

# Syringomatous Squamous Tumors of the Breast

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Four cases are reported of syringomatous squamous tumors of the breast occurring in women aged 37 to 70 years. The lesions were characterized histologically by relatively well-circumscribed tumor-like nodules composed of a proliferation of teardrop or comma-shaped islands of squamous epithelium. The squamous epithelial islands contained central lumens lined by eosinophilic cuticles and were surrounded by a densely cellular fibrous matrix, thus closely resembling the growth pattern of dermal eccrine syringomas. The lesions appeared to arise *de novo* from breast parenchyma without evidence of transitions with the surrounding normal or hyperplastic mammary epithelium and were not associated with the overlying skin or nipple epidermis. In all cases, the surrounding breast tissue showed fibrocystic and benign proliferative changes, and in one case, the lesion was found in the vicinity of a large cyst surrounded by microcalcifications. All patients were treated by local surgical excision and have shown no evidence of recurrence over a follow-up period of 1 to 6 years. The histologic differential diagnosis and the possible pathogenesis of these lesions are discussed. *Cancer* 67:2350-2355, 1991.

**M**ALIGNANT BREAST NEOPLASMS with squamous differentiation are relatively rare tumors with various morphologic appearances, including mucoepidermoid carcinoma,<sup>1,2</sup> adenosquamous carcinoma,<sup>3,4</sup> spindle cell ("metaplastic") carcinoma,<sup>5,6</sup> and the more conventional forms of keratinizing squamous cell carcinoma.<sup>7-9</sup> Benign breast tumors with squamous features have been even more rarely reported and generally are regarded as a manifestation of squamous metaplasia arising from benign hyperplastic or neoplastic epithelial elements in the breast.<sup>10-13</sup> Benign neoplastic squamous proliferations in the breast thus are rare.

We studied four patients with syringomatous squamous tumors that were located deep within breast parenchyma and unrelated to the nipple. The morphologic and clinical features indicated a benign process. The histologic differ-

ential diagnosis of the lesions is discussed with their possible cause and pathogenesis.

## Materials and Methods

Four cases of squamous cell proliferations of the breast with the distinctive features we describe were reviewed. The cases were found in the surgical pathology files of the Pathology Department at Yale University School of Medicine between the years 1978 and 1989. Hematoxylin and eosin-stained sections were available for review in all cases. Two of the cases were submitted in consultation from outside institutions. Clinical and follow-up information was obtained from the patients' medical records or through direct contact with the referring physician.

## Results

### Clinical Data

The clinical and pathologic features in our patients are summarized in Table 1. The patients' ages ranged from 37 to 70 years (average, 60 years). The lesions were located in the left breast in three cases and in the right breast in one. All patients had a palpable mass. In one patient (Case 1), an infiltrating ductal carcinoma (Stage 1A) was found in the contralateral breast. Preoperative mammograms in three cases showed stippled calcifications suggestive of carcinoma. All lesions were treated by local excision only.

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TABLE 1. Clinical and Pathologic Features in Four Female Patients With Syringomatous Squamous Tumors of the Breast

Patient no.	Age (yr)	Location	Size (cm)	Pathologic findings	Treatment	Follow-up
1	65	Left breast	0.5	Sclerosing adenosis, papillomatosis, fibrocystic changes Infiltrating ductal carcinoma (Stage IA) in contralateral breast	Local excision	A&W, 6 yr
2	37	Right breast	0.8	Fibrocystic changes	Local excision	A&W, 4 yr
3	60	Left breast	1.5	Sclerosing adenosis with fibrocystic changes and microcalcifications	Local excision	A&W, 2 yr
4	70	Left breast, deep seated, retroareolar	1	Large cyst surrounded by microcalcifications	Local excision	A&W, 1 yr

A&W: alive and well.

The follow-up of 1 to 6 years has shown no evidence of recurrence or new lesions in any patient.

#### Pathologic Findings

The lesions ranged from 0.5 to 1.5 cm in greatest diameter. Grossly they were described as irregular, rubbery to firm, ill-defined nodules with a tan-gray cut surface.

Histologic examination on scanning magnification revealed a relatively well-circumscribed proliferation of

small epithelial islands with irregular borders (Fig. 1). The central portion of the lesions had small, haphazardly distributed islands of squamous epithelium surrounded by a highly cellular fibrous matrix (Fig. 2). The islands of squamous epithelium were characterized by their pavement-like architecture with prominent intercellular bridges and scattered keratohyalin granules. Many of these islands had a central lumen and were lined by a thin, eosinophilic cuticle; some of them had a characteristic teardrop or "tadpole" configuration, with long, tapering

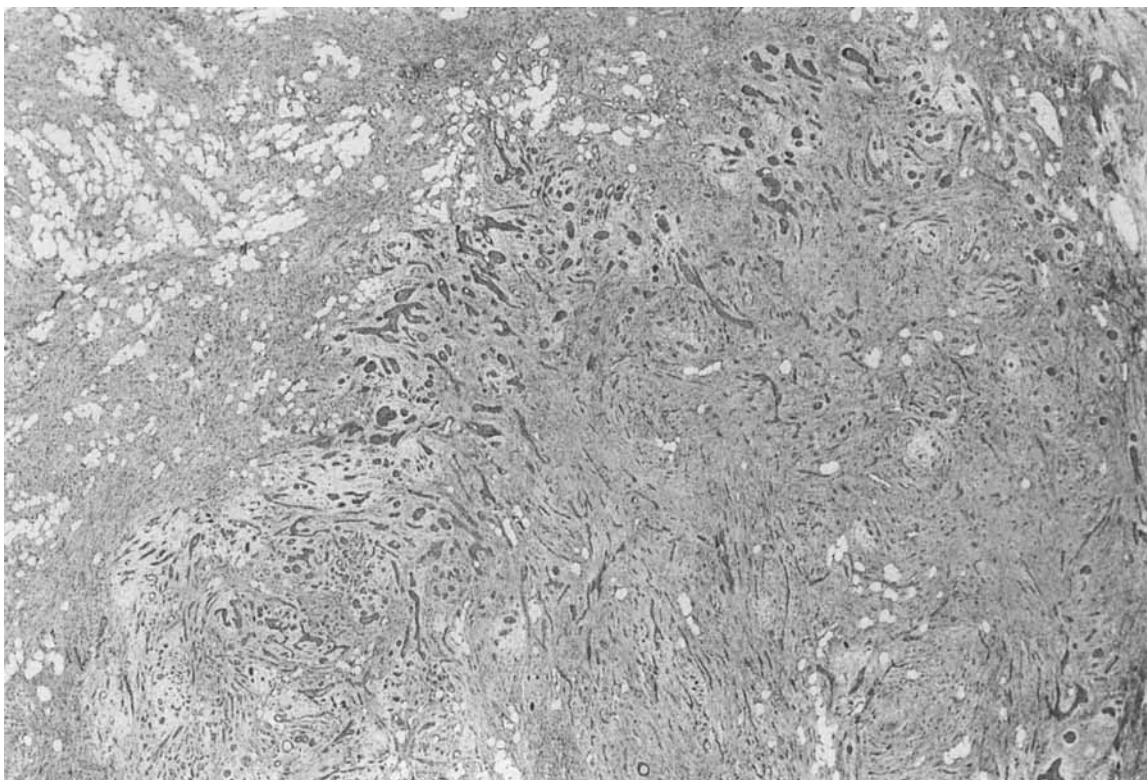


FIG. 1. Scanning magnification of the lesion in Patient 1, showing discrete, relatively well-circumscribed proliferation of epithelial elements (H&E,  $\times 20$ ).

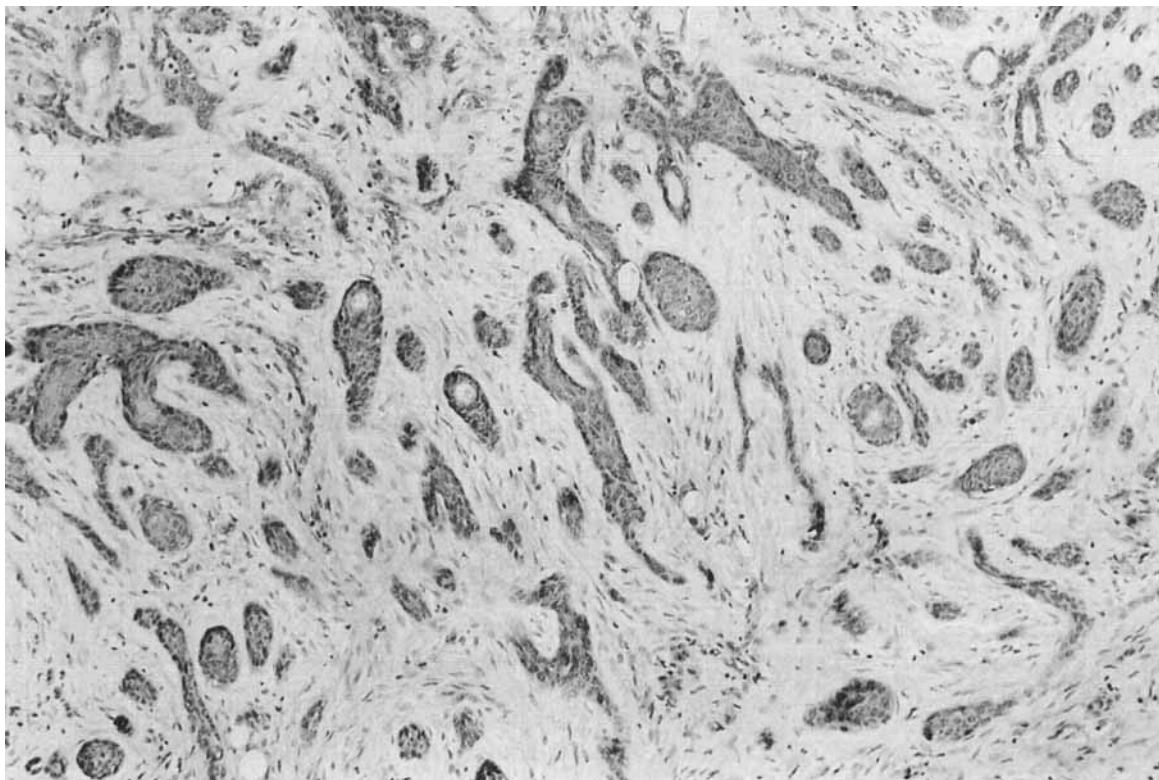


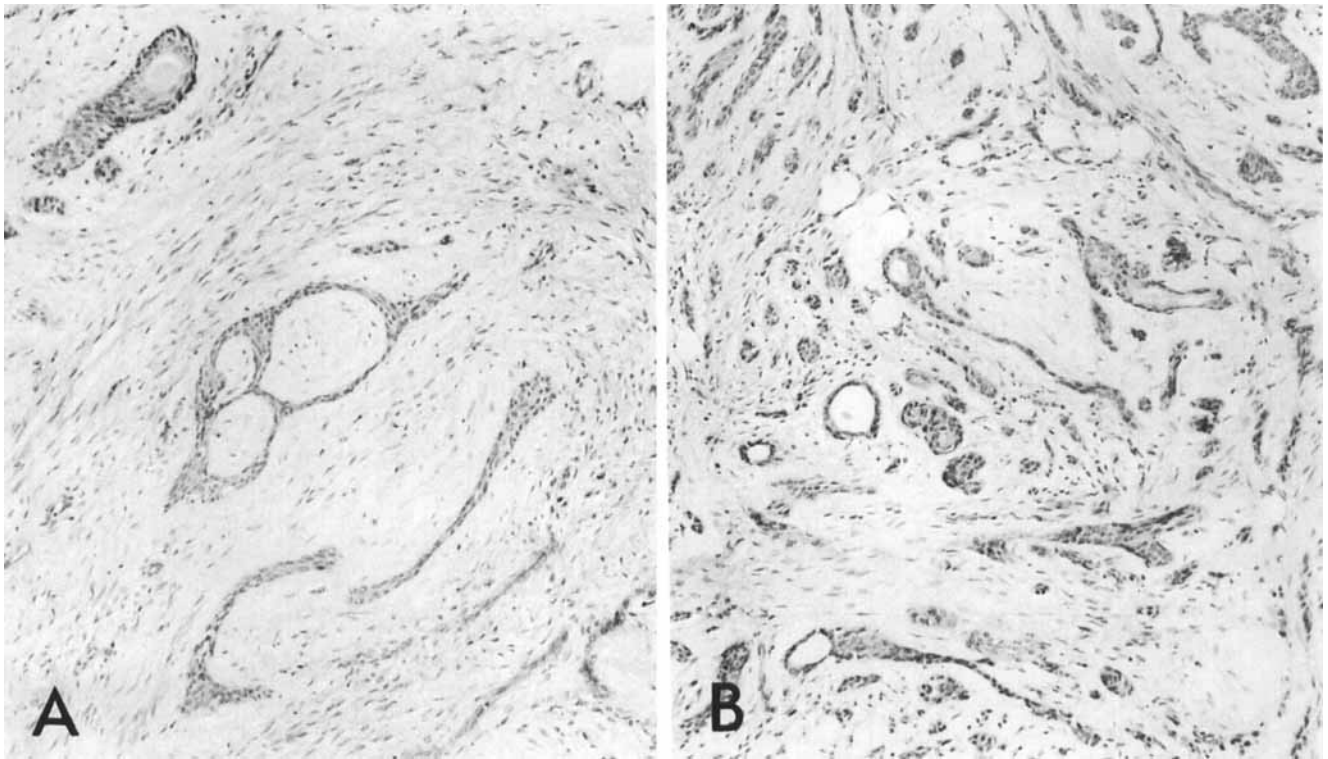
FIG. 2. Closer view of preceding field showing islands of squamous epithelium surrounded by densely cellular fibrous matrix (H&E,  $\times 200$ ).

comma-shaped tails (Fig. 3). Occasional small, scattered duct-like structures formed by one or two cell layers were also seen that contained open lumens but lacked an eosinophilic cuticle. There were no identifiable direct transitions between any of these duct-like structures and the epidermoid epithelium. The peripheral portions of the lesions had larger cyst-like structures with keratin cyst formation (Fig. 4A). Some of the squamous islands in the periphery, in addition to lumen formation, had occasional "squamous eddies," structures which have been observed in various dermal adnexal tumors and are believed to represent an attempt at differentiation toward the intra-epidermal portion of sweat ducts. Other areas had focal invaginations of the squamous islands by connective tissue elements that resulted in a close resemblance to the pilomatrical apparatus of the cutaneous hair papilla (Fig. 4B). No basaloid or matrical cells could be found in these structures. In all cases, there was no encapsulation, and the lesions had ill-defined, pseudoinfiltrative borders which could often only be discerned by identifying the characteristic pale, edematous fibrous stroma surrounding the squamous islands. There was no cytologic atypia, mitoses, or necrosis in any of the lesions. Scattered microcalcifications were found in the lesions in three cases; in most instances, these occurred within the lumens of some of the larger cystic structures. The breast parenchyma ad-

acent to the lesions was fibrocystic, with focal intraductal epithelial hyperplasia and apocrine metaplasia. In one of the cases, the proliferation of syringomatous squamous elements was found in the vicinity of a large, dilated cystic cavity lined by a layer of stratified squamous epithelium (Fig. 5A). The squamous elements surrounding the cystic cavity had abundant keratin cyst formation and calcification and were surrounded by a loose, edematous fibrous stroma containing occasional foreign body-type giant cells and a dense lymphoplasmocytic infiltrate (Figs. 5B and 5C).

### Discussion

We described four cases of syringomatous squamous tumors of the breast that were characterized by relatively well-circumscribed nodules composed of small, teardrop or comma-shaped islands of squamous epithelium. The squamous epithelial islands had central lumen formation and were lined by an eosinophilic cuticle and surrounded by a densely cellular fibrous matrix. The squamous cells comprising these structures were characterized by their pavement-like architecture, with prominent intercellular bridges and keratohyalin granules, and they were devoid of mitotic activity. The overall growth pattern and histologic features of the lesions thus had an adnexa-like

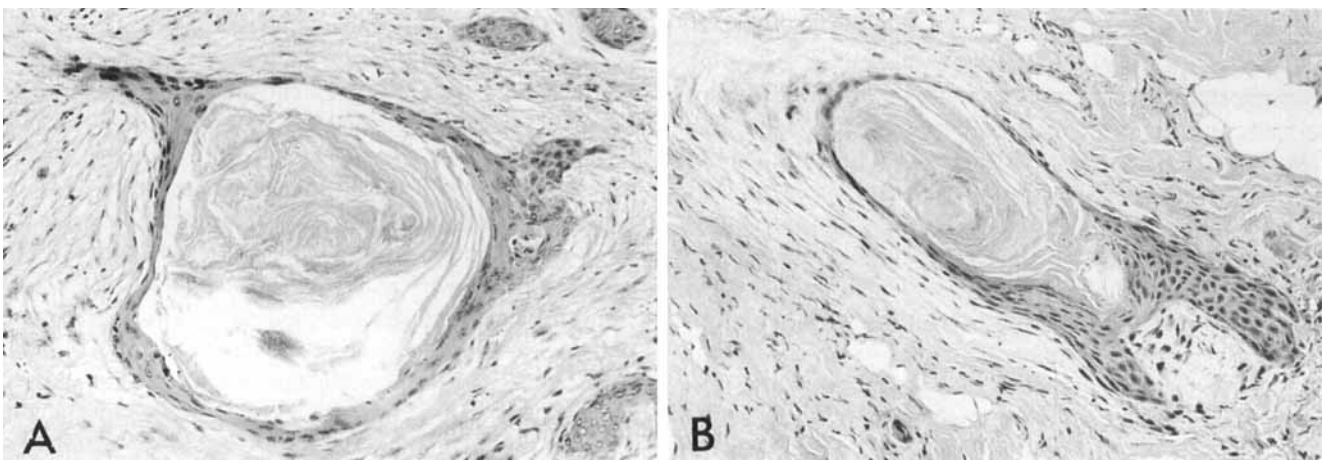


FIGS. 3A AND 3B. (A) Comma-shaped islands of squamous epithelium showing central lumen formation, some of which contain collagenized central cores with a fibroepitheliomatous appearance (H&E, original magnification  $\times 100$ ). (B) An elongated tadpole configuration is seen in many of the squamoid structures (H&E, original magnification  $\times 100$ ). (Patient 2).

quality that closely resembled that of dermal eccrine syringomas.

Breast tumors with adnexa-like features have been rarely described in the literature and, in general, have been characterized by the same histologic features as their dermal counterparts.<sup>14-18</sup> Tumors specifically with syringo-

matous features are even more rarely reported. The earliest example of such a tumor was a case quoted by Johnson and Lawrence<sup>19</sup> from the German literature (reported in 1912 by Konjenty) of a tumor-like proliferation of small squamous islands in which no connection could be found between the squamous structures and the surrounding



FIGS. 4A AND 4B. (A) Large cyst-like squamous island with concentric layers of keratinous material within the lumen (Patient 3) (H&E, original magnification  $\times 400$ ). (B) Squamous island showing invagination of the lower portion by connective tissue ingrowth resulting in a striking resemblance to the dermal hair papilla (Patient 3) (H&E, original magnification  $\times 400$ ).

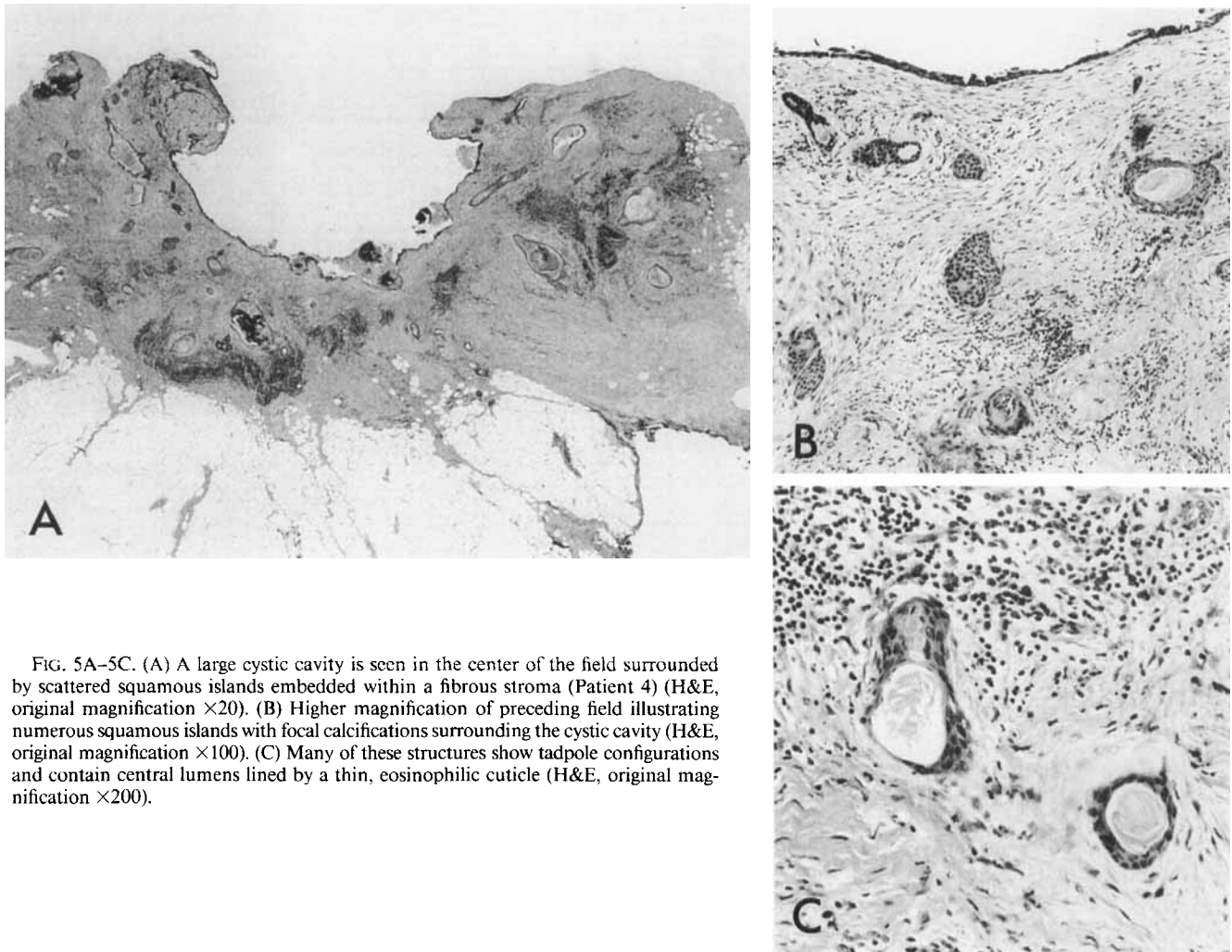


FIG. 5A-5C. (A) A large cystic cavity is seen in the center of the field surrounded by scattered squamous islands embedded within a fibrous stroma (Patient 4) (H&E, original magnification  $\times 20$ ). (B) Higher magnification of preceding field illustrating numerous squamous islands with focal calcifications surrounding the cystic cavity (H&E, original magnification  $\times 100$ ). (C) Many of these structures show tadpole configurations and contain central lumens lined by a thin, eosinophilic cuticle (H&E, original magnification  $\times 200$ ).

breast parenchyma, leading the author to postulate that the lesion had its origin in an early embryonic ectodermal rest. Oliver<sup>20</sup> in 1940 illustrated two additional examples of squamous tumors of the breast with features similar to those reported here, including proliferation of small, comma-shaped squamoid structures containing central lumens and surrounded by a dense fibrous stroma that closely resembled dermal syringomas. The author interpreted the lesions as the result of squamous metaplasia arising from preexisting ductal structures. More recently, several breast conditions have been defined that are also characterized by the proliferation of squamous elements with syringomatous features, including syringomatous adenoma of the nipple,<sup>21</sup> syringomatous tumor of the nipple,<sup>22</sup> infiltrating syringomatous adenoma,<sup>23</sup> and low-grade adenosquamous carcinoma.<sup>3</sup> With the exception of the latter, all these conditions have been related to the nipple epidermis and are therefore most likely related to preexisting dermal adnexal structures. Similar lesions have also been reported in the skin at other sites and

mucosa,<sup>24-26</sup> it has been recently proposed that they may all belong to a family of low-grade neoplasms characterized by their locally infiltrative growth, lack of cytologic atypia, and microscopic resemblance to benign dermal syringoma.<sup>22</sup> The tumors described by Rosen and Ernsberger<sup>3</sup> as "low-grade adenosquamous carcinoma," however, were located deep in breast parenchyma and, like our cases, were unrelated to the overlying skin or nipple epidermis. Such tumors, however, despite having focal syringoma-like features, were also characterized by clear-cut areas of intraductal carcinoma, with foci of spindle-cell growth and osteocartilaginous metaplasia; four of the eight patients in their study who were treated by local excision alone had recurrences in 1 to 3.5 years, further attesting to the malignant nature of these lesions. Our cases share some features with low-grade adenosquamous carcinoma of the breast, and as such, they may represent a precursor stage for them. They significantly differ, however, in that they lack the areas of infiltration and destruction of adjacent breast tissue, the clearly iden-

tifiable intraductal malignant component, or areas of spindle-cell or osteocartilaginous metaplasia. The latter features set these lesions apart from low-grade adenosquamous carcinoma of the breast.

The pathogenesis of syringomatous squamous tumors of the breast is obscure. It is not yet clear whether they represent a neoplastic proliferation or part of a metaplastic process. Squamous metaplasia with features of adnexal differentiation has been previously reported in the breast; however, in all such cases the lesions have been shown to arise from underlying hyperplastic or neoplastic epithelial breast elements.<sup>10,27</sup> The possibility that the tumors in our cases may have arisen on the basis of a metaplastic process involving germinative mammary epithelium or undifferentiated stromal cells, such as has been observed for other tissues,<sup>28</sup> cannot be discounted. Also, the possibility that these lesions may represent extensive squamous metaplasia in sclerosing adenosis or other form of benign proliferative process in the breast has to be considered. Arguing against this possibility, however, is the absence of the characteristic lobular architecture seen in sclerosing adenosis, the lack of a myoepithelial cell layer, and the absence of transitions of the squamous elements with any other proliferative mammary epithelial components. Additionally, syringomatous features have not been reported in cases of squamous metaplasia arising from benign proliferative breast conditions.<sup>10-13,29,30</sup>

The relationship that exists between the lesions we described and other squamous cell proliferations affecting the breast must be clarified. It is possible that these lesions represent a precursor stage for well-differentiated squamous cell or adenosquamous carcinoma. In this regard, it is interesting to note that three of the patients in Rosen and Ernsberger's<sup>3</sup> series who were treated by local excision alone also had no evidence of recurrence despite histologic features of malignancy (the follow-up period in those three patients, however, was relatively short).<sup>3</sup> In our cases, the lack of atypia and mitotic activity, absence of heterologous metaplastic elements, or any identifiable *in situ* or infiltrative malignant component, strongly argue against a diagnosis of malignancy. Although the follow-up in our patients was also relatively short, the absence of recurrences in a period ranging from 1 to 6 years after local excision would seem to support this interpretation. Whether these tumors represent a preneoplastic or low-grade neoplastic condition is an issue that will only be resolved through long-term follow-up of additional cases. Because of the uncertainty as to the exact pathogenesis of the lesions, the designation of "syringomatous squamous tumors" appears at present to be the most appropriate.

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