, Scully C, Macaita MG, Lo Muzio L, Favia G, Mairoano E, et al. Bilateral intraosseous adenoid cystic carcinoma of the mandible: report of a case with lung metastases at first clinical presentation. *Oral Dis.* 2005; 11(2): 109-112.
12. Binesh F, Akhavan A, Masumi O, Mirvakili A, Behniafard N. Clinicopathological review and survival characteristics of adenoid cystic carcinoma. *Indian J Otolaryngol Head Neck Surg.* 2015; 67(Suppl 1): 62-66.

13. Burke CJ, Thomas RH, Howlett D. Imaging the major salivary glands. *British Journal of Oral and Maxillofacial Surgery*. 2011; 49(4): 261-269.
14. Deng RX, Xu X, Zhang CP, Zhang ZY, He Y. Primary intraosseous adenoid cystic carcinoma of the jaw: clinical and histopathologic analysis. *J Oral Maxillofac Surg*. 2014; 72(4): 835 e1-10.
15. Ren ZH, Chickooree D, Liu JB, Wu HJ. Primary intraosseous ACC of mandible of possible salivary origin: A rare clinical entity. *Int J Surg Case Rep*. 2014; 5(5): 222-225.
16. Gondivkar SM, Gadbaile AR, Chole R, Parikh RV. Adenoid cystic carcinoma: a rare clinical entity and literature review. *Oral Oncol*. 2011; 47(4): 231-236.
17. Batsakis JG, Luna MA, el-Naggar A. Histopathologic grading of salivary gland neoplasms: III. Adenoid cystic carcinomas. *Ann Otol Rhinol Laryngol*. 1990; 99(12): 1007-1009.
18. Fordice J, Kershaw C, El-Naggar A, Goepfert H. Adenoid cystic carcinoma of the head and neck: predictors of morbidity and mortality. *Arch Otolaryngol Head Neck Surg*. 1999; 125(2): 149-152.
19. Andreadis D, Epivatianos A, Pouloupoulos A, Nomikos A, Papazoglou G, Antoniadis D, et al. Detection of C-KIT (CD117) molecule in benign and malignant salivary gland tumours. *Oral Oncol*. 2006; 42(1): 57-65.
20. Shen C, Xu T, Huang C, Hu C, He S. Treatment outcomes and prognostic features in adenoid cystic carcinoma originated from the head and neck. *Oral Oncol*. 2012; 48(5): 445-449.
21. Spiro RH, Huvos AG. Stage means more than grade in adenoid cystic carcinoma. *The American Journal of Surgery*. 1992; 164(6): 623-628.
22. Mendenhall WM, Morris CG, Amdur RJ, Werning JW, Hinerman RW, Villaret DB, et al. Radiotherapy alone or combined with surgery for adenoid cystic carcinoma of the head and neck. *Head Neck*. 2004; 26(2): 154-162.
23. Chen AM, Bucci MK, Weinberg V, Garcia J, Quivey JM, Schechter NR, et al. Adenoid cystic carcinoma of the head and neck treated by surgery with or without postoperative radiation therapy: prognostic features of recurrence. *Int J Radiat Oncol Biol Phys*. 2006; 66(1): 152-159.
24. Laurie SA, Ho AL, Fury MG, Sherman E, Pfister DG. Systemic therapy in the management of metastatic or locally recurrent adenoid cystic carcinoma of the salivary glands: a systematic review. *The Lancet Oncology*. 2011; 12(8): 815-824.
25. Hitre E, Budai B, Takacs-Nagy Z, Rubovszky G, Toth E, Remenar E, et al. Cetuximab and platinum-based chemoradio- or chemotherapy of patients with epidermal growth factor receptor expressing adenoid cystic carcinoma: a phase II trial. *Br J Cancer*. 2013; 109(5): 1117-1122.
26. Hotte SJ, Winquist EW, Lamont E, MacKenzie M, Vokes E, Chen EX, et al. Imatinib mesylate in patients with adenoid cystic cancers of the salivary glands expressing c-kit: a Princess Margaret Hospital phase II consortium study. *J Clin Oncol*. 2005; 23(3): 585-590.
27. Agulnik M, Cohen EW, Cohen RB, Chen EX, Vokes EE, Hotte SJ, et al. Phase II study of lapatinib in recurrent or metastatic epidermal growth factor receptor and/or erbB2 expressing adenoid cystic carcinoma and non adenoid cystic carcinoma malignant tumors of the salivary glands. *J Clin Oncol*. 2007; 25(25): 3978-3984.