Rapidly Progressive and Metastatic Mucoepidermoid Carcinoma: Application of Serological Tumor Markers

REINHARD E. FRIEDRICH¹, RAINER KLPDOR² and SYLVA BARTEL-FRIEDRICH³

¹Maxillofacial Surgery, Eppendorf University Hospital, University of Hamburg, Hamburg; ²ZeTDT, Center for Clinical and Experimental Tumor Marker Diagnosis and Therapy, Hamburg; ³Otorhinolaryngology, Martin Luther University, Halle a. d. S., Germany

Abstract. Mucoepidermoid carcinoma (MEC) of the salivary gland is a rare entity. A distinction of 2 variants has been proposed: the low-grade tumor with a favourable prognosis and the high-grade tumor with a poor prognosis. Indeed, MEC is a cancer with a relative favourable outcome and more than 90% of patients survive for more than 5 years after diagnosis, reduced to about 70% after 10 years. This excellent prognosis might contribute to the unacceptable retention of the term "mucoepidermoid tumor" in the medical terminology, even in current medical textbooks. However, the distinction of MEC by grading is a guideline only and it is not appropriate to use this histological term as a prediction for individual cases. We describe the rapid fatal outcome of a patient with MEC in order to emphasize the malignant characteristics of this tumor and the possible application of tumor markers for the diagnosis of metastasizing MEC.

Malignant tumors of the salivary glands are rare (1, 2). The mucoepidermoid carcinoma (MEC) is the third most frequent tumor arising from minor salivary glands (2). Until the WHO reclassification of salivary gland neoplasm in 1991, MEC was termed 'mucoepidermoid tumor'. Now the WHO defines this tumor as a 'carcinoma' due to the increasing number of reports on mucoepidermoid tumors with distant metastasis and fatal outcome (3). However, the judgement of the tumor biology in MEC remains debateable due to the fact that the overall survival of MEC is excellent in studies with a large sample size (4, 5). The capacity to metastasize is attributed to a histological subtype, described as high-grade malignancy (6). However, histological subtyping is a guideline only and offers no prediction for individual cases (6). Additional markers are warranted that adequately describe the differences of tumor biology. We describe a metastasizing MEC with altered levels of serological tumor markers.

Case Report

A 62-year-old male was admitted to our oncology outpatient clinic for diagnosis and therapy of oral findings that had developed over the previous few months. Oral inspection revealed a tumor of the right side of the maxilla distal to the front teeth. The mucosa covering the tumor was intact, excluding a small ulcerative portion. The maximum diameter of the defect was less than 2 cm. A computed tomogram of the head and neck region revealed several lymph nodes of both sides of the neck suspected of being metastatic lesions. However, maxillary bone invasion was seen neither on plain nor on computed radiographs. Chest radiographs and computed tomograms of the thorax and abdomen revealed multiple lung tumors and liver lesions. On whole body scintigram, multiple focal scintillations of different bones supported the diagnoses of disseminated tumor spread. Tumor grading prior to therapy was T1N2cM1. Therapy was palliative and included local maxillary resection in order to identify the entity. Histopathological findings were in accordance with the diagnosis of high-grade MEC of the minor salivary gland (University of Hamburg Registry of Salivary Glands). Sera were collected at the time of palliative treatment (CYFRA 21-1: 33.8 μg/ml, SCC: 101 μg/ml, TPA: 669 U/l, CEA: 162 μg/ml, CA19-9: 62.4 U/ml, CA12-5: 2649 U/ml, CA15-3: 1649 U/ml, TAG 72: 259 U/ml, NSE: 15.5 ng/ml). Polychemotherapy was ineffective. Six weeks following admission the patient died with evidence of disseminated tumor growth.

Discussion

This report shows that out of a panel of proteins serving as serological tumor markers, several protein levels were elevated beyond the cut-off levels in a case of metastatic MEC. Some of these markers showed exceedingly high levels.
Usually MEC are diagnosed following physical inspection and histological diagnosis of representative specimens, supported by endoscopy or external imaging techniques like magnetic resonance tomography or ultrasonography. Even in the case of recurrent disease, these measures are the first choice diagnostics for a salivary gland cancer. Serological markers are not well established in MEC primary diagnostics and follow-up control (7). Indeed, distant tumor spread is rare in MEC and usually occurs many years after diagnosis (4). However, elevated CEA levels were found in an MEC (3). In the case of Noriyuki et al. (8), a low-grade bronchial MEC was associated with an elevated CEA level in serum (12.4 ng/ml) and immunohistochemical identification of CEA in carcinoma cells. The expression of CEA was also demonstrated in carcinoma cells from salivary gland MEC (8). The presented case shows the same peculiarities (10). The primary tumor was rather small compared to the large sized and multiple localized metastases. Furthermore, the distant tumors grew rapidly leading to definite bronchial occlusion and atelectasis over a period of several weeks. Bone metastases in MEC are rare (4). Differential diagnosis of a mucoepidermoid carcinoma of the lung metastatic to the oral cavity was ruled out due to the multilocality of lung tumors (11). Moreover, metastasis to the oral cavity of salivary gland tumors arising in primaries outside the head and neck region is extremely rare (12). However, the definite diagnosis of a primary oral MEC in this case was concluded on clinical findings.

Conclusion

Whereas serological tumor markers are currently not an established tool in the diagnosis of MEC, elevated markers might have a prognostic significance, in particular in metastatic disease.

Acknowledgements

The authors appreciate the skilful technical assistance of M. Bahlo, Hamburg.