

## Cylindroma (Dermal Analog Tumor) of the Breast

### A Comparison With Cylindroma of the Skin and Adenoid Cystic Carcinoma of the Breast

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#### Abstract

*We compared 4 breast cylindromas with 50 dermal cylindromas and 8 adenoid cystic breast carcinomas. Except for a modest increase in the number of eccrine ducts and reactive Langerhans cells in dermal cylindromas, breast and dermal cylindromas showed identical histologic and immunohistochemical features. Both were characterized by epithelial islands containing central basaloid cells and peripheral myoepithelial cells surrounded by a thickened, continuous, periodic acid–Schiff–positive basement membrane that was immunoreactive for collagen IV. Clusters of sebaceous cells and a few eccrine ducts are described in breast cylindromas. Cytokeratin 7 labeled predominantly the central basaloid cells, and smooth muscle actin stained peripheral myoepithelial cells in breast and dermal cylindromas. Eccrine ducts were highlighted by epithelial membrane antigen and carcinoembryonic antigen. S-100 protein and CD1a showed a variable number of dendritic Langerhans cells. Cylindromas of the breast and skin did not express cytokeratin 20, gross cystic disease fluid protein 15, or estrogen or progesterone receptor. Breast cylindroma might be confused with the solid variant of adenoid cystic carcinoma, especially in needle core biopsy specimens, because they share nodular and trabecular patterns, basaloid cells, myoepithelial cells, eccrine ducts, and hyaline globules of basement membrane material. However, adenoid cystic carcinoma displays an infiltrative growth pattern, cytologic atypia, and mitotic figures and lacks the continuous, thickened basement membrane.*

In 2001, one of us (J.A.-S.) coauthored an article in which the first cylindroma of the breast was described.<sup>1</sup> The tumor, which was an incidental finding in a lumpectomy specimen for infiltrating pleomorphic lobular carcinoma, was morphologically similar to dermal cylindroma. Four cases of breast cylindroma subsequently reported essentially confirmed the original observations.<sup>2</sup>

The aim of the present study was to analyze morphologically and by immunohistochemical analysis 4 cases of breast cylindroma (including 3 cases not previously reported) and to compare them with 50 dermal cylindromas and 8 adenoid cystic carcinomas of the breast. Their similarities and differences are emphasized.

#### Materials and Methods

The consultation files of Louisiana State University Health Sciences Center and the surgical pathology files of Delta Pathology, both in Shreveport, LA, were searched for the diagnosis of breast and dermal cylindroma and adenoid cystic carcinoma of the breast. In addition, files of the Dermatopathology Laboratory, New York University, New York, NY, were searched for the diagnosis of dermal cylindroma. Four cases of breast cylindroma, 50 cases of dermal cylindroma, and 8 cases of adenoid cystic carcinoma of the breast were found.

Clinical information was obtained from the clinical charts, pathology reports, and communication with the referring pathologist. Representative H&E-stained sections were available in all cases for review. Immunohistochemical stains were performed on formalin-fixed, paraffin-embedded sections on 3

breast and 10 dermal cylindromas. Paraffin blocks were not available for any of the adenoid cystic carcinomas. Immunohistochemical staining was performed on a BioTek Solutions Tech Mate 1000 automated immunostainer (BioTek Solutions, Santa Barbara, CA) using the standard avidin-biotin peroxidase complex technique and a heat-induced epitope retrieval buffer. The antibodies, dilutions, and sources are listed in **Table 1**. In addition, sections from 10 dermal cylindromas and 3 breast cylindromas were stained with periodic acid–Schiff (PAS) stain with and without diastase.

## Results

The 4 patients with breast cylindroma were women, 63 to 78 years old (mean, 70 years). Two tumors were palpable, and 2 represented incidental findings in lumpectomy specimens excised for infiltrating breast carcinomas (1 lobular and 1 ductal). Two cylindromas arose in the left and 2 in the right breast. One was located in the retroareolar region.

All 4 patients were treated by local excision, and 2 who also had infiltrating breast carcinoma underwent axillary node dissection. The axillary lymph nodes of these 2 patients showed metastatic breast carcinoma but no cylindroma. The 2 patients with breast carcinoma are living with metastases, but no recurrence of the cylindroma has developed from 1 to 5 years after local excision. None of the 4 patients had coexisting cylindroma in the skin or major salivary glands. Likewise, there was no family history of cylindroma in any of the 4 patients.

The 50 patients, 27 men and 23 women, with dermal cylindroma all had small solitary tumors located in the head and neck, predominantly the scalp. The ages of the patients ranged from 36 to 87 years (mean, 59 years).

The 8 patients with adenoid cystic carcinoma were women 43 to 64 years of age (mean, 51 years). The initial symptom was a palpable mass in all cases. Five tumors arose in the left and 3 in the right breast.

## Gross Features

Gross descriptions were available for 3 breast cylindromas. The remaining tumor was overlooked during gross examination. The size of the tumors ranged from 0.8 to 1.3 cm. They were described as relatively well-circumscribed, firm, and nodular masses. Fatty breast tissue surrounded 3 of the tumors.

## Histologic Features

Except for minimal variations, the microscopic features of the 4 breast cylindromas were similar to those of the 50 dermal cylindromas. Both the breast and dermal cylindromas were nonencapsulated but well-demarcated lesions that showed the characteristic jigsaw pattern of epithelial basaloid nests, trabeculae, and lobules **Image 1**.

A dual population of central basaloid cells and peripheral myoepithelial cells was seen in all tumors. Scant stroma separated the epithelial structures. The nests, trabeculae, and lobules were surrounded by a thickened band of basement membrane material that was PAS-positive and showed immunoreactivity for collagen IV **Image 2**. Likewise, hyaline globules often seen within the epithelial nests, trabeculae, and lobules also were PAS-positive and immunoreactive to collagen IV **Image 3**. There were no mitotic figures or nuclear pleomorphism.

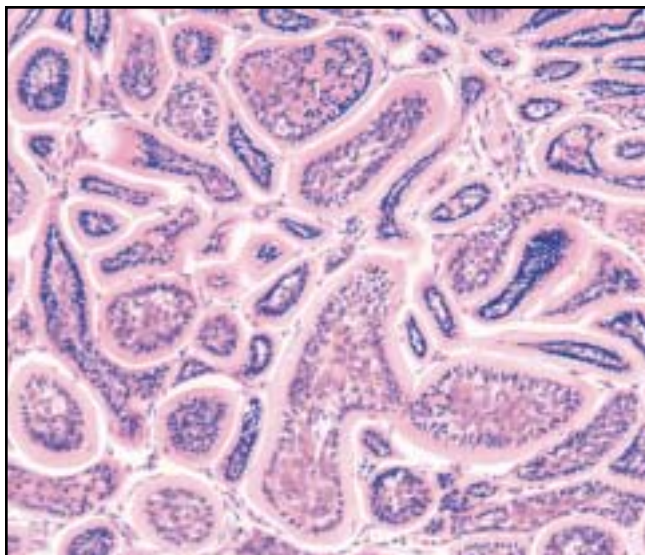
One breast cylindroma was located in proximity to large lactiferous ducts. Involvement of several ductal-lobular units was observed in the retroareolar cylindroma. Whether this feature represented *in situ* change or direct extension could not be determined with certainty.

Eccrine ducts were seen in 41 (82%) of 50 dermal cylindromas and 3 breast cylindromas (**Image 3**) **Image 4**. The eccrine ducts, some of which had inspissated secretions, were more numerous in dermal than in breast cylindromas (**Image 4**).

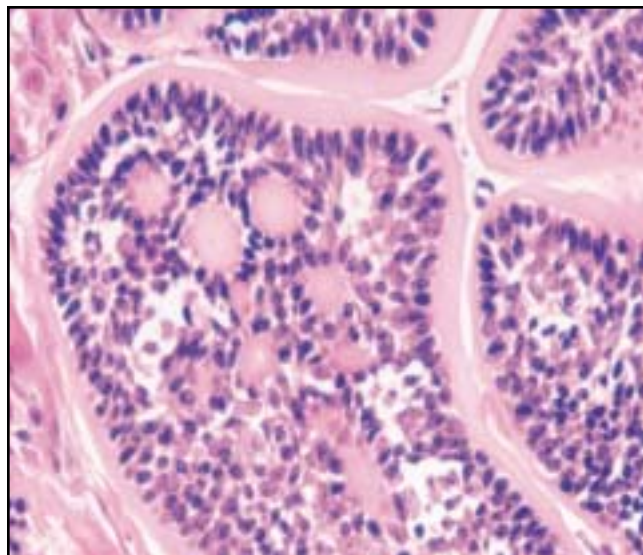
Clusters of cells with clear, finely multivacuolated PAS-negative cytoplasm and central nuclei were identified in 1 (25%) of 4 breast and 19 (38%) of 50 dermal cylindromas. These clear, multivacuolated cells were interpreted as sebaceous cells

**Table 1**  
Panel of Antibodies

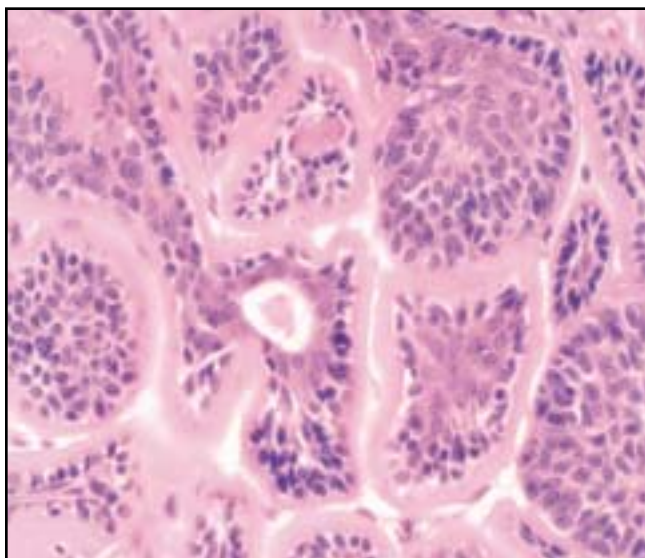
Antibody	Dilution	Source	Clone
Cytokeratin 7	Prediluted	Ventana, Tucson, AZ	K72
Cytokeratin 20	Prediluted	Ventana	KS20.8
Epithelial membrane antigen	Prediluted	Ventana	MCS
Carcinoembryonic antigen, polyclonal	Prediluted	Ventana	TF-3H8-1
Smooth muscle actin	Prediluted	Ventana	14A
S-100 protein	Prediluted	Ventana	—
Estrogen receptor	Prediluted	DAKO, Carpinteria, CA	1DS
Progesterone receptor	Prediluted	DAKO	PGR636
Collagen IV	1:40	DAKO	—
CD1a	Prediluted	Ventana	—
Gross cystic disease fluid protein 15	Prediluted	Cell Marque, Austin, TX	—



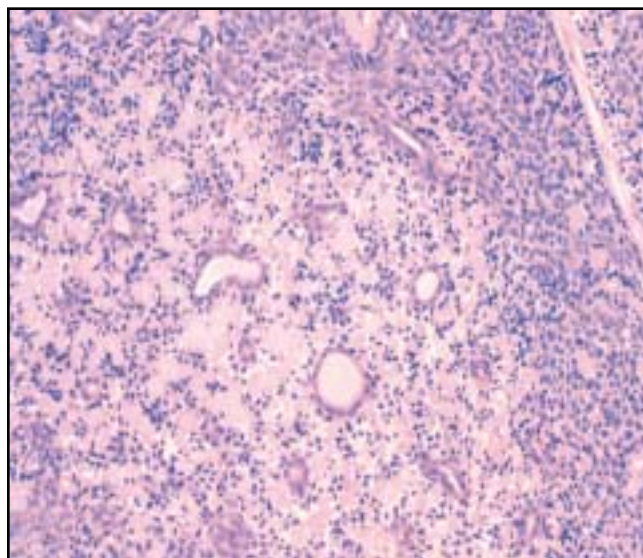
**Image 1** Low-power view of breast cylindroma showing the typical jigsaw pattern of epithelial basaloid nests (H&E, x125).



**Image 2** Breast cylindroma. Higher magnification of basaloid trabecula surrounded by a thickened basement membrane. Hyaline globules of basement membrane are seen within the trabecula (H&E, x250).



**Image 3** A single eccrine duct was present in this breast cylindroma (H&E, x200).



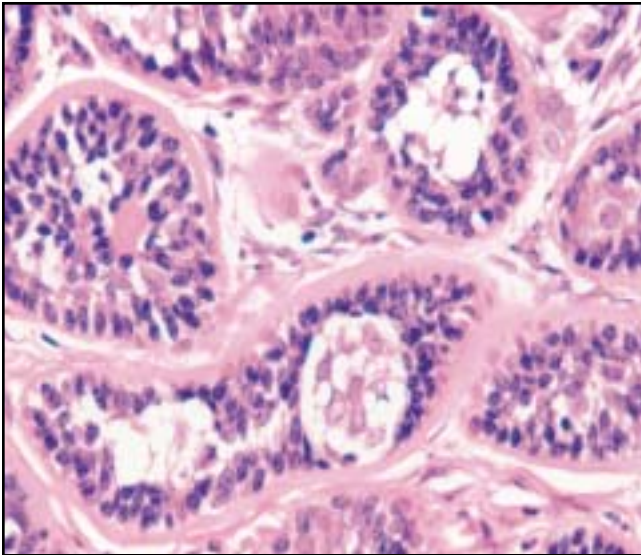
**Image 4** Numerous eccrine ducts were identified in this dermal cylindroma (H&E, x150).

**Image 5** and **Image 6**. Of 50 dermal cylindromas, 16 (32%) contained eccrine ducts and sebaceous cells. Foci of squamous metaplasia closely associated with eccrine ducts were seen in 3 (6%) of 50 dermal cylindromas and were not identified in any breast cylindromas that showed squamoid areas not associated with ducts **Image 7** and **Image 8**.

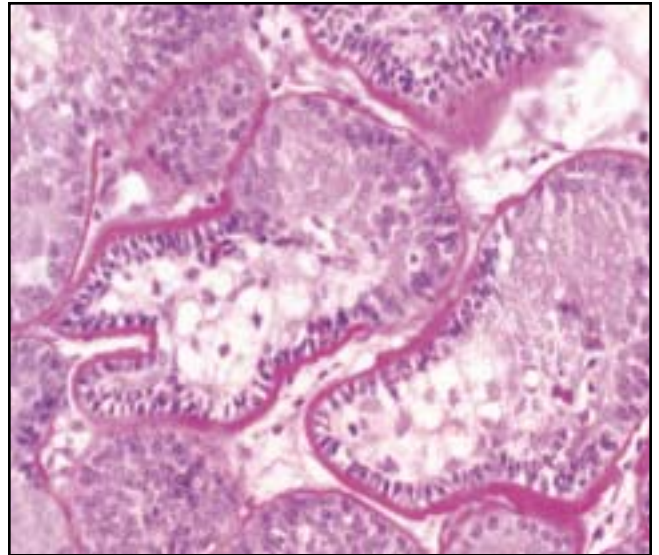
Five adenoid cystic carcinomas of the cribriform type were distinguished easily from breast cylindromas because of the crisp cribriform pattern, presence of mucin, lack of a thickened basement membrane around the epithelial nests, and presence of cytologic atypia and mitotic figures. Moreover, one

adenoid cystic carcinoma arose in a background of microglandular adenosis and another originated from an intraductal papilloma. Foci of microglandular adenosis with atypical features and changes consistent with adenoid cystic carcinoma in situ were present. Likewise, gradual transition from the intraductal papilloma to the adenoid cystic carcinoma was noted.

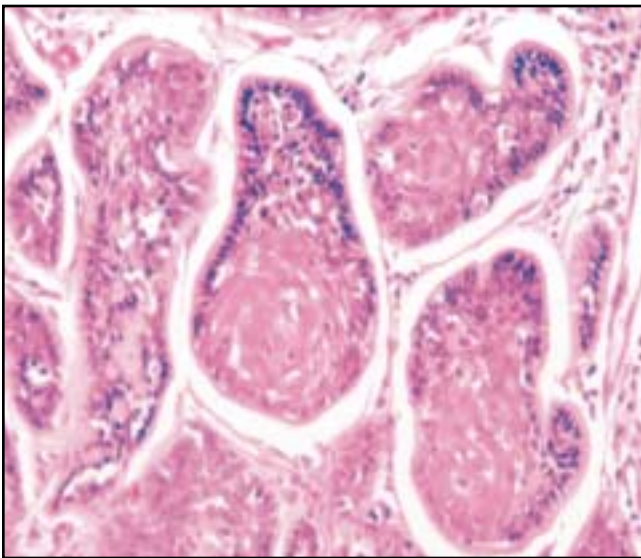
In contrast, 3 adenoid cystic carcinomas of the solid type showed some similarities to the breast cylindromas. They consisted of nests, nodules, or anastomosing broad trabeculae of hyperchromatic basaloid cells lacking cribriform structures or mucin **Image 9**. A few small, poorly defined ductal structures



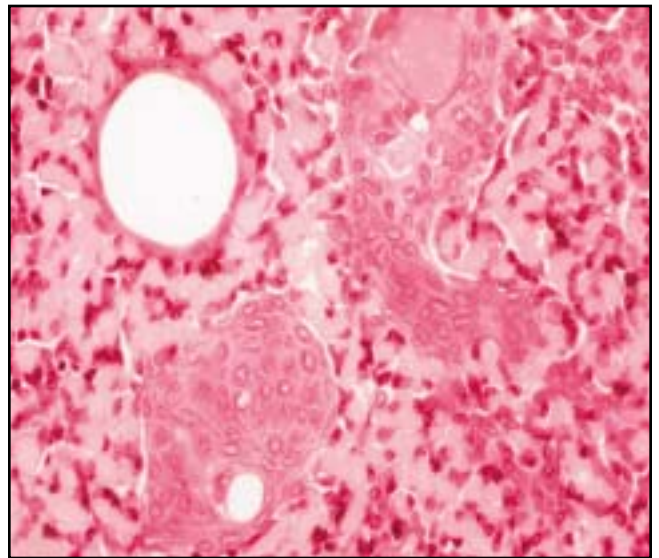
**Image 5** Cluster of multivacuolated clear cells interpreted as sebaceous cells in a breast cylindroma (H&E,  $\times 250$ ).



**Image 6** The thickened peripheral basement membrane is positive, whereas the sebaceous cells are negative (periodic acid-Schiff,  $\times 250$ ).



**Image 7** Squamoid foci in a breast cylindroma (H&E,  $\times 200$ ).

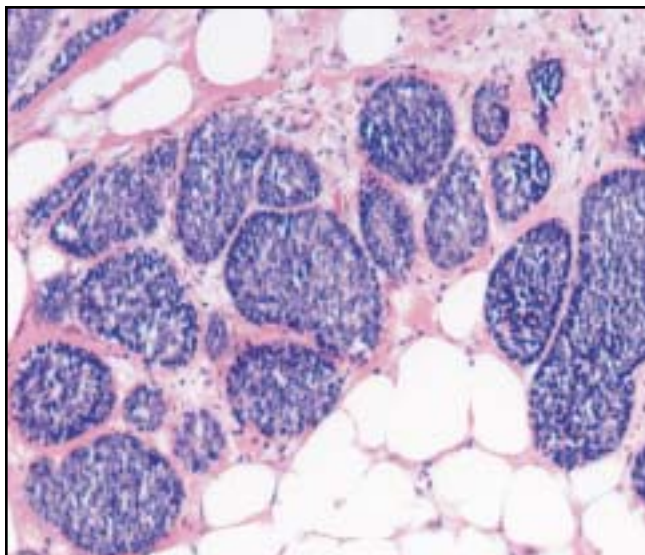


**Image 8** Squamous foci immediately adjacent to eccrine ducts in a dermal cylindroma (H&E,  $\times 200$ ).

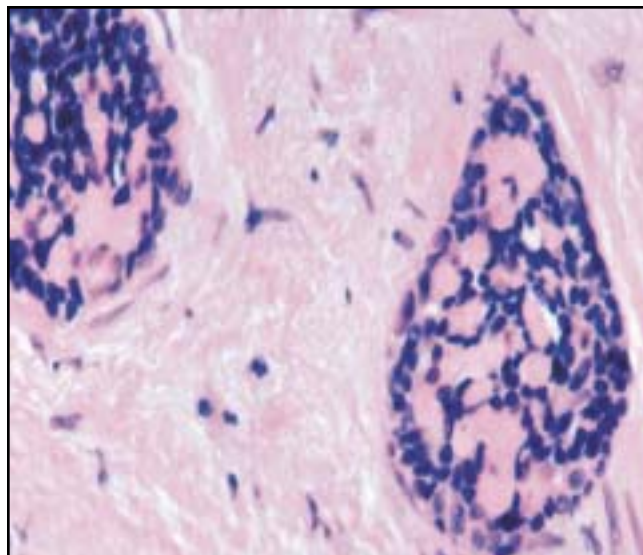
were recognized. Within some of the trabeculae or nodules, hyaline PAS-positive globules similar to those of breast and dermal cylindromas were seen **Image 10**. However, the thickened band of basement membrane material that surrounded the epithelial structures of breast and dermal cylindromas was not recognized in the adenoid cystic carcinomas with conventional H&E-stained sections. The neoplastic cells of the solid adenoid cystic carcinomas showed nuclear atypia and mitotic figures, features not seen in the breast or dermal cylindromas. There were no squamous or sebaceous cells in any of the adenoid cystic carcinomas.

### Immunohistochemical Analysis

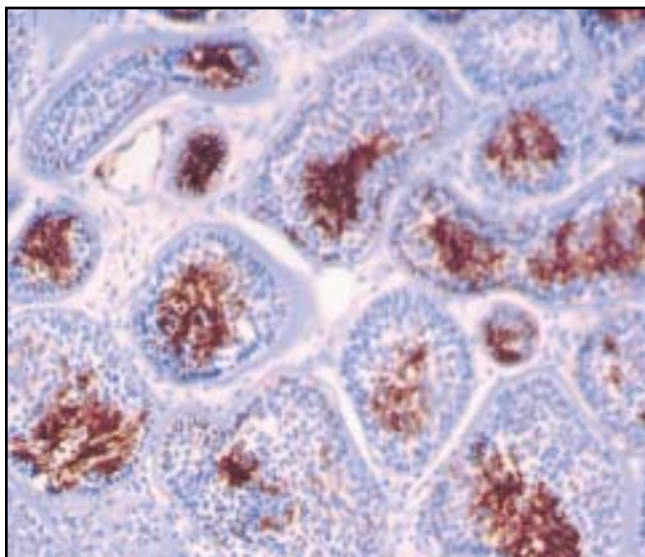
The basaloid epithelial cells of the breast and dermal cylindromas were positive for cytokeratin (CK) 7. These cytokeratin-positive cells more often were located in the central portion of the epithelial structures **Image 11**. However, in some lobules or nests, all epithelial cells, central and peripheral, showed immunoreactivity for cytokeratin 7. CK20 was negative in 3 breast and 10 dermal cylindromas. On the other hand, the peripheral cells of the epithelial structures stained with smooth muscle actin most likely reflecting myoepithelial differentiation **Image 12**. Epithelial membrane antigen (EMA)



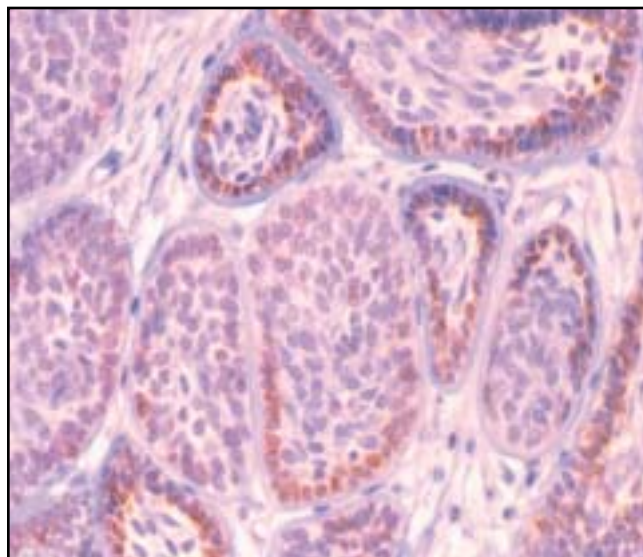
**Image 9** Solid variant of adenoid cystic carcinoma. Multiple nodules of basaloid cells are depicted (H&E,  $\times 150$ ).



**Image 10** Solid variant of adenoid cystic carcinoma. Two basaloid islands contain globules of basement membrane similar to those shown in Image 2 (H&E,  $\times 250$ ).



**Image 11** Cylindroma of skin showing cytokeratin (CK) 7 positivity. The CK7+ cells tend to be centrally located (immunostain for CK7,  $\times 125$ ).



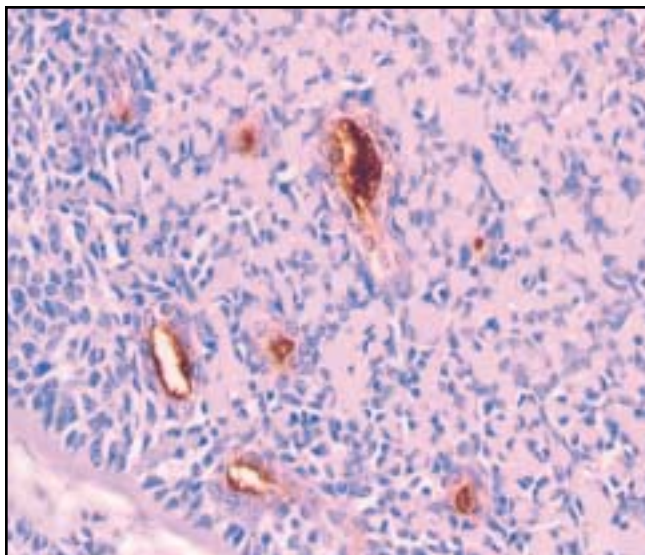
**Image 12** Peripheral myoepithelial cells are positive (immunostain for smooth muscle actin,  $\times 200$ ).

and carcinoembryonic antigen (CEA) stained exclusively the eccrine ducts and their secretions. The luminal border of the ductal cells was highlighted by EMA and CEA stains **Image 13** and **Image 14**. The cell borders of the multivacuolated sebaceous cells stained with EMA and CK7. These cells were negative for smooth muscle actin and S-100 protein, excluding the possibility of them being myoepithelial cells. A population of reactive dendritic Langerhans cells was demonstrated in 10 dermal and 3 breast cylindromas with S-100 protein and CD1a stains. These Langerhans cells were admixed with basaloid cells and were more abundant in dermal than in breast

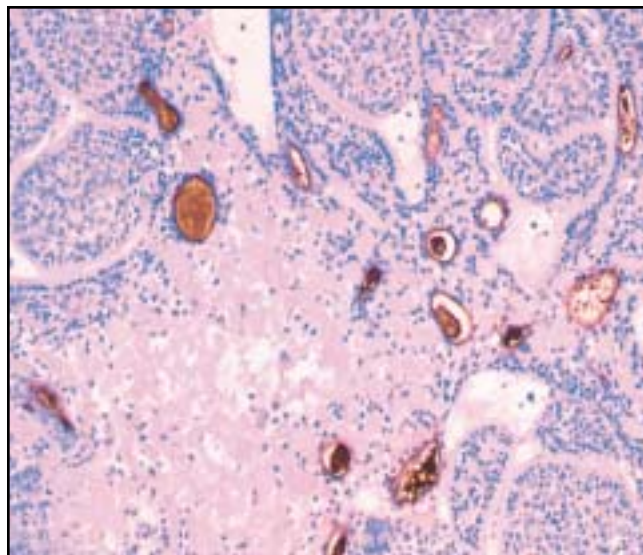
cylindromas **Image 15** and **Image 16**. Estrogen receptor, progesterone receptor, and gross cystic disease fluid protein 15 were negative in breast and dermal cylindromas.

## Discussion

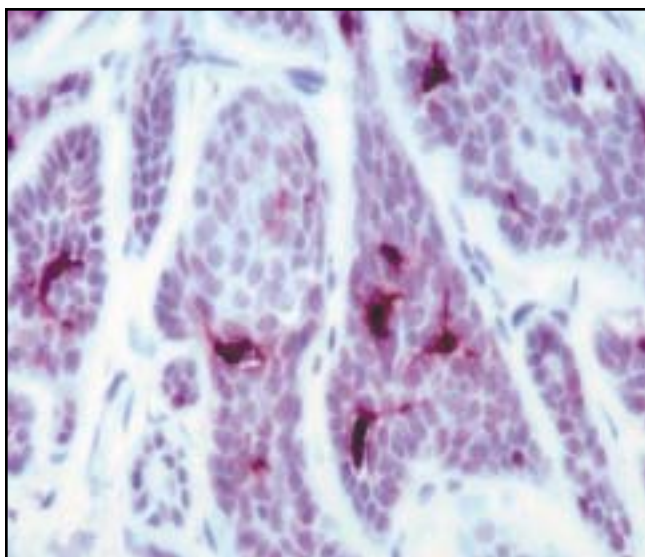
The occurrence of primary breast neoplasms with eccrine and apocrine phenotypes is not surprising because the breast is considered a modified sweat gland. Benign and malignant tumors similar to those that arise in the sweat glands have



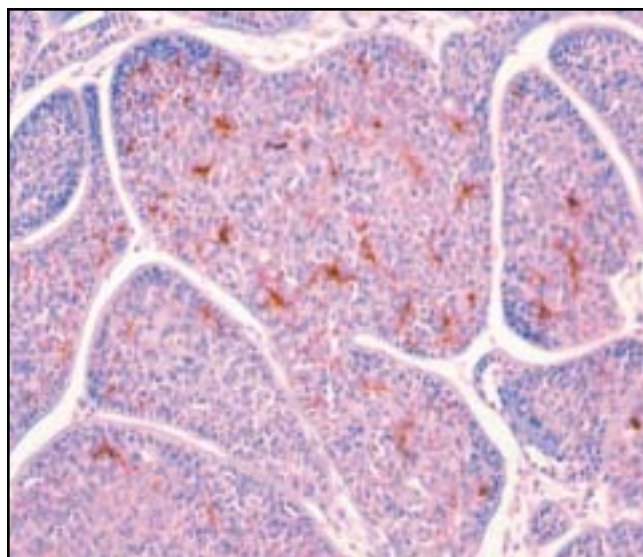
**Image 13** Few positive eccrine ducts were present in this breast cylindroma (immunostain for polyclonal carcinoembryonic antigen,  $\times 200$ ).



**Image 14** Numerous positive eccrine ducts were present in this dermal cylindroma (immunostain for polyclonal carcinoembryonic antigen,  $\times 125$ ).



**Image 15** Few CD1a+ Langerhans cells were seen in this breast cylindroma (CD1a immunostain,  $\times 200$ ).



**Image 16** Numerous CD1a+ Langerhans cells were present in this dermal cylindroma (CD1a immunostain,  $\times 150$ ).

been described in the breast, including syringoma,<sup>3,4</sup> eccrine spiradenoma,<sup>5,6</sup> eccrine spiradenoma with carcinosarcoma,<sup>7</sup> eccrine poroma,<sup>8</sup> clear cell hidradenoma,<sup>9</sup> mixed tumor,<sup>10-12</sup> syringocystadenoma papilliferum,<sup>13</sup> and cylindroma.<sup>1</sup>

Cylindroma is a rare but distinctive benign tumor of the breast histologically similar to its dermal counterpart. It was first described in 2001,<sup>1</sup> and, to our knowledge, only 8 cases (including 3 cases in the present series) have been reported to date.<sup>2</sup> Most cylindromas of the breast occur in women older than 60 years and are sporadic, small, and solitary. One case occurred in a 37-year-old woman with hereditary

cylindromatosis, an autosomal dominant syndrome characterized by cutaneous adnexal tumors, including cylindromas.<sup>2</sup> In affected families, mutations in the *CYLD* gene located on chromosome 16q12-13 have been demonstrated.<sup>14-18</sup> Sporadic cylindromas also have been reported in the major salivary glands,<sup>19,20</sup> whereas cylindromas in the lung and kidney occur in patients with familial cylindromatosis.<sup>16,21</sup>

Although some cylindromas are seen in proximity to the major lactiferous ducts of the nipple, they are not connected to the overlying skin. In the 4 cases in the present series, the average size of the tumors was 10 mm. Because they were so

small, 2 tumors were incidental findings in lumpectomy specimens excised for infiltrating breast carcinoma (1 lobular and 1 ductal). The smallest cylindroma, in fact, was overlooked during gross examination.

The morphologic similarities between cylindromas of the breast and skin include the cytologic composition of the epithelial structures characterized by central basaloid cells, peripheral myoepithelial cells, occasional clusters of sebaceous cells, squamous cells, and a constant population of reactive Langerhans cells. In addition, a thickened basement membrane that is immunoreactive to collagen IV surrounds the epithelial structures. Hyaline globules composed of basement membrane material occurred within the epithelial structures and, in some tumors, led to hypocellularity secondary to atrophy.

Breast and dermal cylindromas displayed eccrine ducts, some containing inspissated secretions. These eccrine ducts, which are an integral component of these tumors, were more numerous in dermal than in breast cylindromas and were highlighted by EMA and CEA stains. Foci of squamous differentiation seen in close association with eccrine ducts were identified only in dermal cylindromas. Eccrine ducts in dermal cylindromas were first recognized by Crain and Helwig<sup>22</sup> in 1961 and later confirmed by others.<sup>23,24</sup> Although lipid-rich clear cells have been described in dermal cylindroma since 1977, they were not identified as sebaceous cells.<sup>20</sup> We are not aware of previous studies describing sebaceous cells in breast cylindromas. The presence of basaloid cells, myoepithelial cells, sebaceous cells, squamous cells, and eccrine ducts in breast and dermal cylindromas suggests that these tumors probably arise from stem cells that are able to differentiate along different cell lines. This hypothesis could explain the existence of cylindromas in the salivary glands, lung, and kidney.

Adenoid cystic carcinoma of the breast is a morphologically heterogeneous neoplasm. Its cribriform variant can be distinguished easily from breast cylindroma because of its cribriform structures, mucin content, cytologic atypia, mitotic figures, and invasive growth pattern. It is of interest that this variant of adenoid cystic carcinoma of the breast can arise in a background of microglandular adenosis<sup>25</sup> or intraductal papilloma, as occurred in 2 of our cases. As reported by others,<sup>25</sup> transition from atypical microglandular adenosis to in situ and invasive adenoid cystic carcinoma was observed in 1 of our cases. Likewise, gradual transition from papilloma cells to adenoid cystic carcinoma was noted in another tumor. So far, no cylindroma has originated from these benign proliferative breast lesions.

In contrast, the solid variant of adenoid cystic carcinoma might be confused with cylindroma, especially in needle core biopsy specimens. Both tumors share nodular and trabecular patterns, basaloid cells, myoepithelial cells, and, rarely, squamous cells.<sup>25-27</sup> Moreover, eccrine ductal structures and hyaline globules of basement membrane also have been recognized in both mammary tumors. The presence of eccrine ducts

and sebaceous cells has been described in adenoid cystic carcinoma of the breast.<sup>28,29</sup> With immunohistochemical stains for collagen IV, a thin, discontinuous band of basement membrane surrounded the trabeculae or nodules of adenoid cystic carcinoma.<sup>25</sup> In contrast, a thickened, continuous band of basement membrane was seen around the epithelial structures of breast cylindromas with conventional stains. Langerhans cells, which are a constant feature of cylindromas, are absent in adenoid cystic carcinomas.<sup>23,24</sup> Moreover, these tumors display an infiltrative pattern of growth, greater cytologic atypia, and more mitotic figures than cylindromas.

Our study suggests that dermal cylindromas contain more eccrine ducts and Langerhans cells than breast cylindromas. The remaining histologic and immunohistochemical features are essentially identical. Breast cylindromas can be confused with the solid variant of adenoid cystic carcinoma, especially in needle core biopsy specimens, because they share a population of basaloid cells, myoepithelial cells, ducts, and, occasionally, squamous and sebaceous cells and hyaline globules of basement membrane within the epithelial structures. However, the solid variant of adenoid cystic carcinoma differs from cylindroma by its infiltrative growth pattern, cytologic atypia, mitotic figures, and the lack of a thickened basement membrane around the epithelial structures. Moreover, adenoid cystic carcinomas can arise in a background of microglandular adenosis or intraductal papilloma.

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