Pleomorphic adenoma of the breast initially misdiagnosed as metaplastic carcinoma in preoperative stereotactic biopsy: A case report and review of the literature

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Summary

Pleomorphic adenoma (PA) is a benign mixed tumor found commonly in the salivary glands but rarely in the breast. PA might be misinterpreted clinically and pathologically as a malignant tumor. The differential diagnoses include fibroadenoma, phyllodes tumor and metaplastic carcinoma. Metaplastic carcinoma is the most important entitiy with respect to differential diagnoses, as surgical overtreatment, i.e., mastectomy may be the result. We describe one of the first cases of PA initially misdiagnosed as metaplastic carcinoma (osteoid-chondroid type) in a preoperative stereotactic biopsy and review the literature regarding this entity.

Key words: Pleomorphic adenoma; Breast; Metaplastic carcinoma; Stereotactic biopsy.

Introduction

Pleomorphic adenoma (PA) is a benign tumor frequently encountered in the salivary gland. Some authors describe this type of tumor as a special variant of adenomyoepithelioma [1]. Histopathology is characterized by a mixture of epithelial and myoepthelial cells and can display areas of chondroid or myxoid differentiation [2]. In the mammary gland, however the histopathological diagnosis of PA is extremely rare and thus, only 70 cases of this benign condition have been reported to the best of our knowledge [3]. Due to the mixed histology of PA and its infrequent occurrence in the mammary gland, this entity is often misdiagnosed as reviewed by Lyengar *et al*. [4]. In particular, the misdiagnosis of invasive carcinoma is common if only limited sampling is available for histopathological review [4]. Differential diagnoses include malignant and benign conditions, such as metaplastic carcinoma, mucinous carcinoma, and phyllodes tumor as well as fibroadenoma.

PA can be detected by mammography and is reported as a well circumscribed, round or ovoid mass, sometimes with irregular shape and calcification [5]. Breast ultrasound may reveal an irregulary shaped tumor with heterogenous echoes and partially ill-defined margins which may suggest an invasive carcinoma [6, 7].

In the majority of the cases reported in the literature PA was excised with a cuff of normal tissue and thus, surgical excision with free margins is the treatment of choice [8]. Of note, recurrency [9, 10] or malignant transformation [11] ex PA of the breast has been described in three cases, which underlines the importance of follow-up after surgery. Due to the fact that PA was occasionally misdiagnosed as invasive carcinoma some patients were submitted to unnecessarily aggressive surgical treatment, i.e., mastectomy [12, 13]. In the current study, we report a case of PA of the breast misdiagnosed as metaplastic carcinoma in a preoperative stereotactic biopsy and discuss the histopathologic findings of wide local excision.

Case Report

A 58-year-old Caucasian woman was referred to us with an externally performed stereotactic biopsy which had led to a histopathologic diagnosis of metaplastic carcinoma of the breast (osteoid-chondroid type). The patient was healthy with no underlying diseases with no risk factors for and no family history of breast cancer. Routine mammographic features showed a well circumscribed lobulated tumor measuring 1.8 cm in the upper outer quadrant 5.5 cm behind the areola. The mass had internal pleomorphic microcalcifications. Retrospective review of a two-year-old prior mammogramm showed the nodule measuring 6 mm only. Thus, radiographic findings were considered suspicious (BIRADS 0) (Figure 1). Stereotactic biopsies consisted of five samples measuring 12 mm each.

Upon physical examination the tumor was not palpable. Axillary lymph nodes were not enlarged. Ultrasonography showed no reliable correlation to the mammographic findings. Stereotactic biopsy led to the diagnosis of a metaplastic carcinoma. The tumor markers CEA and CA15-3 were within normal range, however.

The patient underwent a wide excision and sentinel lymph node biopsy. Intraoperatively, frozen section of the resected tissue revealed morphologic features consistent with either PA, phyllodes tumor or fibroadenoma. The excision was complete with adequate margins of more than a 3 mm cuff of normal tissue. Final histopathologic diagnosis was conclusive for PA. Workup of the sentinel lymph node showed no evidence of carcinoma. Further treatment was not recommended. A one-year follow-up period was clinically uneventful.

Histologic findings

The externally performed preoperative stereotactic biopsy revealed a chondroid and osteoid matrix embedded in epithelial

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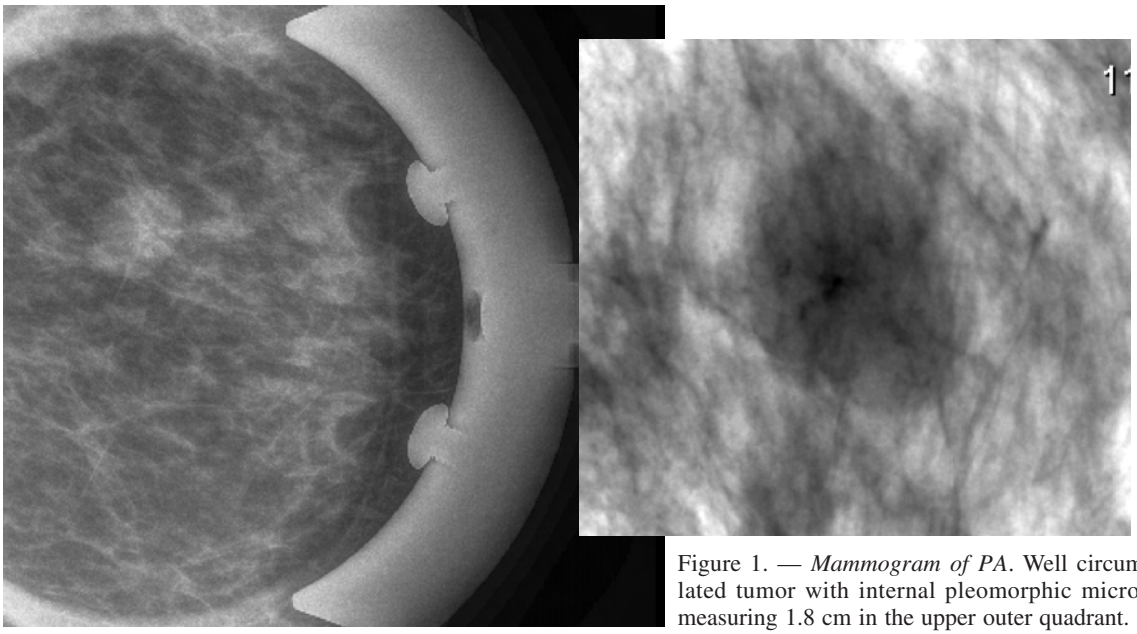

Figure 1. — *Mammogram of PA*. Well circumscribed lobulated tumor with internal pleomorphic microcalcifications measuring 1.8 cm in the upper outer quadrant.

cells and a nuclear polymorphism, which initially led to the diagnosis of metaplastic carcinoma.

Preliminary analysis of the frozen section suggested the differential diagnoses of PA versus phyllodes tumor or fibroadenoma.

The wide excision specimen contained a 1.3 cm well circumscribed bright mass with a lobulated and myxoid cut surface. Microscopic examination revealed a fibrous pseudo-capsule surrounding the tumor. Furthermore, a small satellite nodule was noticed. Epithelial hyperplasia and numerous enlarged mammary ducts were present. The neoplasm had biphasic morphology consisting of trabecular and glandular structures with an inner luminal layer of epithelial cells surrounded by an outer layer of myoepithelial cells. The myxoid stroma contained epithelial cell clusters, spindle and stellate cells. Within the mesenchymal differentiated areas there was an extensive chondroid metaplasia and also small areas of osseous metaplasia with focal calcifications (Figure 2a, 2b).

Immunohistochemical studies confirmed the biphasic cellular composition. Myoepithelial cells showed reactivity for CK5/ 6, 34ßE12, S100, GFAP, actin and CD10 (Figure 3a, 3b). Only few myoepithelial cells were immunoreactive for p63. CK7 stained strongly positive in the luminal epithelial cell layers. Epithelial and myoepithelial cells expressed focal and weak estrogen and progesterone receptors.

The sentinel lymph node contained no metastases.

Discussion

PA usually is located in the salivary gland but also occurs in the skin, larynx and lacrimal gland. The breast as a modified sweat gland shares its common embryological ectodermal origin with salivary glands and skin. PA of the breast is extremly rare and to date only 70 cases have been reported [3]. The tumor is more often described in females than in males [14]. Patient age ranges from 23 to 78 years.

Histopathologic reports describe a mixture of epithelial and myoepithelial cells embedded in the extracellular matrix. The extracellular matrix might be myxoid, chondroid and/or osteoid [2]. A fibrous pseudo-capsule surrounds the mass and infiltration by nests of neoplastic cells through the capsule can exist [15].

The histogenesis of PA of the breast is uncertain. Some authors postulate a myoepithelial derivation. The frequent occurrence in the periareolar region [16, 17] could be explained with the high densitiy of myoepithelial cells along the large subareolar mammary ducts. Pia-Foschini *et al*. showed that PAs of the salivary gland frequently occur with chromosomal translocations in the long arms of chromosomes 8 (8q12) and 12 (12q15) and the short arm of chromosome 6 (6p21) [9]. Recurrent chromosomal alterations of PA of the breast have not yet been demonstrated [18].

PA of the breast might be a palpable indolent mass. The ultrasound findings can vary. They can show a solid mass with partially ill-defined borders or sharp margins, and sometimes with a homogeneously hypoechoic internal signal. The mammographic findings have demonstrated a well-circumscribed round or ovoid mass, sometimes with irregular shape and microcalcifications. Lyengar *et al*. reported a solid mass of 2.4 cm suspicious for a mucinous carcinoma and an enlargement over time as revealed by retrospective analysis of prior mammograms. In our case, this growth in dimension was considered suspicious (BI-RADS 0) and a stereotactic biopsy was performed.

The presence of calcifications in mammogramms has not been described in many reports. Authors who identified calcifications described numerous coarse calcifications, diffuse irregular central calcifications or the appearance was described as densely and partly calcified. In the present case, pleomorphic central microcalcifications were identified.

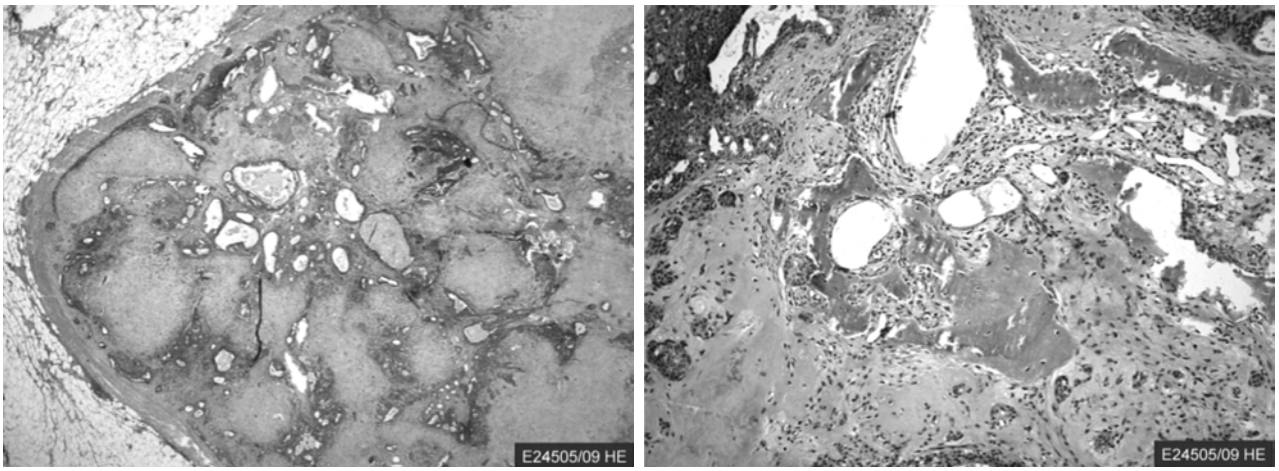

Figure 2a, 2b. — *Histopathological features*. Extensive chondroid metaplasia and small areas of osseous metaplasia with focal calcifications in the mesenchymal differentiated areas.

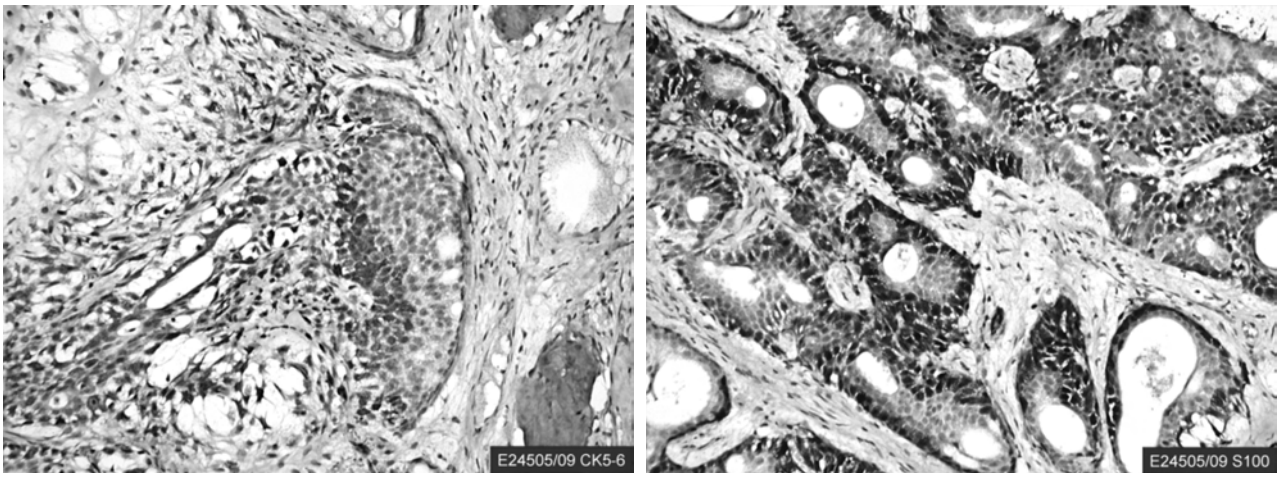

Figure 3a, 3b. — *Immunhistochemical features*. Myoepithelial cells showed reactivity for CK5/6, S100.

Because of the extreme rarity and confusing imaging findings suggestive of carcinoma a correct preoperative diagnosis might be difficult. Many authors have reported misdiagnoses. Fine-needle aspiration material might yield a too limited amount of tissue for histopathologic exam and this might lead to the diagnosis of malignancy. Of the cases reported 30-50% were initially misdiagnosed as carcinoma [4, 19, 20]. Likewise in the present case the stereotactic biopsy was interpreted as a metaplastic carcinoma.

Metaplastic carcinoma is one of the most important differential diagnoses of PA. This special subtype of mammary carcinoma shows variable morphology. One percent of all invasive breast carcinomas are metaplastic carcinomas [21]. Histopathology shows an abundant extracellular matrix with clusters of chondroid and/or osteoid islands. The epithelium displays foci of poorly differentiated ductal carcinoma. The presence of nuclear atypia with an abundance of mitosis and necrosis can be helpful in differentiating between carcinoma and PA [11]. Carcinoma has an infiltrative nature and no pseudocapsule [21].

The surgical procedure in most cases has been wide local excision and sentinel lymph node biopsy. Multifocality has been described but the extent of involvement (segmental vs entire breast) is unclear [16]. Three cases of carcinoma ex-PA of the breast have been reported recently. The regional lymph nodes had shown no metastasis. The long-term follow-up of these cases is yet unknown.

Pathologists and clinicians should be aware of this extremly rare tumor to avoid unnecessary aggressive surgical treatment [12, 13]. Complete excision with an adequate cuff is the therapeutic treatment of choice [22]. Despite the excellent prognosis patients should be informed about the moderate risk of recurrance. A follow-up period of five years with yearly examinations should be recommended.

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