Histologically Benign Pleomorphic Adenoma of the Calvaria

Mark Girson,1 Dianne B. Mendelsohn,1 Dennis Burns,2 and Bruce Mickey3

Pleomorphic adenoma or benign mixed tumor is the most common salivary gland tumor. It is most frequently located in the parotid gland, and is considered to be a benign neoplasm accounting for 70–80% of all benign tumors of the salivary glands [1]. Benign metastasizing pleomorphic adenoma is extremely rare, with only a handful of cases described. We report a case of a histologically benign mixed tumor in the diploic space of the skull in a patient who had a benign pleomorphic adenoma (BPA) of the parotid gland resected 16 years previously. This case may represent an unusual example of a histologically benign mixed tumor of salivary origin metastasizing to the calvaria without evidence of local recurrence, a previously unreported phenomenon. An alternative, less likely, possibility would be a metachronous chondroid syringoma arising from displaced cutaneous adnexal structures.

Case Report

A 33-year-old man presented with an enlarging scalp mass over a period of 6 months and left-sided hemi-cranial headaches for the past 3 months. Sixteen years prior to admission he had a left superficial parotidectomy for a 2.5-cm BPA.

Skull radiographs and a CT scan showed a large intradiploic expandable mass lesion, with thinning of the adjacent inner and outer skull tables and mild enhancement upon contrast administration (Figs. 1 and 2). A radionuclide bone scan showed a central photopenic area surrounded by a rim of increased uptake. No additional abnormal foci were noted in the rest of the skeleton. MR imaging performed on a 1.5-T scanner showed the mass to have slightly decreased signal intensity relative to the adjacent brain parenchyma on the T1-weighted, 550/20/2 (TR/TE/excitations), sequences with a marked increase in signal intensity on the T2-weighted, 2500/90/1, spin-echo sequences. Following the administration of gadopentetate dimeglumine, intense inhomogeneous enhancement was noted within this mass, with enhancement and thickening of the adjacent meninges (Fig. 3). This dural enhancement likely represents reactive changes caused by loose connective tissue proliferation, hypervascularity, and vascular dilatation; it does not necessarily imply neoplastic infiltration [2]. Selective left external carotid angiography showed the mass to be hypervascular, being fed by the middle meningeal artery (Fig. 4).

An MR study of the neck and skull base revealed no evidence of residual or recurrent parotid tumor. En bloc surgical resection was performed with rigorous histological and ultrastructural examination, confirming the diagnosis of a histologically benign mixed tumor (Fig. 5). The original histology was unavailable for review.

Discussion

Pleomorphic adenomas (benign mixed tumors) of the salivary glands are benign neoplasms characterized by slow intermittent growth, which may remain unchanged in size for many years. They occur most commonly in the parotid gland, and account for the large majority of parotid neoplasms. They are slightly more common in women, and the peak age is between 30 and 50 years [3].

Two to nine percent of mixed tumors of salivary gland origin have malignant characteristics [4]. Three morphological pat-
terns of these malignant mixed tumors have been described. The vast majority have been termed carcinoma ex-pleomorphic adenoma, characterized by the presence of malignant epithelial elements, usually of ductal origin, within the stroma of the pleomorphic adenoma. Carcinoma in situ or preinvasive carcinoma ex-pleomorphic adenoma, is a microfocus of carcinoma ex-pleomorphic adenoma with no invasive characteristics [5, 6]. Carcinosarcoma, or true malignant mixed tumor, is a rare variant in which there are both carcinomatous and sarcomatous malignant components in a single tumor [4, 5, 7]. The third and rarest variety, which has been called a medical curiosity, is the histologically benign metastasizing mixed tumor that has no morphologic evidence of malignancy. Likewise, the metastases are histologically benign. Thorough histological examination is imperative in all cases of presumed pleomorphic adenoma, and the entire tumor must be sectioned, since malignant change can be focal and possibly overlooked [8].

Benign mixed tumor is characterized by histological diversity, containing both mesenchymal and epithelial components. The most common variety of malignant mixed tumor, namely carcinoma ex-pleomorphic adenoma, derives from a malignant transformation of the epithelial component, with a carcinoma arising within a preexisting benign mixed histological
Fig. 4.—A, Left external carotid arteriogram shows that tumor is supplied predominantly by the middle meningeal artery (arrow). B, Delayed subtraction image reveals the diffuse blush (arrows) within the adenoma.

Fig. 5.—A, Low-power photomicrograph of calvarial neoplasm shows well-demarcated border of lesion (thin arrow) at its interface with native bone (thick arrow). (H and E ×50) B, Higher magnification of neoplasm shows intimate admixture of glandular (epithelial) and stromal (myoepithelial) elements characteristic of benign mixed tumor. Glandular spaces (thin arrow) are lined by uniformly bland low cuboidal epithelium. Adjacent polygonal to stellate stromal cells (thick arrow) are dispersed in a loose myxomatous matrix (asterisk), typical of mixed tumor. (H and E ×250)

pattern. Under these circumstances the metastases of the carcinoma ex-pleomorphic adenoma are epithelial, similar to the malignant areas within the primary lesion. True malignant mixed tumors are appropriately designed carcinosarcomas, and are composed of both malignant mesenchymal and epithelial elements, both or either of which may be present within metastatic foci. Metastases from these tumors may contain carcinomatous as well as sarcomatous elements [3, 7]. Metastases from mixed tumors may become clinically apparent for up to 50 years after the initial treatment of the primary salivary gland neoplasm, and they most commonly involve bone and lung [9]. Total excision is the treatment of choice for metastases in surgically accessible sites. Multiple local recurrences in the parotid bed are the most important predictors of distant metastases of primary benign mixed tumors. Recurrences complicate the course in 5–50% of patients with BPA and are related to the adequacy of initial surgical resection [3, 7]. In the rare patient with histologically benign metastasizing mixed tumors, it is postulated that numerous primary recurrences and subsequent surgical manipulations result in vascular implantation at the time of surgery with subsequent hematogenous spread and the development of metastases.

An alternative theory would be development of a synchronous lesion in an ectopic rest of salivary gland tissue. While ectopic salivary gland tissue has been described in numerous locations—such as the pharynx, gums, lips, mandible, subcutaneous tissues, trachea, and mediastinum—salivary gland rests have not been described within the calvaria of the skull [9–12]. Salivary parenchyma shares biological features with cutaneous adnexa, which may give rise to neoplasms similar to those of salivary gland origin [13]. Chondroid syringoma is a cutaneous adnexal neoplasm ultrastructurally and immunohistochemically similar to the pleomorphic adenoma of salivary gland [3, 14–16]. The proximity to the coronal suture in our case raises the additional possibility of a neoplasm arising within skin appendages sequestered within the coronal suture. The fact that the expansile mass was adjacent to rather than centered at the suture speaks against this hypothesis.

Most of the previously reported benign metastasizing pleomorphic adenomas are characterized by at least one local recurrence prior to the metastatic presentation [4, 5, 8, 12]. We believe our case to be a rare example of a BPA with delayed osseous metastasis without clinical or MR evidence of local recurrence. The validity of previous reports of met-
astatic BPA [17, 18] in the absence of local recurrence has been disputed by El Naggar et al. [8], who believe that the published photomicrographs are those of malignant neoplasms rather than benign lesions. Many cases of benign metastasizing lesions reported in the older literature are, by today’s criteria, histologically malignant neoplasms, most commonly carcinoma pleomorphic adenomas. It has been suggested that so-called benign metastasizing pleomorphic adenomas may in fact represent an as yet unclassified malignancy [8].

In conclusion, we have described an extremely rare case of metastasis of a histologically benign mixed tumor to the diploic space 16 years after resection of a parotid BPA with no clinical or MR evidence of local recurrence. BPA may metastasize many years after surgery and should be considered in the differential diagnosis of a lytic bone lesion given the history of a prior salivary gland tumor.

ACKNOWLEDGMENT

We thank Cherie McCann for typing this manuscript.

REFERENCES