Metastasizing pleomorphic adenoma presenting as an asymptomatic kidney tumor twenty-nine years after parotidectomy – urological viewpoint and overview of the literature to date

Jan Ebbing,1 Carolin Blind,2 Harald Stein,2 Kurt Miller,1 Christoph Loddenkemper2
1Department of Urology, and 2Institute of Pathology, Charité–Universitätsmedizin Berlin, Campus Benjamin Franklin, Berlin, Germany

Abstract

Pleomorphic adenomas (benign mixed tumors) are the most common tumors of glandular origin in the head and neck and are one of the few benign neoplasms that can undergo malignant transformation.1 Mixed tumors that are seemingly benign at the microscopic level but metastasize have been termed metastasizing mixed tumors (MZMTs). The entity of metastasizing benign mixed tumors has been reported since the early 1940s, with up to approximately 50 cases described in the literature to date. Despite their bland morphologic appearance, MZMTs have been associated with an overall mortality rate of about 20-40%. We report the case of a MZMT of the kidney almost 30 years after lateral parotidectomy owing to the same tumor entity. For benign mixed tumors, we are unaware of more than two other cases of metastasis to the kidney that have been published, whereas metastases to the bone, lung, and lymph nodes are more common. Parotidectomy is widely accepted as the first choice of treatment,13 but once metastases have occurred the therapeutic strategy is uncertain with surgery being the only curative option in cases with resectable disease. This case report provides information about the rare event of metastatic disease to the kidney and points out therapeutic strategies. However, in view of the general lack of adequate information in the literature, the best therapy for systemic disease still remains unresolved.

Case Report

A 49-year-old woman suffered from a car accident and was brought to our clinic. A routine ultrasound scan of the abdomen in the emergency unit detected a kidney tumor on the right side. The patient did not report any symptoms that would point to a disease of the urogenital tract. The physical examination was without pathological findings. A computerized tomography (CT) scan of the abdomen revealed the presence of two suspect cortical tumors (20 mm and 50 mm in diameter) in the right kidney. In addition, the CT scan was suspicious for pulmonary metastases and a CT scan of the chest confirmed the presence of multiple pulmonary lesions in both lungs, with a maximal diameter of 11 mm in the right lower lobe. The right kidney was removed by laparoscopic radical nephrectomy as clinically renal cell carcinoma was suspected, without complications.

Pathological Findings

Gross findings

On sectioning the cut surface of the kidney, revealed a white, solid, lobulated, well-circumscribed tumor in the middle third of the parenchyma, which measured 55x55x50 mm and penetrated the capsule (Figure 1A). Another smaller, similar focus of 10 mm in diameter was found in the surrounding parenchyma close to the hilus.

Histological findings

The microscopic features of both tumors showed a mixed cell composition with mesenchymal elements demonstrating chondroid differentiation embedded in a myxoid matrix, as well as epithelial components consisting of ductal structures without atypia (Figure 1B). Immunohistochemical studies showed that the epithelial component stained positive for pan-cytokeratin AE1/AE3 with partial expression of the myoepithelial markers p63 (Figure 1C) and a very low Ki-67 proliferation rate (Figure 1D).

Figure 1. (A) Gross appearance of the dissected nephrectomy specimen showing a well-defined tumor with a homogeno- nous tan cut surface. (B) Histology displays the typical features of a benign (metastasizing) pleomorphic adenoma in the right kidney: a mesenchymal cartilaginous component and an epithelial ductal component within renal tissue (left lower corner). (C) The myoepithelial cells showing expression of p63. (D) The Ki-67+ proliferative index is seen as extremely low (≤1%). (E) Macroscopy of the paraffin block from 1978 showing a small nodular tumor of the parotid gland with a white-to-tan cut surface. (F) The identical morphology of a pleomorphic adenoma in the salivary gland tissue is demonstrated (left lower corner).
Statement of the pathologist

The histopathological features of the tumors disclosed a mixed tumor of salivary gland origin, in particular for a metastasizing pleomorphic adenoma, but were not typical of a primary tumor of the kidney.

The past history of the patient revealed that a lateral parotidectomy on the left side had been performed 29 years previously because of a tumor mass of the parotid gland diagnosed as a pleomorphic adenoma. The pathological report described a 45x35x28 mm gland with a tumor 22 mm in diameter. It was possible to retrieve the old paraffin blocks from the archives of the Institute of Pathology of the Charité–Campus Benjamin Franklin, which showed a white cut surface of the tumor (Figure 1E). On histology, even in retrospect, no signs of malignancy were detected and the tumor was still classified as a pleomorphic adenoma with characteristic epithelial and mesenchymal composition (Figure 1F) and great morphological similarity to the kidney metastasis 29 years later.

Discussion

We report the case of a metastasizing “benign” pleomorphic adenoma of the kidney almost 30 years after a lateral parotidectomy owing to the same tumor entity. A CT scan revealed suspect pulmonary masses in both lungs that have remained stable over a period of three months. After discussion with an oncologist a surveillance strategy of the asymptomatic patient was agreed.

Mixed tumors of the salivary glands generally are divided into benign mixed tumors and malignant mixed tumors, represented by carcinomas and so-called carcinoma ex-mixed tumors, which can develop within a benign mixed tumor over an extended period of time.1 Rarely will a mixed tumor that is seemingly benign at the microscopic level metastasize. These tumors have been termed metastasizing mixed tumors (MZMTs) and have been classified as metastasizing pleomorphic adenomas within the category of malignant epithelial tumors of the salivary gland by the WHO. Some authors suggest that a MZMT could be the intermediate link in the transformation of a pleomorphic adenoma into a carcinoma ex-mixed tumor.2 A published case report from Czader et al.2 underlined the suggestion that MZMT and carcinoma ex-mixed tumor could represent different stages along a common biological pathway.3

Histopathological and clinical criteria to differentiate metastatic mixed tumors from non-metastatic mixed tumors are lacking. There are no predictive factors available to determine which mixed tumor may have the potential to metastasize and which patient may die of metastatic disease.4 However, the probability that a benign mixed tumor will become malignant depends on the period of time it has been allowed to develop without treatment. The risk of malignant transformation – usually into a carcinoma ex-pleomorphic tumor – ranges from 1.5% in the first five years to 9.5% after 15 years.5 It is estimated that approximately 20-40% of patients with MZMT will die from the disease eventually.6 Surgical manipulations are thought to create a metastatic potential but do not truly explain the occurrence of metastases.7 Metastases were discovered from 6 to 52 years after the primary tumor was removed.8 About 40-50% of patients suffering from carcinoma ex-pleomorphic adenoma develop local recurrence and up to 70% develop local or distant metastases.9 Systematic data for MZMTs concerning recurrence and metastatic rates are lacking. In contrast to our case, the patients normally have at least one episode of tumor recurrence at the primary site before the development of metastases, which may occur many years after the presentation of the primary mixed tumor. The metastatic potential of mixed tumors is related to the accumulation of key genetic alterations. The development of a carcinoma ex-mixed tumor apparently could be, in part, the consequence of the accumulative loss of chromosomes at loci at 3p, 9p, and 17p.10 A number of case reports describe the simultaneous appearance of benign and malignant components of mixed tumors in the same tumor manifestation.11,12 The order of genetic alterations along tumor progression seems to be variable and may differ for each salivary tumor, but for MZMT no recurrent genetic defect has been reported. Parotidectomy is widely accepted as the first choice of treatment,13 but once metastases have occurred, the therapeutic strategy is uncertain with surgery being the only curative option in cases with resectable disease.

Conclusions

Metastatic pleomorphic adenoma of the salivary gland to the kidney is a very rare neoplasm, which requires a careful patient history and knowledge of the lesion for pathologists and clinicians to reach the correct diagnosis. There is no approved hypothesis as to how a morphologically benign tumor may metastasize. Surgery of resectable disease with curative intent should be attempted whenever possible. In view of the general lack of adequate information in the literature, the best therapy for systemic disease still remains unresolved.

References

1. Klijanienko J, El-Naggar AK, Servois V, et al. Clinically aggressive metastasizing pleomorphic adenoma: report of two cases. Head Neck 1997;19:629-33.
2. Czader M, Eberhart CG, Bhatti N, et al. Metastasizing mixed tumor of the parotid: initial presentation as a solitary kidney tumor and ultimate carcinomatous transformation at the primary site. Am J Surg Pathol 2000;24:1159-64.
3. Li X, Lu XY, Zhu XZ, et al. Metastasising pleomorphic adenoma of the parotid: presenting as a solitary kidney mass. Pathology 2008;40:87-9.
4. Fujimura M, Sugawara T, Seki H, et al. Carcinomatous change in the cranial metastasis from a metastasising mixed tumor of the salivary gland - case report. Neurol Med Chir (Tokyo) 1997;37:546-50.
5. Minic AJ. Unusual variant of a metastasizing malignant mixed tumor of the parotid gland. Oral Surg Oral Med Oral Pathol 1993;76:330-2.
6. Batsakis JG. Malignant mixed tumor. Ann Otol Rhinol Laryngol 1982;91:342-3.
7. Seifert G, Sobin LH. The World Health Organization's Histological Classification of Salivary Gland Tumors. A commentary on the second edition. Cancer 1992;70:379-85.
8. Ellis G. Tumors of the Salivary Glands. In: Tumors of the Salivary Glands. Ellis GL, Auclair PL, eds. Washington, DC: 1996, pp 155-373.
9. Wenig BM, Hitchcock CL, Ellis GL, et al. A clinicopathologic and flow cytometric analysis of metastasizing mixed tumor of salivary glands. Am J Surg Pathol 1992;16:485-58.
10. Bradley P. Metastasizing pleomorphic salivary adenoma should now be considered a low-grade malignancy with a lethal potential. Curr Opin Otolaryngol Head Neck Surg 2005;13:123-6.
11. Johns MM 3rd, Westra WH, Califano JA, et al. Allelotype of salivary gland tumors. Cancer Res 1996;56:1151-4.
12. Hellquist H, Michaels L. Malignant mixed tumour. A salivary gland - case report. Neurol Med Chir (Tokyo) 1997;37:546-50.
13. Paris J, F felon F, Chrestien MA, et al. Recurrences of pleomorphic adenomas of the parotid: changing attitudes. Rev Laryngol Otol Rhinol (Bord) 2003;124:229-34.