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LETTER TO THE EDITOR

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Malignant adenomyoepithelioma of the breast metastasizing to the liver

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Sir,

Tumors with myoepithelial cell component have been recognized for some time within the salivary gland and, although rare, have also been described in the breast [2, 3, 5]. Examples include adenoid cystic carcinoma, adenomyoepithelioma, low-grade adenosquamous (syringomatous) carcinoma, pure malignant myoepithelioma (myoepithelial carcinoma) and poorly differentiated myoepithelial-rich breast carcinoma.

The morphology of tumors showing myoepithelial differentiation is generally different to that of tumors derived from luminal cells. Pure myoepithelial carcinomas tend to resemble sarcomas by having a predominantly spindle cell pattern of growth. Although there are only a few reports in the literature, it seems that no fewer than 50% of the published cases had an aggressive behavior [2]. Metastases have been described in five reports, with sites including ribs, lumbar spine, bones, lung and brain, lung, regional lymph nodes and jaw.

We have previously reported molecular cytogenetic data on pure myoepithelial carcinomas using comparative genomic hybridization (CGH) analysis [4]. While myoepithelial carcinomas showed overlap in the regions of DNA copy number change relative to ductal carcinomas of no special type (IDC-NST), they exhibited far fewer genetic alterations. The most common changes were losses at 11q, 16p, 16q, 17p and 17q, aberrations frequently seen in invasive ductal carcinomas. Given the rarity of myoepithelial cell transformation, and their aggressive behavior, these regions may harbor critical genes in breast tumorigenesis.

Unlike pure myoepithelial carcinomas, adenomyoepitheliomas of the breast contain a proliferation of both the luminal glandular component as well as myoepithelial cells. Reports in the literature are primarily as single case reports or small series [1]. Although generally considered to be benign, malignant and metastatic adenomyoepitheliomas have been reported. The epithelial component may form solid nests or groups, ducts, cystic trabecular, pseudo-papillary or papillary structures. The myoepithelial component is arranged around the epithelial component and can form solid strands, trabeculae or even larger sheets, and are usually polygonal or spindle shaped.

We report a case of adenomyoepithelioma in the breast with a pure spindle cell tumor metastases to the liver. CGH analysis was used to investigate the clonal relationship between the glandular and myoepithelial components of the primary lesion and the spindle cell metastasis.

Case report

A 71-year-old woman presented with a 2-month history of a right breast mass which may have been present longer, as she had not undertaken breast self-examination for 3 years. A 2×3-cm mass in the lower outer quadrant of the right breast was reported as suspicious of carcinoma by mammography and fine-needle aspiration (FNA) cytology. Right segmental mastectomy with axillary node clearance was performed. The patient was treated with tamoxifen which was continued for 2 years until her death. At postmortem, multiple tumor deposits were found in the right lobe of the liver. No other evidence of metastatic disease was present. Detailed examination of the breast did not reveal any residual or recurrent tumor.

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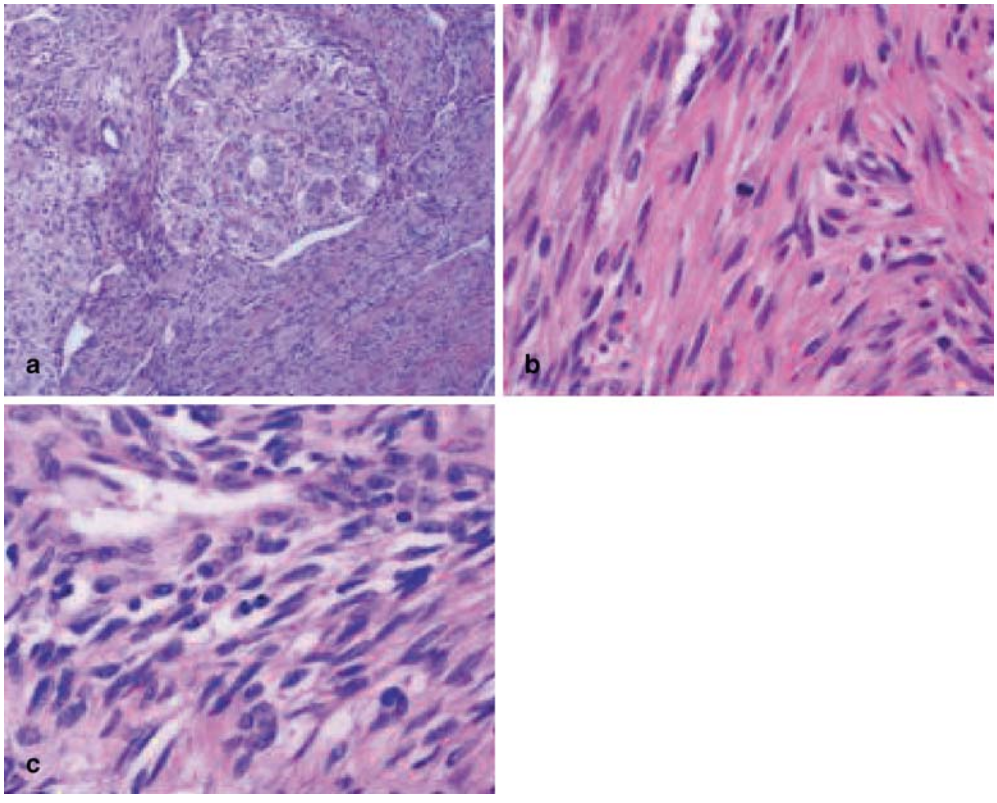

Fig. 1 Malignant adenomyoepithelioma of the breast. **a** Adjacent glandular and spindle cell components, hematoxylin and eosin (H&E) ×100. **b** Spindle cell component, high power showing mitoses, H&E ×400. **c** Spindle cell metastasis in the liver, high power, showing mitoses, H&E ×400

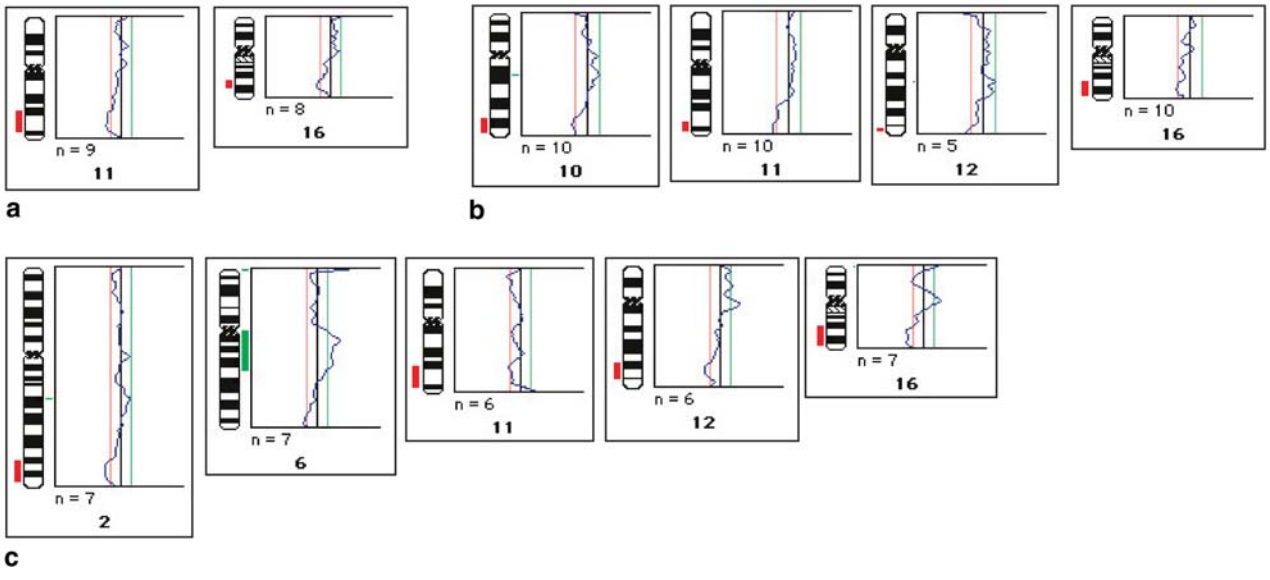

Fig. 2 **a** Comparative genomic hybridization (CGH) data from adenomyoepithelioma, glandular component, showing losses at 11q23–q24 and 16q22–q23. **b** CGH data from myoepithelial carcinoma, spindle component, showing losses at 10q25, 11q23–q24, 12q24 and 16q22–q23. **c** CGH data from liver metastasis showing loss at 2q35–q37, gain at 6q12–q16, loss at 11q23–q24, loss at 12q24 and loss at 16q22–q24

The breast tumor was a circumscribed mass measuring 3×3×2 cm within 0.5 cm of the inferior line of resection. Microscopically, the tumor showed a mixed glandular and spindle cell morphology. (Fig. 1a). The spindle cell component was extensive in some areas and had increased mitotic activity (up to 4 per 10 high power fields, Fig. 1b) and focal areas of necrosis. Although a diagnosis of an adenomyoepithelioma was made, it was noted that the mitotic activity and necrosis was suggestive of a more aggressive phenotype. No vascular invasion was seen, and staging investigations were negative. At autopsy, multiple tumor deposits were seen in the right lobe of the liver. Microscopically, these were pure spindle cell tumors with a fascicular and focally haemangiopericytomatous pattern, and no evidence of a glandular/epithelial component (Fig. 1c).

Table 1 Immunohistochemical findings

Antibody	Primary tumor			Metastasis
	Glandular areas		Spindle cells	
	Inner cells	Outer cells		
MNF116	Positive	Negative	Negative	Negative
AE1/AE3	Positive	Negative	Negative	Negative
Vimentin	Positive	Positive	Positive	Positive
SMA	Negative	Positive	Negative	Negative
S100	Negative	Positive	Negative	Negative
SMMHC	Negative	Positive	Negative	Negative
GFAP	Negative	Negative	Negative	Negative
Desmin	Negative	Negative	Negative	Negative
CD34	Negative	Negative	Negative	Negative
Calponin	Negative	Positive	Negative	Negative
CK14	Positive	Positive	Negative	Negative

The results of immunohistochemical staining of the primary tumor and metastasis against a range of myoepithelial markers are given in Table 1. The inner cells of the glandular component of the primary tumor showed immunopositivity against MNF116, AE1/AE3 and vimentin. This was in contrast to the outer epithelial cells which showed positivity for vimentin, SMA, S100, SMMHC, calponin and CK14, consistent with myoepithelial cells. The solid spindle cell component in the primary tumor was negative for all markers apart from vimentin. The same pattern was seen in the metastatic spindle cell tumors in the liver.

Microdissection, DNA extraction and CGH analysis were carried out as described previously [4]. The data for the CGH analysis of primary tumor and metastasis is shown in Fig. 2. Both the breast and liver tumors showed an overall pattern of genetic alterations by CGH resembling myoepithelial tumors, with few regions of copy number change compared with invasive ductal carcinomas [4]. The glandular component of the primary tumor showed losses at 11q23–q24 and 16q22–q23 (Fig. 2a), while the spindle cell component of the primary tumor showed these losses as well as loss at 10q25 and 12q24 (Fig. 2b). The liver metastasis showed losses at 2q35–q37, 11q23–q24, 12q24 and 16q22–q24, and a gain at 6q12–q16 (Fig. 2c).

Discussion

Our interpretation of these results is that the losses at chromosomes 11q and 16q indicate a common origin for the two components of the primary adenomyoepithelioma. The undifferentiated spindle cell component then acquired an additional loss at 12q prior to metastasis to the liver, any further genetic alterations occurring subsequent to this event.

As well as adding to the literature on distant metastases of malignant adenomyoepithelioma, this data has implications for the origin of the two components of these biphasic tumors, suggesting a common origin prior to differentiation and metastasis. The spindle cell component, which morphologically resembles a pure myoepithelial cell tumor, also has a molecular cytogenetic profile that is similar to pure myoepithelial carcinomas. Given the clinically aggressive nature of these lesions, it is perhaps not surprising that it is the spindle cell component of the primary tumor that has metastasized to the liver in this patient. In an analogous manner to pure myoepithelial carcinomas, the few genetic alterations exhibited by this tumor may make it an excellent model to study the critical pathogenic events in breast tumorigenesis and metastasis.

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