

Adenoid Cystic Carcinoma *ex* Pleomorphic Adenoma of the Parotid Gland

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Abstract There is a considerable variation in the histologic subtype of epithelial malignancies among carcinoma *ex* pleomorphic adenomas (CXPA) and virtually any known carcinoma entity can develop. To our knowledge, adenoid cystic carcinoma (AdCC) *ex* PA is quite rare despite the fact that *de novo* AdCC is the fourth most common salivary gland malignancy. We describe a new case of AdCC *ex* PA in the parotid gland of a 62 year-old woman. In our patient, there was a short interval of time between parotidectomy and local recurrence and rapid development of distant metastases. Although most of the reported cases are considered low-grade, evidence is presented here that AdCC can take the form of a high-grade malignancy in PA.

Keywords Adenoid cystic carcinoma ·
Carcinoma *ex* pleomorphic adenoma ·
High-grade malignancy · Parotid gland

Introduction

Carcinoma *ex* pleomorphic adenoma (CXPA), as a group, constitutes 12% of malignant salivary gland tumors [1], and in data from the Armed Forces Institute of Pathology, this ranks it as the sixth most common carcinoma at this location [2]. Of all PA, CXPA accounts for 9.5% [2], and has been noted *ab initio* or at recurrence [1–3]. Although there is no prototypical carcinoma entity, the forms of

malignancy found are most common adenocarcinoma not otherwise specified, salivary duct carcinoma and undifferentiated carcinoma [1–7]. The malignant component is often difficult to subclassify as one of exactly defined carcinoma categories [6], and more than one phenotype may be present [5, 8].

In previous large series [5–12], the cribriform growth pattern considered supportive of a diagnosis of adenoid cystic carcinoma (AdCC) was observed in 4–33% of CXPA, many of which comprised only a limited portion of poorly differentiated adenocarcinoma [5, 11]. Of six reports, four lacked illustrations of the AdCC component [5–7, 12], and only two involved histopathologic findings of AdCC *ex* PA with no information of the individual case [8, 11]. In the study of Moberger and Eneroth [10], a single convincing example was detailed and the same case was also briefly described in the paper of Eneroth et al. [9]. Our literature search disclosed six additional cases of pure AdCC *ex* PA described by name [13–17]. The following is a rare emergence of AdCC from a primary PA in the parotid gland which pursued an unpredictable aggressiveness on behavioral basis.

Case Report

A 62 year-old woman presented with an 8 month history of a painless mass of the right parotid gland. With magnetic resonance imaging and computed tomography (Fig. 1), a well-circumscribed, 4 cm tumor with evidence of calcification was found in the deep lobe and diagnosed at Stage II (T₃N₀M₀). She had no clinically detectable tumor in any other site and her past medical history was non-contributory. Following the histologic diagnosis of CXPA in the initial parotidectomy specimen, the definitive surgery with

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Fig. 1 Computed tomography scan shows a heterogeneously enhanced and well-circumscribed tumor of the right parotid gland

dissection of parapharyngeal area and upper neck was completed one month later. Microscopically, there was neither residual carcinoma nor positive cervical lymph node. Nineteen months postoperatively, local recurrence was noted in the posterior pharyngeal wall and small metastatic foci in the lung and liver were diagnosed on the basis of computed tomography and magnetic resonance imaging. At the patient's wish, both lesions were not biopsied and only chemotherapy was carried out at another institution. Although specific details of protocols were not available, she still has evidence of disease two years later.

Macroscopically, the bilobed mass measuring $4 \times 4 \times 3 \text{ cm}^3$ appeared deceptively well-demarcated and on cut surface, contained a large solid nodule with hemorrhage and smaller foci with sclerosis. On microscopic examination, the tumor was found to be not excised with clear margins (Fig. 2a). It was composed of two strikingly contrasting types of tumor; lobulated aggregates of AdCC and densely hyalinized nodules of PA, with the former constituting $>80\%$ of lesion (Fig. 2a, b). The remnants of PA were recognizable by the bilayered ductal structures in the desmoplastic, calcified or ossified stroma (Fig. 2c, d). Solid and cribriform growth patterns occurred together in the AdCC component; tumor cell necrosis including comedo-type was readily apparent in the former and excessive basal lamina was characteristically evident in the latter (Fig. 2e, f). The nuclei of basaloid carcinoma cells were

angular and showed moderate mitotic rate and mild to moderate atypia (Fig. 2g). In the AdCC areas, neural invasion was common, but there was no vascular involvement. Because the solid pattern represented more than 40% of carcinoma, the AdCC element was categorized into Grade III [18, 19]. Even in multiple sampling, the transition between PA and AdCC was difficult to trace because of hypocellularity and hyalinization of the PA component. The coexistence of another high-grade carcinoma or carcinosarcoma was not evident.

Discussion

Among seven cases of AdCC *ex* PA with sufficient data [10, 13–17], five tumors arose in association with a primary PA including a long-standing (>50 years) lesion [13–16], whereas the remaining two developed as a recurrent tumor at the site of a previously excised PA [10, 17]. It is acknowledged that PA and AdCC are composed of variable proportions of ductal and myoepithelial type cells [19–22]. Considering the immunohistochemical result that 19% of supervening carcinoma in CXPA shows the bidirectional line of differentiation into ductal and myoepithelial cells [21, 23], the sequential evolution of PA to AdCC may not be surprising. Circumstantial evidence also comes from cases of PA showing AdCC-like phenotypic manifestations [22, 24]. Conversely, the diagnostic consideration of *in situ* or intracapsular AdCC within PA should be given in such tumors [7, 9, 11, 13, 24]. The cribriform nests in PA are usually limited to small areas and their nuclear features are not hyperchromatic, angular as in the case of AdCC [20, 22].

Conceptually, salivary tumors that occupy a single gland and consisted of two distinct types may be categorized as either synchronous or hybrid [19]. There were only a few reports on simultaneous occurrence of PA and adenocarcinoma; the latter included acinic cell adenocarcinoma, mucoepidermoid carcinoma and salivary duct carcinoma only [25]. An unusual combination of myoepithelioma of spindle cell variant and AdCC of cribriform type was also described [26]. Importantly, synchronous tumors never demonstrate a confluence between two separable entities as seen in CXPA [25]. It is our understanding that hybrid lesions show transitional areas between two histologically different tumors in a single mass, suggesting their clonal origin [27]. This rare condition can be seen as a combination of hybrid adenomas, hybrid carcinomas or carcinoma with adenoma [19] and the most commonly reported partner of AdCC was salivary duct carcinoma and epithelial-myoepithelial carcinoma [27]. In contrast to CXPA, hybrid tumors are usually characterized by the mixture of two well-defined carcinomas [27], and hybrids exhibiting both benign and malignant components are

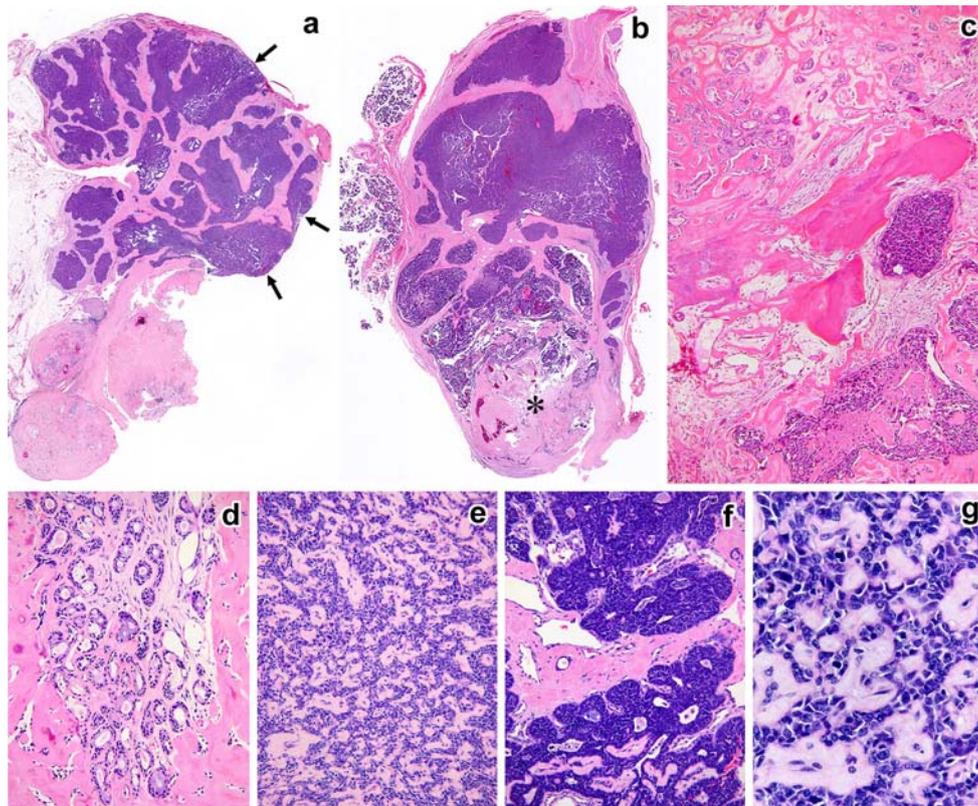


Fig. 2 (a) Scar-like discrete foci of pleomorphic adenoma (PA) and multilobulated nodule of adenoid cystic carcinoma (AdCC) are juxtaposed to each other without a transitional zone. Arrows indicate positive surgical margins, (b) PA (asterisk) and AdCC are blending each other in another section, (c) woven bone trabeculae are present between residual PA (upper) and solid nests of AdCC with

comedonecrosis (lower), (d) nidus of unmistakable PA surrounded by sclerotic stroma, (e) intercellular basal lamina material is conspicuous within cribriform areas, (f) small pseudocystic and ductal spaces are filled with necrotic debris, (g) nuclei of carcinoma cells are hyperchromatic, angular and irregular shaped (Hematoxylin-Eosin, a and b, $\times 3$; c, $\times 40$; d, e, and f, $\times 200$; g, $\times 400$)

exceptional, with a sole combination of basal cell adenoma and AdCC [19].

One of the important pathologic factors associated with patient prognosis in AdCC includes tumor grade [18–20, 28]. Unfortunately, the universally accepted grading system for *de novo* AdCC, i.e., the proportion of the tumor with a solid pattern, has not yet been used in any case of AdCC *ex* PA. Judging from the photomicrographs and/or descriptions, most of the previously reported cases of AdCC *ex* PA were low-grade [6, 8, 11, 13–15, 17]. The present AdCC component was regarded as Grade III and the solid growth pattern was predominant in two remaining cases that developed metastasis [9, 16]. In *de novo* AdCC, distant metastasis frequently occurs without regional lymph node involvement, even after local control of tumor [20, 28]. Given that two of three cases with metastatic spread had negative cervical nodes [15, 16], AdCC *ex* PA is certainly no exception; notably, two patients represented skin metastasis that is very rare in *de novo* AdCC [9, 15]. In the present high-grade case, clinical signs of local recurrences and distant metastases were evinced within 19 months on follow-up imaging;

nevertheless, our patient is alive with disease two years postoperatively. This is in keeping with the fact that some of patients with *de novo* AdCC pursue prolonged survivals despite distant metastasis [28].

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