Mucoepidermoid Carcinoma - Unknown Primary Affecting the Neck

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Abstract. *The present report describes therapy and follow-up of a patient who experienced a localized swelling of the neck that proved to be a mucoepidermoid carcinoma. Extensive staging revealed no primary site. Therapy was modified neck dissection followed by external application of chemotherapy combined with fractionated radiotherapy. Over a period of 43 months, the patient has remained free of local tumour growth and distant metastasis. Whereas prognosis of mucoepidermoid carcinoma in general is good, prognosis of patients affected by mucoepidermoid carcinoma with carcinoma of unknown primary is ambiguous.*

Mucoepidermoid carcinoma (MEC) is a malignant tumour predominantly arising from the salivary glands; the minor glands preferentially give rise to MEC (1, 2). MEC is the most frequent malignant salivary gland tumour in children (1) and adults (2). The term 'mucoepidermoid' reflects the mixture of different epithelial cells comprising the tumour. Varying proportions of epidermoid and mucus-producing cells comprise the well-delineated epithelial components of the tumour, embedded in intermediate cells forming a solid tumour (2). The malignancy of MEC was recognized after many years of observational studies (4). The entity is also genetically distinct (3). Tumour biology is related to morphological characteristics, allowing grading of the tumour. Low-grade tumours appear to have a better prognosis than high-grade ones (2). However, overall survival of patients affected with MEC is greater than 10 years for more than 90% (5). The prognosis is worse in patients with local or distant spread of MEC (1-5). In very rare cases, MEC was reported at distant sites with no detection of a primary tumour (6, 7). Therapy and prognosis of patients with MEC and carcinoma of unknown primary (CUP) is an individual decision alluding to therapy protocols for metastatic salivary gland cancer. This report adds a new case of CUP in MEC.

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Key Words: Mucoepidermoid carcinoma, carcinoma unknown primary, salivary gland neoplasm, neck metastasis, radiotherapy head neck.

Case Report

A 48-year-old male was submitted to the Department of Oral and Maxillofacial Surgery, Eppendorf University Hospital for treatment for a swelling of the left side of the neck. The otherwise healthy patient had experienced a painless swelling during the previous 6 months. On admission, a palpable, firm mass was found in the anterior of the mid region of the sternocleidomastoid. The integument showed no signs of inflammation. Ultrasound imaging displayed an encapsulated echo-free oval lesion of about 2.6 cm in diameter covered in part by the sternocleidomastoid muscle (Figure 1). The vascularization of the distinct mass was sparse, allowing no clear distinction between seroma and neoplasm of a lymph node. Under general anaesthesia, the left sternocleiodomastoid muscle was exposed. Adhering to the muscle and other surrounding soft tissues, the firm tumour was detached and completely resected. Wound healing was uneventful following primary closure of the wound in anatomical layers. After histological diagnosis, the patient underwent modified radical dissection of the neck of the affected side followed by radiochemotherapy of the head and neck. Staging revealed no further manifestation of the disease (magnet resonance imaging of head and neck region and thorax, positron-emission tomography combined with computed tomography of the whole body). Forty-three months after diagnosis, the patient has experienced no further disease related to MEC. However, during the follow-up, he had to be treated for a severe deep venous thrombosis of the lower left leg (positive family history for thrombosis) and is under continuous anticoagulatory medication.

Histology. A soft-tissue resection specimen (4.0×2.5×2.0 cm^3) contained three lymph nodes, one of them showed neoplastic infiltrates destroying the lymph node capsule (2.4 cm maximum diameter). Based on conventional histology, we suspected an MEC of the neck, of low grade (Figure 2). No invasion of the neural sheath was present. Fluorescence *in situ* hybridization (FISH) (PathVysion™; Abbott, Chicago, IL, USA) excluded a mutation of the human epidermal growth factor receptor 2 (*HER2*)/*neu* gene; however, it did reveal split signals in the tumour cells consistent with translocation of mastermind like protein 2 (*MAML2*) gene, characteristic of MEC (*MAML2* break-apart probe; Zytovision, Bremerhaven, Germany).

Discussion

This report details the diagnosis and therapy of a patient with MEC and a CUP manifesting in the head and neck region. Malignant salivary gland tumours are rare (2). Other localizations can also give rise to tumours resembling the features of MEC (8-14). In particular, certain carcinomas of the lung are revealed to be true MEC (8). Repeated investigation disclosed no primary lung cancer in the present case. Furthermore, MEC may occasionally arise from the skin (9), the nasopharynx (10), larynx (14), and breast (13). These organs showed no primary tumour during the follow-up period. Indeed, MEC arising from these organs are rarities (8-14).

MEC is the most frequent salivary gland neoplasm (2). Tumour biology varies considerably in individual cases. The current grading allows, with some restrictions, an estimation of prognosis (2, 5). Grade I MECs are described as low-grade cancer having a better prognosis, lower recurrence rate, and overall survival rate greater than 90% during the first 10 years (5). Grade II and III have a considerable poorer prognosis; the recurrence rates are calculated at about 30% and 70%, respectively (15). Survival rates of patients with high-grade MEC with positive neck lymph nodes was 70% after application of ablative surgery and radiotherapy (15).

Surgical excision of the tumour with safety margins is the therapy of choice (5, 16). Neck dissection should be considered in CUP affecting the neck (2, 5). However, neck dissection should be limited to the affected side. Occult metastasis to the neck region may be present at the time of first notice of a neck swelling (16, 17). Radiosensitivity of the primary tumour and regional lymph node metastases is ambiguous in MEC (18). Benefits of chemotherapy are also not clear (19).

The present case was managed by adequate surgical excision followed by postoperative radiotherapy. Local control was achieved by this strategy. However, MEC can arise in the field of irradiation (20). Recently an MEC case was reported with CUP of the neck and further tumour spread, despite ablative surgery and radiotherapy (6). In clinical studies on MEC of the salivary glands, the primary is usually identified (5, 15, 16).

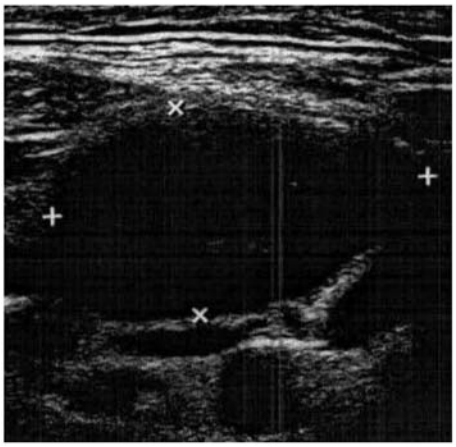

Figure 1. *Cropped image of a print-out of the B-scan ultrasonogram of the left neck. The anechoic oval lesion appeared to have distinct borders. The lesion had displaced the sternocleidomastoid muscle (left). Its ultrasonographic appearance makes invasive growth of the lesion unlikely.*

Metastasis is usually confined to regional lymph nodes, allowing local tumour resection and tumour control (1-3). However, rapid distant spread with poor prognosis is detailed in the literature (5), in particular to the lungs, liver and brain (2). Therefore, prognosis of MEC with CUP manifestation remains uncertain. MEC with unknown primary should be classified as a salivary gland carcinoma with distant metastasis. Further reports on this special condition are needed in order to better understand the benefit patients can expect from combined therapies.

Conclusion

MEC of unknown origin is an extremely rare clinical finding. In the head region, adequate resection of tumour and adjacent structures is the therapy of choice. Surgical therapy should seriously consider the indication for neck dissection, in particular in cases with extracapsular spread. In these cases, adjuvant radiotherapy may improve local tumour control.

References

1 Strutz J and Mann WJ: Praxis der HNO-Heilkunde. Thieme, Stuttgart, p. 579, 2009.

2 Goode RK and El-Naggar AK: Mucoepidermoid carcinoma (Head and Neck). *In*: Barnes L, Eveson JW, Reichart P and Sidransky D (eds.): Pathology and genetics of Head and Neck Tumours. World Health Organization Classification of Tumours. IARC Press, Lyon, pp. 219-222, 2005.

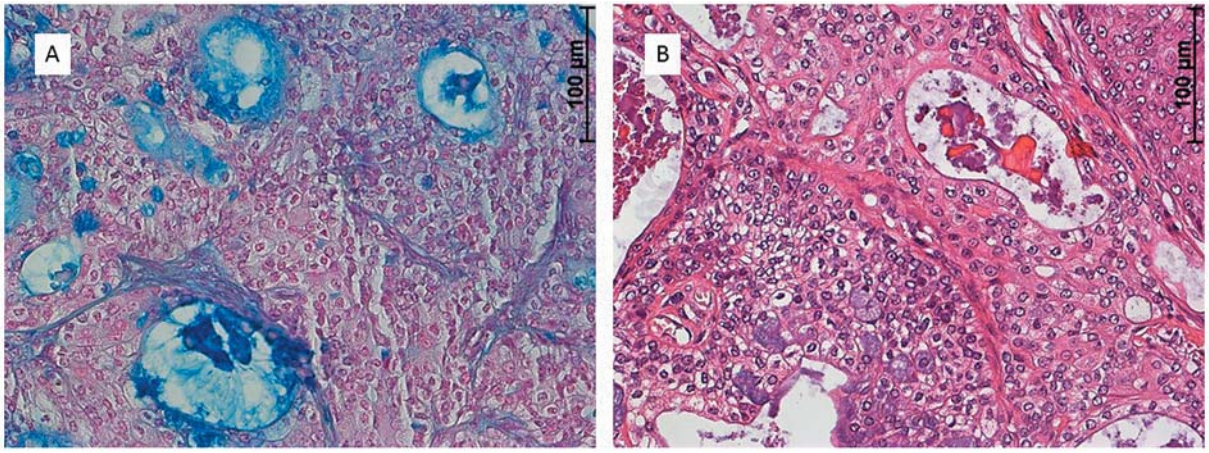

Figure 2. *Mucoepidermoid carcinoma. A: Using histochemical staining methods (Alcian blue), the content of cysts and tumour cell vacuoles was proven to be mucus. B: Microscopic analysis revealed sheaths and nodules of atypical epithelioid infiltrates with focal cystic formations. Several tumour cells exhibited vacuolae filled with bluish material (haematoxylin-eosin). Original magnification: ×200.*

3 Weinreb I: Translocation-associated salivary gland tumors: a review and update. Adv Anat Pathol *20*: 367-377, 2013.
4 Lentrodt J and Hafke G: Clinical aspects and especially dignity of mucoepidermoid tumors of salivary glands. Dtsch Zahnarztl Z *29*: 615-622, 1974 (In German).
5 Plambeck K, Friedrich RE and Schmelzle R: Mucoepidermoid carcinoma of salivary gland origin: classification, clinical-pathological correlation, treatment results and long-term follow-up in 55 patients. J Craniomaxillofac Surg *24*: 133-139, 1996.
6 Prabhu V, Johnston J, Ingrams D and Passant C: Mucoepidermoid carcinoma – unknown primary and late distant metastasis: an unusual course of the disease. Clin Pract *1*: e97, 2011.
7 Trosman S, Chute D, Wood B and Lamarre E: Unknown primary mucoepidermoid carcinoma: Diagnosis and treatment. Head Neck *48*: 101-119, 2015
8 Graham DM, O'Connor KM, Hinchion J, Coate LE, Burke L and Power DG: Mucoepidermoid carcinoma of lung masquerading as urothelial carcinoma of bladder. Rep Pract Oncol Radiother *19*: 62-64, 2013.
9 Yu R, Salama S and Alowami S: Primary cutaneous *versus* salivary gland origin mucoepidermoid carcinoma. Am J Dermatopathol *37*: e26-e30, 2015.
10 He Y, Wang J, Fu HH, Zhang ZY and Zhuang QW: Intraosseous mucoepidermoid carcinoma of jaws: report of 24 cases. Oral Surg Oral Med Oral Pathol Oral Radiol *114*: 424-429, 2012.
11 Prichard RS, Lee JC, Gill AJ, Sywak MS, Fingleton L, Robinson BG, Sidhu SB and Delbridge LW: Mucoepidermoid carcinoma of the thyroid: a report of three cases and postulated histogenesis. Thyroid *22*: 205-209, 2012.
12 Ollero JM, Morón AH, Luis AM, Sánchez SM, Nazarewsky AA, López MJ and Aguerri AR: Nasopharyngeal mucoepidermoid carcinoma: A case report and review of literature. Rep Pract Oncol Radiother *18*: 117-120, 2012.
13 Basbug M, Akbulut S, Arikanoglu Z, Sogutcu N, Firat U and Kucukoner M: Mucoepidermoid carcinoma in a breast affected by burn scars: comprehensive literature review and case report. Breast Care *6*: 293-297, 2011.
14 Alimoglu Y, Mamanov M and Kaytaz A: High-grade mucoepidermoid carcinoma of the larynx. J Craniofac Surg *22*: e62-e64, 2011.
15 Emerick KS, Fabian RL and Deschler DG: Clinical presentation, management, and outcome of high-grade mucoepidermoid carcinoma of the parotid gland. Otolaryngol Head Neck Surg *136*: 783-787, 2007.
16 Ozawa H, Tomita T, Sakamoto K, Tagawa T, Fujii R, Kanzaki S, Ogawa K, Kameyama K, and Fujii M: Mucoepidermoid carcinoma of the head and neck: clinical analysis of 43 patients. Jpn J Clin Oncol *38*: 414-418, 2008.
17 Nobis CP, Rohleder NH, Wolff KD, Wagenpfeil S, Scherer EQ and Kesting MR: Head and neck salivary gland carcinomas – Elective neck dissection, yes or no? J Oral Maxillofac Surg *72*: 205-210, 2014.
18 Chen AM, Lau VH, Farwell DG, Luu Q and Donald PJ: Mucoepidermoid carcinoma of the parotid gland treated by surgery and postoperative radiation therapy: clinicopathologic correlates of outcome. Laryngoscope *123*: 3049-3055, 2013.
19 Demirci U, Coskun U, Karaca H, Dane F, Ozdemir NY, Ulas A, Baykara M, Benekli M, Ozkan M and Buyukberber S: Docetaxel and cisplatin in first-line treatment of patients with unknown primary cancer: a multicenter study of the Anatolian Society of Medical Oncology. Asian Pac J Cancer Prev *15*: 1581-1584, 2014.
20 Fortson JK, Rosenthal M, Patel V, Lawrence GE and Lin JS: Atypical presentation of mucoepidermoid carcinoma after radiation therapy for the treatment of keloids. Ear Nose Throat J *91*: 286-288, 2012.

Received March 18, 2016
Revised April 23, 2016
Accepted May 8, 2016