Cutaneous Syncytial Myoepithelioma: Clinicopathologic Characterization in a Series of 38 Cases

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Abstract

Cutaneous myoepithelial tumors demonstrate heterogeneous morphologic and immunophenotypic features. We previously described, in brief, seven cases of cutaneous myoepithelioma showing solid syncytial growth of ovoid, spindled or histiocytoid cells. We now present the clinicopathologic features in a series of 38 cases of this distinctive syncytial variant, which were diagnosed between 1997–2012 (mostly seen in consultation). There were 27 men and 11 women, with a median age of 39 years (range 2 months to 74 years). Primary anatomic sites were upper extremity (11, including 2 on the hand), upper limb girdle (3), lower extremity (14; 3 on the foot), back (6), face (2), chest (1), and buttock (1); the typical presentation was as either a polypoid or papular lesion. Tumors were well-circumscribed and centered in the dermis and ranged in size from 0.3 to 2.7 cm (median 0.8 cm). Microscopically all tumors showed a solid sheet-like growth of uniformly sized ovoid to spindled or histiocytoid cells with palely eosinophilic syncytial cytoplasm. Nuclei were vesicular with fine chromatin and small or inconspicuous nucleoli, and exhibited minimal to no atypia. Mitoses ranged from 0 to 4 per 10 HPF; 28 tumors showed no mitoses. Necrosis and lymphovascular invasion were consistently absent. Adipocytic metaplasia, appearing as superficial fat entrapped within the tumor, was seen in 12 cases. Chondro-osseous differentiation was seen in one tumor. All tumors examined were diffusely positive for EMA, and the majority showed diffuse staining for S-100 protein (5 showing focal staining). Keratin staining was focal in 1 of 33 tumors and seen in rare cells in 3 other cases. There was also positivity for GFAP (14/33), SMA (9/13), and p63 (6/11). Most lesions were treated by local excision. The majority of tumors tested (14/17; 82%) were positive by fluorescence in situ hybridization for *EWSR1* gene rearrangement; testing for potential fusion partners (*PBX1, ZNF444, POU5F1, DUX4, ATF1, CREB1, NR4A3, DDIT3,* and *NFATc2*) was negative in all *EWSR1*-rearranged tumors. No *FUS* gene rearrangement was detected in two tumors lacking *EWSR1* rearrangement. Follow-up information is available for 21 patients (mean follow-up 15 months). One patient with a positive deep margin developed a local recurrence 51 months after initial biopsy. All other patients with known follow-up, including 11 who had positive deep margins, are alive with no evidence of disease and no reported metastases. In summary, cutaneous syncytial myoepithelioma is a

morphologically distinct variant that more frequently affects men, occurs over a wide age range, and usually presents on the extremities. Tumors are positive for S-100 protein and EMA, and unlike most myoepithelial neoplasms, keratin staining is infrequent. *EWSR1* gene rearrangement is present in nearly all tumors tested, and likely involves a novel fusion partner. Prior reports describe some risk of recurrence and metastasis for cutaneous myoepithelial tumors; however, the syncytial variant appears to behave in a benign fashion and only rarely recurs locally.

Keywords

myoepithelioma; syncytial; skin; soft tissue; *EWSR1*

INTRODUCTION

Cutaneous myoepithelial tumors demonstrate heterogeneous morphologic and immunophenotypic features, similar to primary myoepithelial neoplasms in other sites. Myoepithelial neoplasms in skin and soft tissue have been increasingly characterized over the past ten years (1–9), and are classified as chondroid syringoma/benign mixed tumor (defined by tubulo-ductal differentiation), myoepithelioma, and myoepithelial carcinoma. In common with lesions showing myoepithelial differentiation, a wide variety of cytologic and architectural features may be present both within a given lesion and between different tumors. Myoepithelial tumors typically coexpress epithelial antigens (keratin and/or EMA), S100 protein and/or GFAP; staining for p63, SMA and calponin is variable. To date, studies have shown that approximately 40–50% of myoepithelial tumors (more often carcinomas) in soft tissue sites harbor *EWSR1* rearrangement (and rarely alternate *FUS* rearrangement) (10), and documented fusion partners include *POU5F1*, *PBX1*, and *ZNF444* (10–12). Reports of the frequency of *EWSR1*-rearrangement has been variable in cutaneous myoepithelial tumors, ranging from 29% (10) to 44% (13), while mixed tumors more often show *PLAG1* gene rearrangement, comparable to their salivary counterparts (14). Up to 20% of myoepitheliomas and myoepithelial carcinomas in skin and soft tissue are known to recur, and the risk appears higher with incomplete resection. Myoepithelial carcinoma, which is distinguished by the presence of at least moderate cytologic atypia, has a significant risk of metastatic spread to distant sites.

The majority of cutaneous myoepitheliomas show a typically lobular or multinodular architecture with epithelioid, spindled, plasmacytoid, or clear cells associated with a prominent myxoid or hyalinized stroma. In 2004, among a series of 14 cutaneous myoepitheliomas, we described a morphologically and immunohistochemically distinct subset (7 cases) showing solid syncytial growth of ovoid, spindled or histiocytoid cells with eosinophilic cytoplasm, with an immunophenotype of EMA and S-100 positivity but infrequent keratin staining (7). Herein we describe the clinicopathologic and molecular features of 38 cases of this distinctive syncytial variant of cutaneous myoepithelioma with the goal of more completely characterizing these lesions.

MATERIALS AND METHODS

Thirty-eight cases of cutaneous syncytial myoepithelioma identified between 1997 and 2012 were retrieved from surgical and consultation files (C.D.M.F. and J.L.H.) at Brigham and Women's Hospital, Department of Pathology, Boston, MA. Hematoxylin and eosin (H&E) stained sections and immunohistochemical stains performed at the time of diagnosis were re-examined, with attention to cytomorphologic features, growth pattern, cytologic atypia, the presence of necrosis, and mitotic count. Clinical and follow-up data were obtained from

referring pathologists using a standardized data sheet (see Acknowledgements). Seven cases have been published previously in a preliminary study (cases 1–7) (7, 15).

Immunohistochemistry had been performed in our laboratory on 4-µm-thick formalin-fixed paraffin-embedded tissue sections using the antibodies and conditions listed in Table 1. The Envision Plus detection system (Dako, Carpinteria, CA) was used for all antibodies. Appropriate positive and negative controls were used throughout.

FISH on interphase nuclei from paraffin embedded 4-micron sections was performed in 17 cases applying custom probes using bacterial artificial chromosomes (BAC), covering and flanking *EWSR1* in 22q12, *FUS* in 16p11, *PBX1* in 1q23, *ZNF444* in 19q13, *POU5F1* in 6p21, *DDIT3* in 12q13.3, *ATF1* in 12q13.3, *CREB1* in 2q33.3, *NR4A3* in 9q31.1, *DUX4* in 4q35.2, and *NFATc2* in 20q13.2 (Table 2). Two of these cases (cases 26 and 35) and two other cases (cases 17 and 27) had initially been tested for *EWSR1* rearrangement at Brigham and Women's Hospital using similar methods. No cases had been submitted for conventional cytogenetic analysis.

BAC clones were chosen according to USCS genome browser (http://genome.uscs.edu). The BAC clones were obtained from BACPAC sources of Children's Hospital of Oakland Research Institute (CHORI) (Oakland, CA) (http://bacpac.chori.org). DNA from individual BACs was isolated according to the manufacturer's instructions, labeled with different fluorochromes in a nick translation reaction, denatured, and hybridized to pretreated slides. Slides were then incubated, washed, and mounted with DAPI in an antifade solution. The genomic location of each BAC set was verified by hybridizing them to normal metaphase chromosomes. Two hundred successive nuclei were examined using a Zeiss fluorescence microscope (Zeiss Axioplan, Oberkochen, Germany), controlled by Isis 5 software (Metasystems). A positive score was interpreted when at least 20% of the nuclei showed a break-apart signal. Nuclei with incomplete set of signals were omitted from the score. All cases were first tested with an *EWSR1* probe. The *EWSR1*-rearranged tumors were then evaluated for break-apart signals using probes for *PBX1, ZNF444, POU5F1, etc.* The *EWSR1* negative tumors were then tested for *FUS* break-apart, since *FUS* may substitute for the *EWSR1* gene in certain translocation-associated sarcomas (10, 16, 17). All 17 cases were tested for *NR4A3* break-apart.

This study was performed with the approval of the Institutional Review Board at the Brigham and Women's Hospital.

RESULTS

Clinical Features

Clinical data are summarized in Table 2. The patient group comprised 27 men and 11 women (2.5:1 ratio), with a median age of 39 years (range 2 months to 74 years). Over half (60%) of the patients were in the third through fifth decades in age. The anatomic distribution was as follows: upper extremity (11, including two on the hand), upper limb girdle (3), lower extremity (14; 3 on the foot), back (6), face (2), chest (1), and buttock (1). These skin lesions were described as either polypoid or papular. Reported preoperative duration ranged from two months to four years. Clinical diagnoses offered included: acrochordon, cutaneous cyst, wart, seborrheic keratosis, actinic keratosis, Kaposi sarcoma, hemangioma, neurofibroma, keratoacanthoma, dermatofibroma, basal cell carcinoma, squamous cell carcinoma, dermal nevus (with or without inflammation), amelanotic melanocytic lesion, Spitz nevus, adnexal tumor, sebaceous hyperplasia, schwannoma, leiomyoma, spiradenoma, and angiolipoma. Proposed diagnoses by submitting pathologists, when provided, included epithelioid sarcoma (3 cases), neurofibroma (2), perineurioma/

sclerosing perineurioma (5), cellular neurothekeoma (3), granular cell tumor, myofibroma/ myopericytoma (4), smooth muscle neoplasm (2), angiomyolipoma, meningioma, dermatofibrosarcoma protuberans, proliferative fasciitis, cutaneous epithelioid angiomatous nodule, fibrous histiocytoma, epithelioid fibrous histiocytoma (2), fibroma, juvenile fibrous histiocytoma, ossifying (non-ossifying) fibromyxoid tumor, and nevus. In only five cases, a myoepithelial neoplasm was suggested.

Most patients were treated by local excision (or re-excision after initial biopsy sampling). Follow-up information was available for 21 patients (mean follow-up 15 months). Many patients were not followed longer because of the benign diagnosis. One patient with a positive deep margin developed a local recurrence 51 months after initial shave biopsy without formal excision (case 37). All other patients with known follow-up, including 6 others who had positive margins and 1 with marginal excision, were reported to be alive with no evidence of disease. No patients received radiation or chemotherapy, and none developed metastases.

Gross and Microscopic Features

Lesions ranged in size from 0.3 to 2.7 cm (median 0.8 cm). Most tumors were well-circumscribed but unencapsulated (Figure 1). All tumors were centered in the dermis and often abutted the overlying epidermis (Figure 2). Microscopically all tumors showed a solid sheet-like growth of uniformly sized ovoid to spindled or histiocytoid cells with palely eosinophilic syncytial cytoplasm (Figures 3a and b). Only occasional focal fascicular growth of spindle cells was seen (Figure 3c). Nuclei were vesicular with fine chromatin and smooth nuclear contours had small or inconspicuous nucleoli, and showed minimal to no atypia. Mitoses ranged from 0 to 4 per 10 high power fields (HPF); 28 tumors showed no mitoses. All tumors lacked evident necrosis and lymphovascular invasion. In 17 cases, minimal-to-moderate lymphoplasmacytic infiltrates were observed at the periphery of or within tumor, frequently surrounding vessels (Figure 4). Adipocytic metaplasia, appearing as superficial fat seemingly entrapped within the tumor, was seen in 12 cases (Figures 1b and 5). Chondro-osseous differentiation was seen in 1 tumor (Figure 6). All tumors lacked ductal differentiation, although entrapment of adnexal structures was common. For the recurrent tumor observed in case 37, no mitoses were found in the primary or recurrent tumor, which appeared morphologically identical to one another.

Immunohistochemical Findings

All tumors examined were diffusely positive for EMA (38/38) (Figure 7a) and the majority showed diffuse staining for S-100 protein (33/38); five showing more focal staining (Figure 7b). Keratin was negative in 31/36 cases tested (Figure 7c) ; there was focal positivity in one tumor rare cells were positive in four other cases. Of 33 tumors tested for GFAP, 14 were positive and most commonly showed weak multifocal staining (Figure 7d), although as few as rare positive cells were observed in some cases. SMA was positive in 9 of 13 cases. p63 was positive in 6 of 11 tumors and typically showed a focal to multifocal nuclear staining pattern.

Molecular genetic findings

Fourteen of seventeen tumors tested showed *EWSR1* rearrangement by FISH (Figure 8).

Two cases did not show break-apart signals for *EWSR1*, and further testing for *FUS* break-apart was negative in both tumors. For the last case, no hybridization signal could be obtained, likely due to DNA degradation. Subsequent testing of all *EWSR1*-rearranged tumors, in hopes of identifying a fusion partner, was negative for all break-apart signals for

PBX1, *ZNF444*, *POU5F1*, *ATF1*, *CREB1*, *NR4A3*, *DDIT3* and *NFATc2*, as well as for *EWSR1-DUX4* fusion

DISCUSSION

Cutaneous syncytial myoepithelioma is a morphologically distinct subtype of myoepithelial neoplasm that is characterized by solid growth of spindled, ovoid, or histiocytoid cells with palely eosinophilic cytoplasm and a distinct immunophenotype of EMA and S-100 positivity and infrequent cytokeratin staining. The tumor affects patients over a wide age range (2 months to 74 years) with a male predominance (2.5:1, M:F). While the anatomic distribution is broad, these tumors are most common on the extremities (74%). The majority of cutaneous syncytial myoepitheliomas tested show *EWSR1* gene rearrangement.

While myoepithelial neoplasms show a wide range of morphologic and immunophenotypic heterogeneity, most tumors at least focally demonstrate characteristic features of epithelioid, plasmacytoid, or spindled cells showing either nested or reticular growth within a collagenous or chondromyxoid stroma. The syncytial variant consistently showed syncytial solid growth with no significant stroma. Most tumors were cytologically bland, with benign-appearing nuclei. The majority of tumors (28/38; 73%) showed no mitotic activity; and the highest mitotic count was 4 per 10 HPF. No necrosis or lymphovascular invasion was observed. Adipocytic metaplasia was seen in approximately one-third of tumors. Interestingly, one prior case report (18) of what was regarded as a cutaneous myoepithelial carcinoma showing "a plexiform growth pattern" showed similar pathologic features, including predominance of solid growth of spindled cells, positivity for EMA and S100, and negativity for keratin; the tumor exhibited adipocytic metaplasia which accounts for the plexiform appearance. The histologic features of spindled and histiocytoid cells and lack of significant stroma, atypia, and necrosis are useful in recognizing the syncytial variant.

Myoepithelial tumors typically express a combination of epithelial antigens (keratin and/or EMA), S-100 protein and/or GFAP, and variably SMA, calponin, and p63. However, the syncytial variant consistently shows positivity for EMA and S-100 protein and most tumors lacked keratin staining; only five cases were positive for keratin and staining was very focal or present in rare cells. Staining for GFAP appeared to be more limited in extent when compared to S-100, with typically multifocal weak positivity. The absence of significant keratin staining may lead to diagnostic pitfalls, and underscores the importance of applying a complete immunohistochemical panel when a myoepithelial neoplasm is suspected.

The differential diagnosis includes, principally, epithelioid benign fibrous histiocytoma (EFH), juvenile xanthogranuloma (JXG), melanocytic lesions, and, less likely, epithelioid sarcoma. EFH frequently presents on the lower extremities of young to middle-aged adults as a well-circumscribed dermal nodule of epithelioid cells with palely eosinophilic cytoplasm, and often shows EMA positivity (19). The predominance of epithelioid cells embedded in collagenous or variably vascular stroma and absence of spindle cells and syncytial architecture favors EFH. Furthermore, binucleate cells are frequently present in EFH but were not observed in any cases of cutaneous syncytial myoepithelioma. While EFH is frequently positive for EMA and negative for keratin, EFH is consistently negative for S-100, GFAP, and p63 (19), and therefore immunohistochemistry can reliably distinguish EFH from cutaneous syncytial myoepithelioma.

Juvenile xanthogranuloma (JXG) in the so-called "early stage" can mimic cutaneous syncytial myoepithelioma, exhibiting an exophytic proliferation of eosinophilic histiocytic cells that lack characteristic lipidization and Touton giant cells (20). While children are most frequently affected by JXG, seven patients with cutaneous syncytial myoepithelioma in this

series were aged 18 years or younger, including a 2-month-old male infant. JXG can be distinguished by histiocytic markers CD163 and CD68, and absent expression of myoepithelial markers.

Melanocytic neoplasms may also enter the differential diagnosis, particularly for lesions showing little cytologic atypia and pleomorphism and those in which a junctional component is not present or visualized. Spitz nevi, which are well-circumscribed and occasionally completely intradermal, can raise diagnostic challenges. Careful examination for the presence of a junctional component, nested growth pattern, Kamino body formation, and downward "maturation" into deeper dermis will identify Spitz nevi. While S-100 positivity is shared by both Spitz nevi (and other melanocytic neoplasms) and cutaneous syncytial myoepithelioma, the application of melanocytic markers HMB-45, MelanA, and MiTF and other myoepithelial markers will usually differentiate the two entities.

Cutaneous syncytial myoepithelioma may also show some morphologic overlap with epithelioid sarcoma, which commonly affects young adults on the distal extremities. Epithelioid sarcoma typically shows an admixture of epithelioid and spindle cells with moderate atypia showing infiltrative growth and often discontiguous nodules; however in some cases solid growth and relatively less atypia can be observed. Both lesions are positive for EMA; positivity for pan-keratin and CD34 and negativity for S-100 and GFAP favors epithelioid sarcoma. While 90% of epithelioid sarcomas show loss of nuclear expression of INI1 (21), the product of a tumor suppressor gene mapped to 22q11.2, INI1 loss has been observed in pediatric myoepithelial carcinomas of soft tissue (8). In fact, since initial recognition of INI1 deficiency in malignant rhabdoid tumors (22), INI1 loss has been observed in several other tumor types (23), including a subset of epithelioid malignant peripheral nerve sheath tumors (21), renal medullary carcinoma (24) and another tumor type typically showing *EWSR1* rearrangement, extraskeletal myxoid chondrosarcoma (25). The mechanism of loss of INI1 protein expression varies between tumor types and is not necessarily correlated with cytogenetic status of the region on 22q11.2 (23), but INI1 staining is not likely to be helpful in accurate diagnosis of syncytial myoepithelioma.

Based on available follow-up information, a benign clinical course is expected for syncytial myoepithelioma, with only one patient showing local recurrence 4 years after initial shave biopsy with positive margins. All other patients with known follow-up showed no evidence of recurrence or metastasis, including six patients with positive margins and one patient with marginal excision. While criteria for malignancy in cutaneous myoepithelial neoplasms have not been well established, myoepithelial tumors in soft tissue with moderate-to-severe cytologic/nuclear atypia show increased risk of recurrence and metastasis and are thus classified as myoepithelial carcinoma (5). Based on a small number of reports, cutaneous lesions showing cytologic atypia, high mitotic rate, and necrosis show more aggressive behavior (4, 7–9); however prior work also suggested a potential risk of recurrence and metastasis even for cytologically bland cutaneous myoepithelial tumors (7). In our prior study of cutaneous myoepitheliomas, the three cytologically benign tumors that recurred (one of which also metastasized) showed increased mitotic counts (up to 6 per 10 HPF); however none of these tumors were the syncytial variant (7). All tumors in our present series lacked significant cytologic atypia, necrosis, and lymphovascular invasion; most tumors showed negligible mitotic activity, and the highest count was 4 per 10 HPF. For the case in which a recurrence developed, the primary tumor did not exhibit atypia or mitotic activity in the sections examined and the recurrent tumor was morphologically identical and lacked any features of malignancy.

Cytogenetic aberrations were first reported in a series of pediatric myoepithelial carcinoma of soft tissue in 2007, in which one case showed loss of chromosome 22 and *EWSR1*

rearrangement was detected in another case (8). In the following two years, Brandal et al reported a balanced translocation t(1;22)(q23;q12) and resultant *EWSR1-PBX1* gene fusion in one case of soft tissue myoepithelioma (11) and one myoepithelial carcinoma with translocation t(19;22)(q13;q12) resulting in a chimeric gene *EWSR1-ZNF444* (12). In a series of 66 myoepithelial neoplasms in skin, soft tissue, bone, and visceral sites, Antonescu et al (10) identified *EWSR1* gene rearrangement in 45% (30/66) of tumors, 47% (14/30) of which were myoepitheliomas and 53% (16/30) of which were malignant. One case showed alternative rearrangement of *FUS*. PBX1 was identified as a partner gene in five cases and *ZNF444* in a single case; *POU5F1* (mapped on chromosome 6p21) was identified as a partner gene in five additional cases showing distinctive clear cell morphology. Myoepithelial neoplasms showing *EWSR1-POU5F1* fusion affected children and young adults and were located in deep soft tissue of the extremities. Of the seven cutaneous tumors examined, only two tumors were positive for *EWSR1* gene rearrangement, neither of which had syncytial features. In a 2011 series of 18 cutaneous myoepithelial tumors, Flucke et al (13) reported that seven (7/16; 44%) cases harbored *EWSR1* rearrangement, including four mixed tumors, two myoepitheliomas (none of which were reported to be syncytial), and one myoepithelial carcinoma. In Flucke et al's series, one case description was consistent with the syncytial variant (their case 11), but was negative for *EWSR1* rearrangement. A fourth partner gene of *EWSR1* was recently reported in a soft tissue myoepithelioma showing *EWSR1-ATF1* gene fusion (26). In contrast to Flucke et al's finding of *EWSR1* rearrangement in mixed tumors (13), Bahrami et al (14) reported that mixed tumors in skin and soft tissue sites showed *PLAG1* aberrations, similar to their salivary gland counterpart.

In summary, cutaneous syncytial myoepithelioma is a distinct variant showing solid growth of spindled, ovoid, or histiocytoid cells with palely eosinophilic cytoplasm that more frequently affects men, occurs over a wide age range, and usually presents on the extremities. Tumors are positive for S-100 protein and EMA, and in contrast to most myoepithelial neoplasms, keratin staining is infrequent. Prior reports describe some risk of recurrence and metastasis for cutaneous myoepithelial tumors; however, based on preliminary follow-up data, the syncytial variant appears to behave in a benign fashion and only rarely recurs locally. The presence of *EWSR1* gene rearrangement in most cases supports a close relationship to other subsets of myoepithelial tumors, but we were unable to demonstrate any of the known fusion gene partners, suggesting that this morphologically distinctive tumor type may prove to be associated with a novel fusion gene.

Acknowledgments

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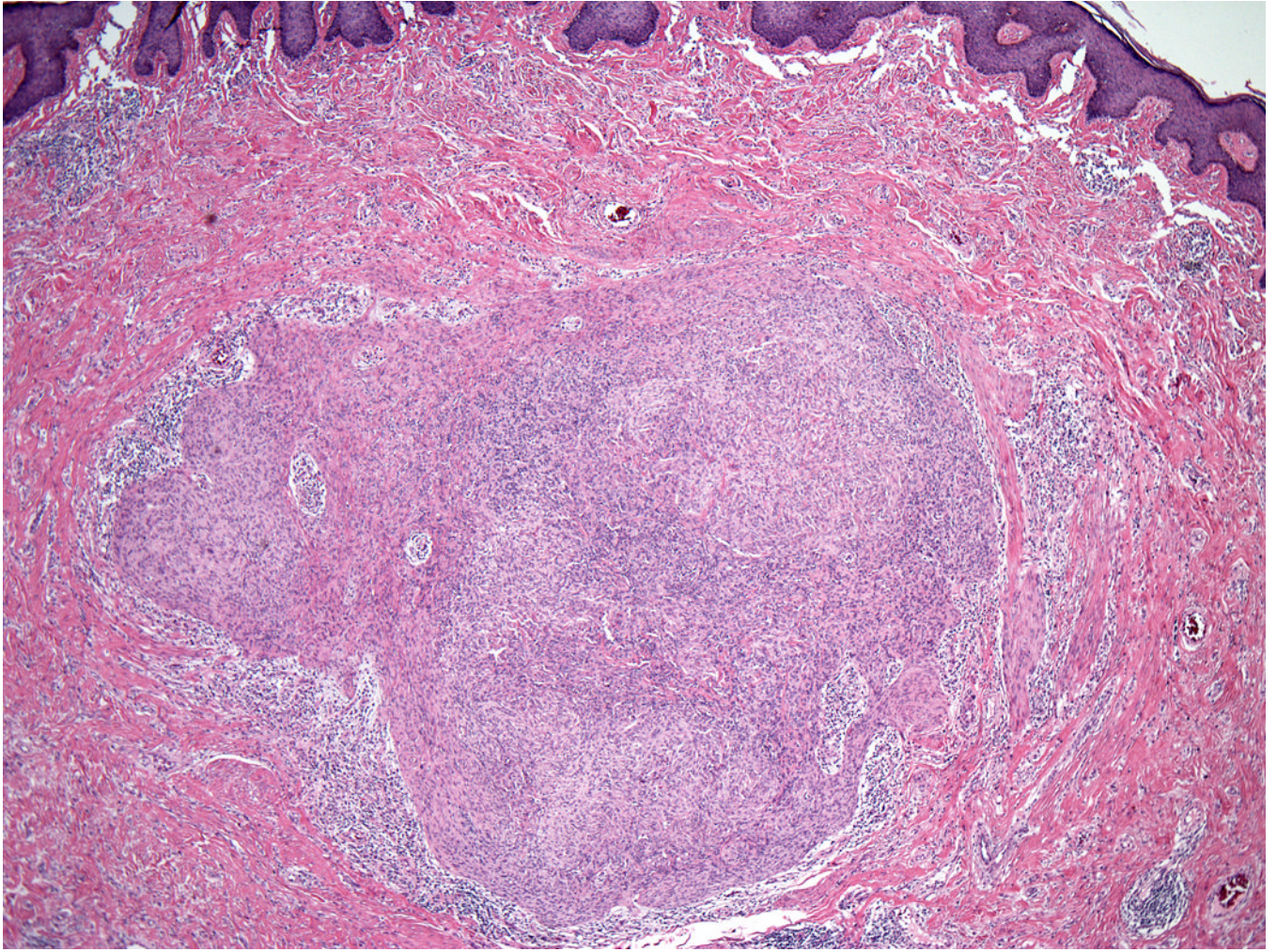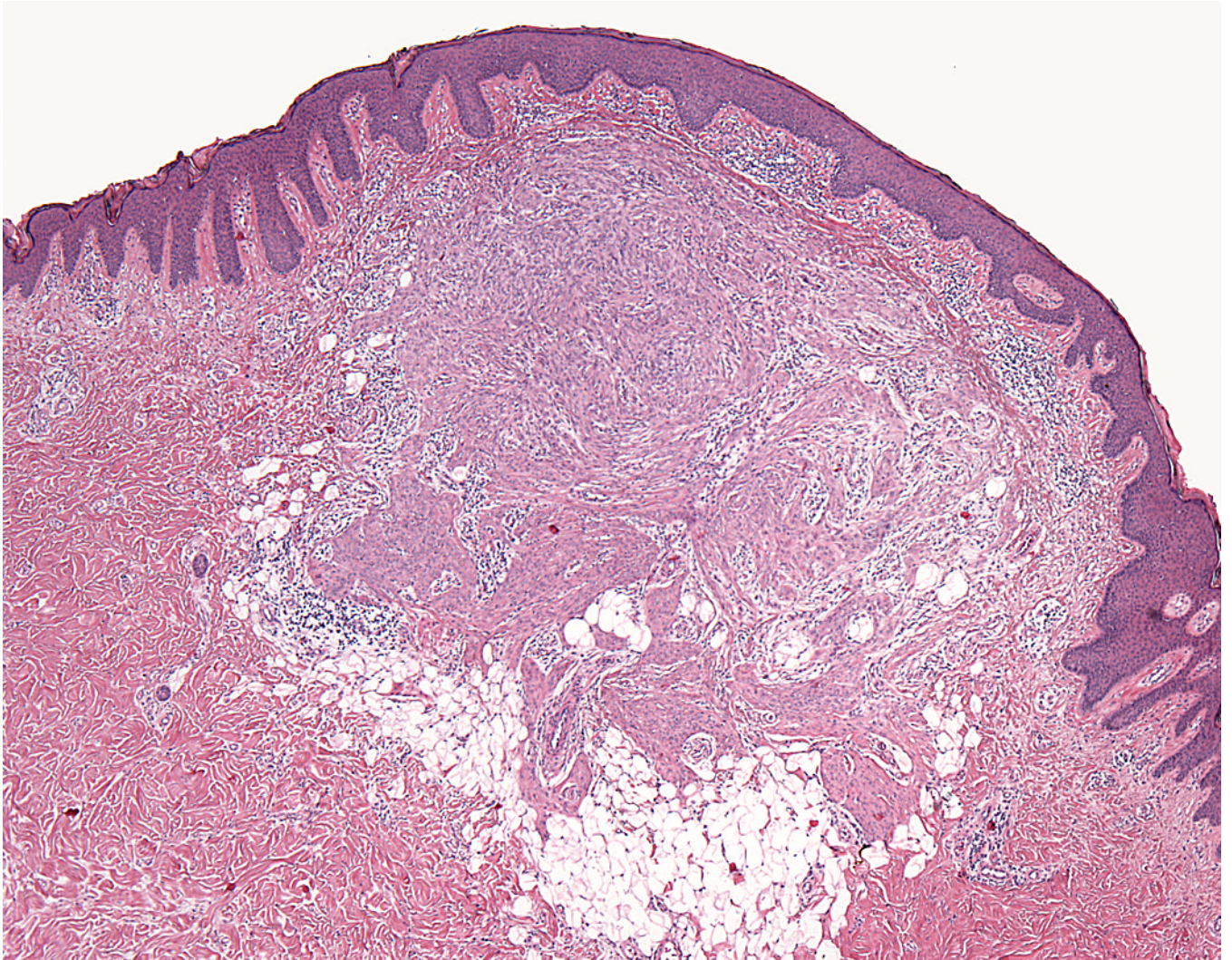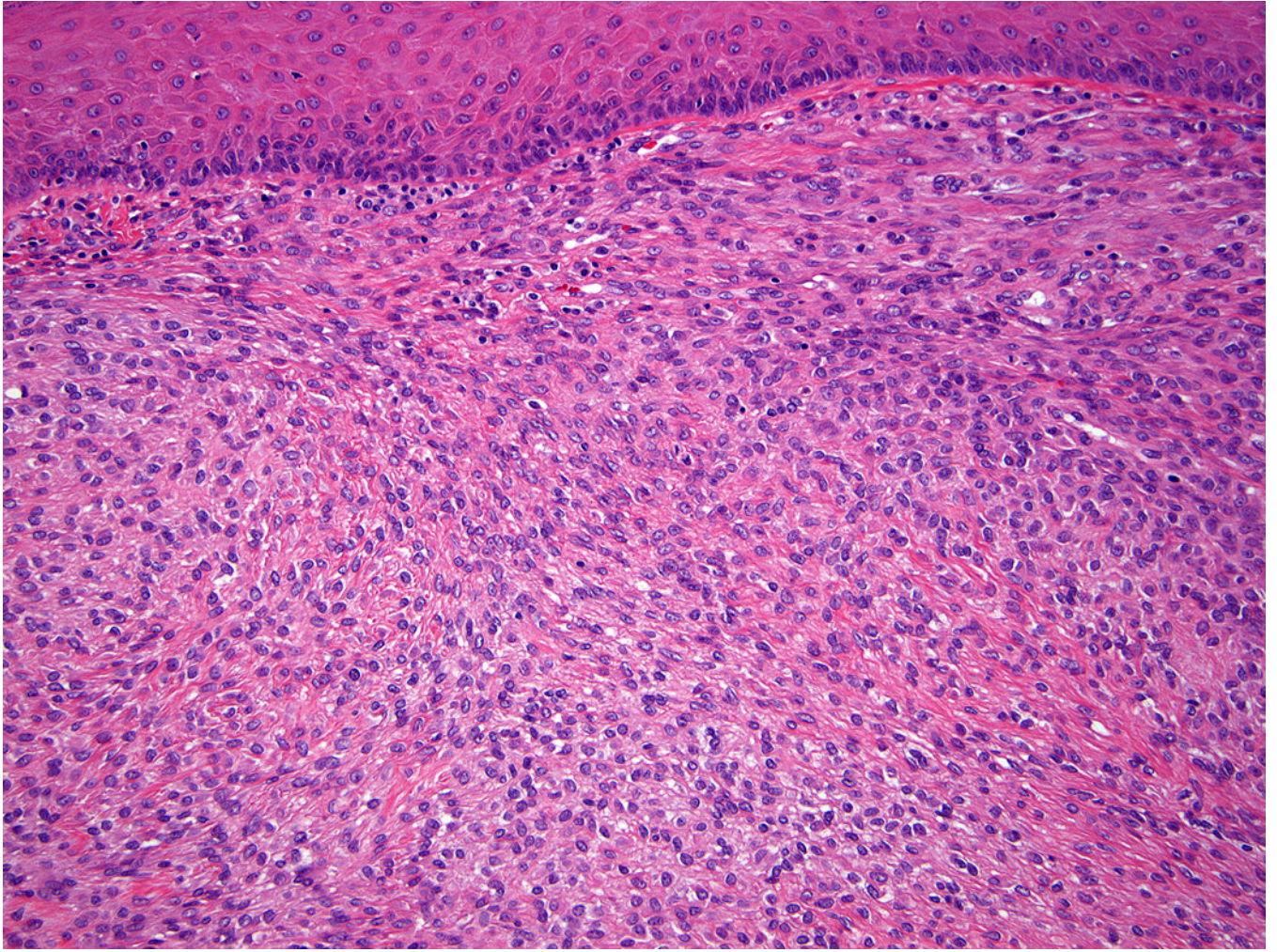
Figure 1.
Most cutaneous syncytial myoepitheliomas were well-circumscribed and unencapsulated
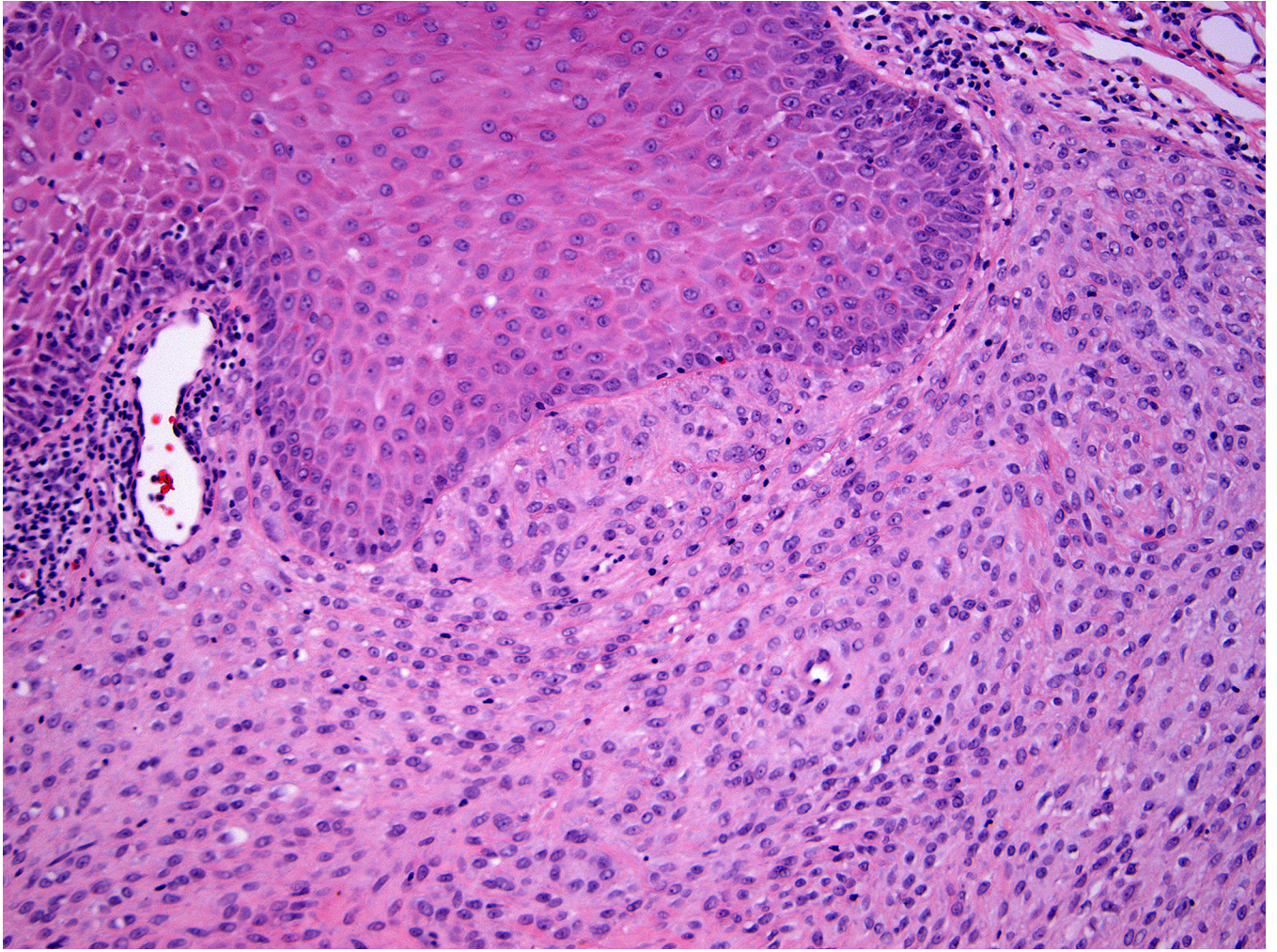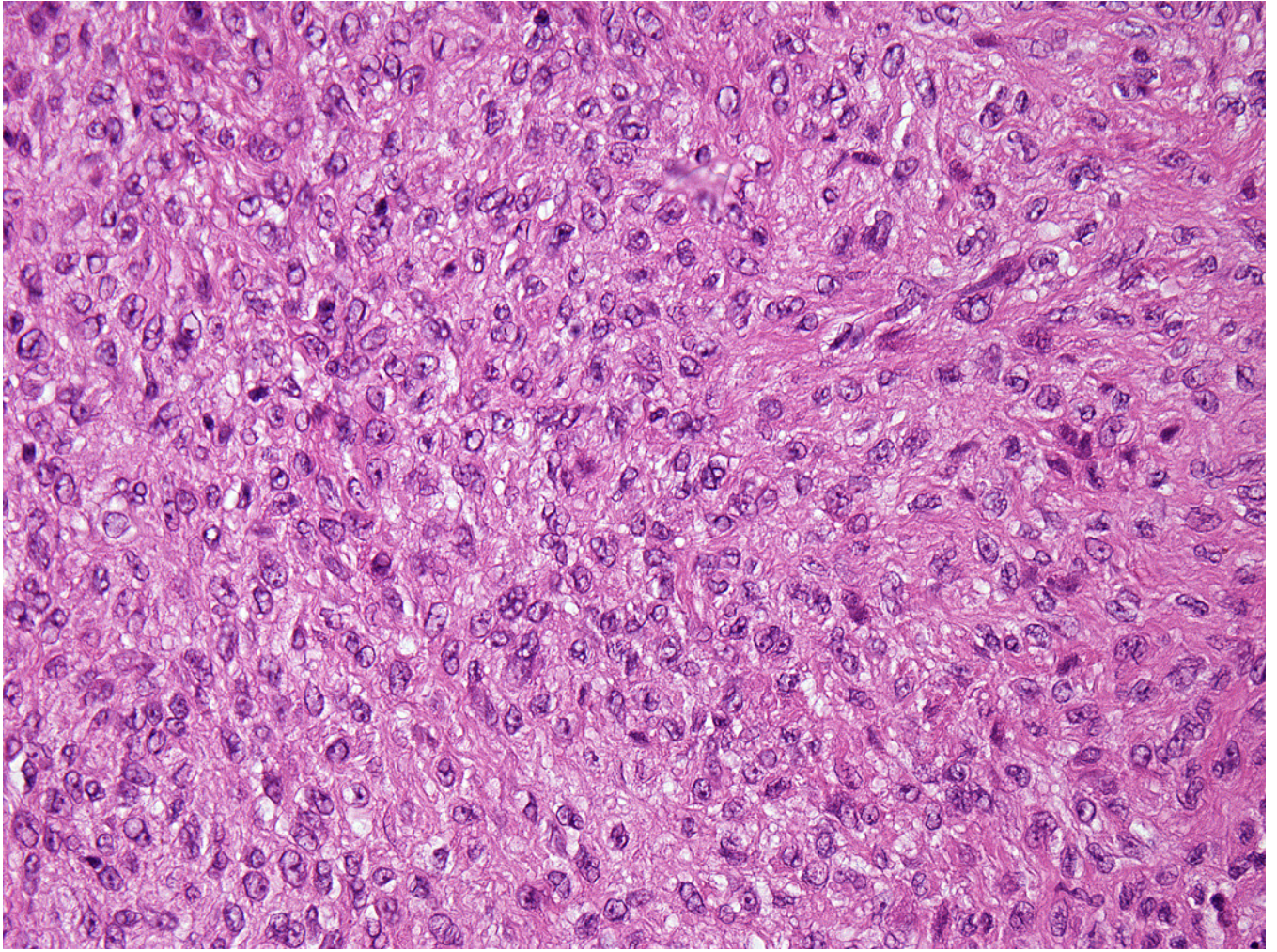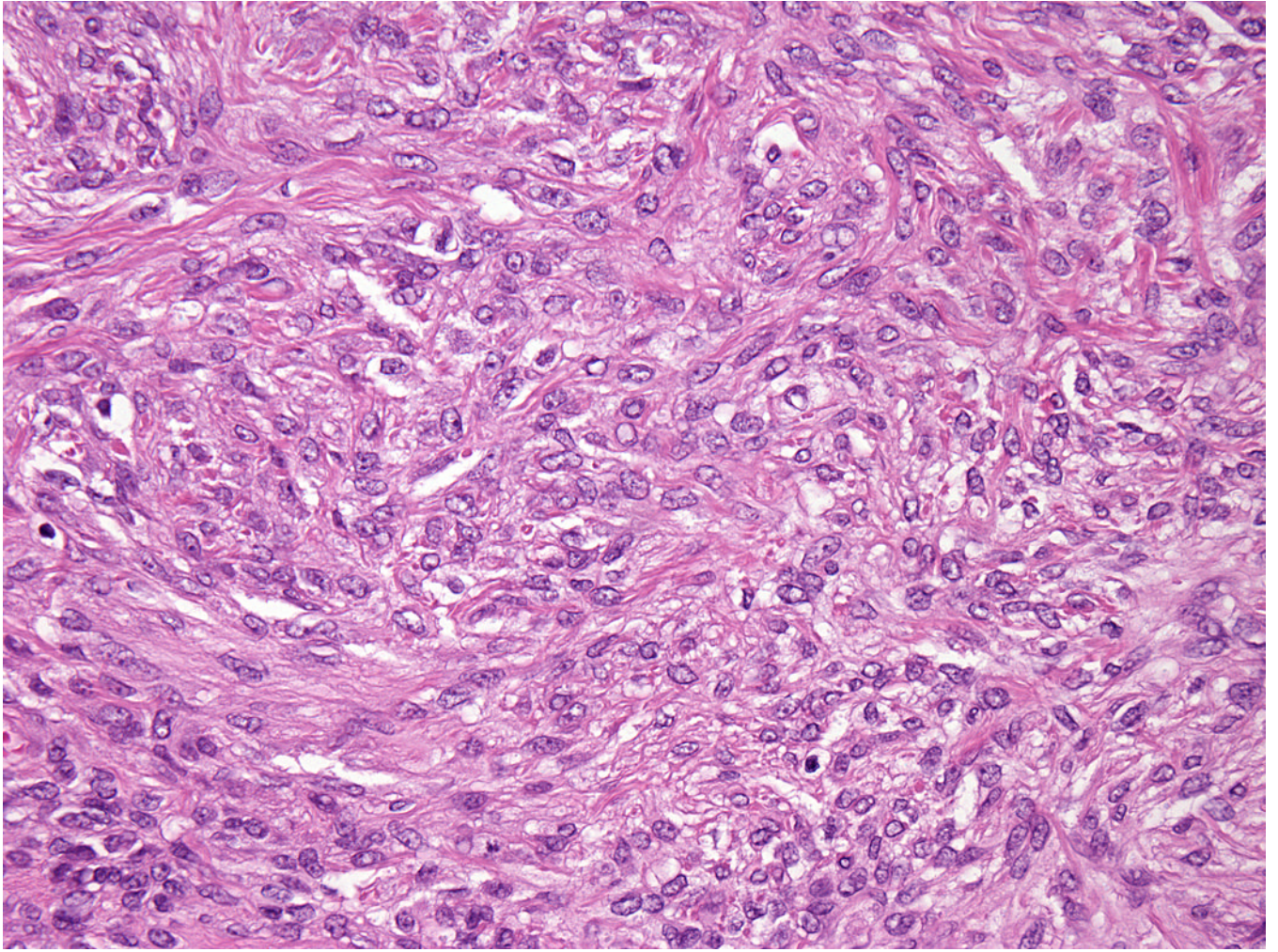(a); some tumors showed adipocytic metaplasia (b).

Figure 2.
Tumors were centered in the dermis and often abutted overlying epidermis (a & b).

Figure 3.
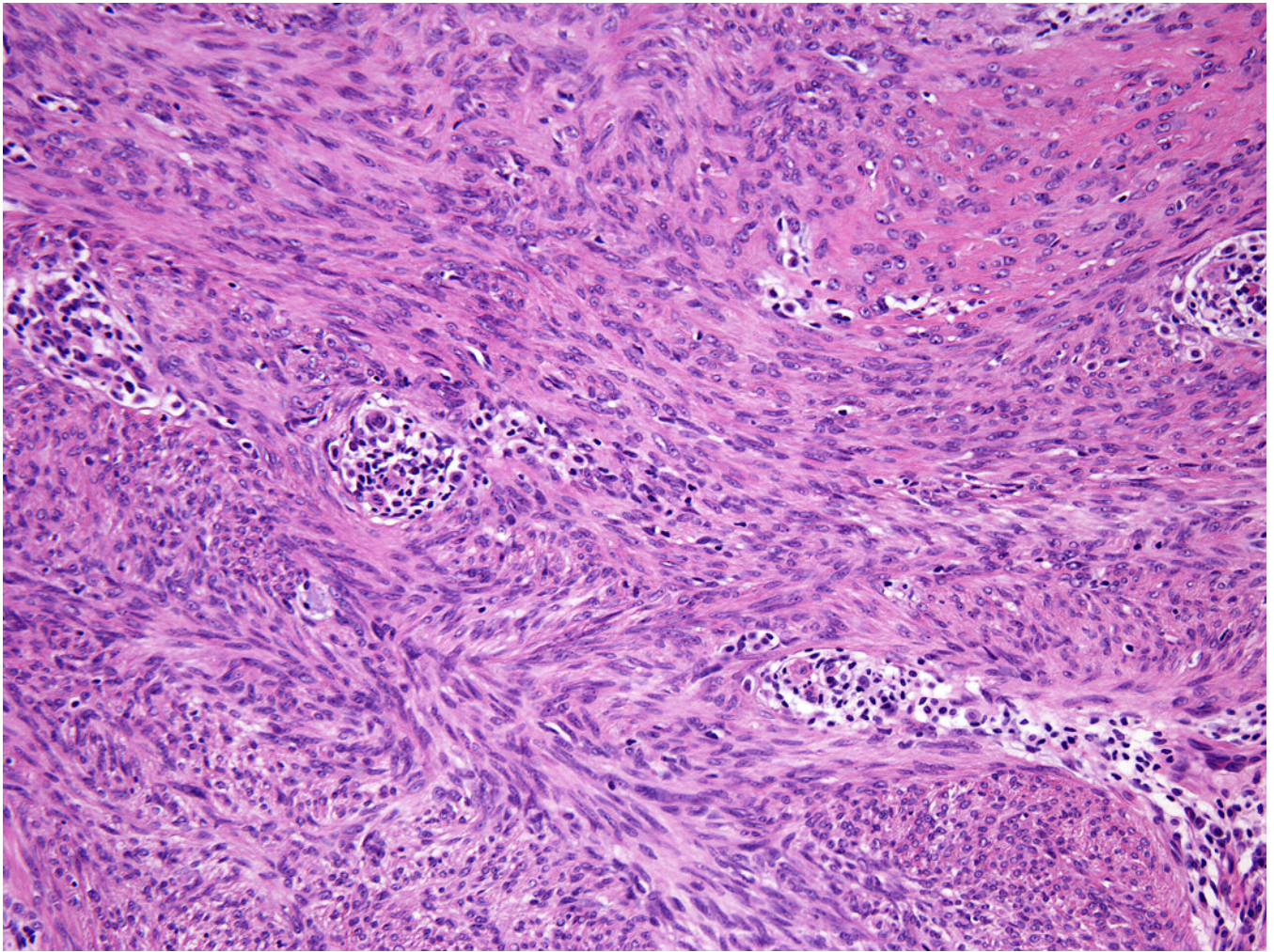All tumors showed a solid sheet-like growth of uniformly sized ovoid to spindled or histiocytoid cells with palely eosinophilic syncytial cytoplasm (3a); most tumors showed no mitotic activity. Nuclei were vesicular with fine chromatin and smooth nuclear contours and had small or inconspicuous nucleoli, with minimal to no atypia (3b). Focally fascicular growth was observed in only one tumor (3c).
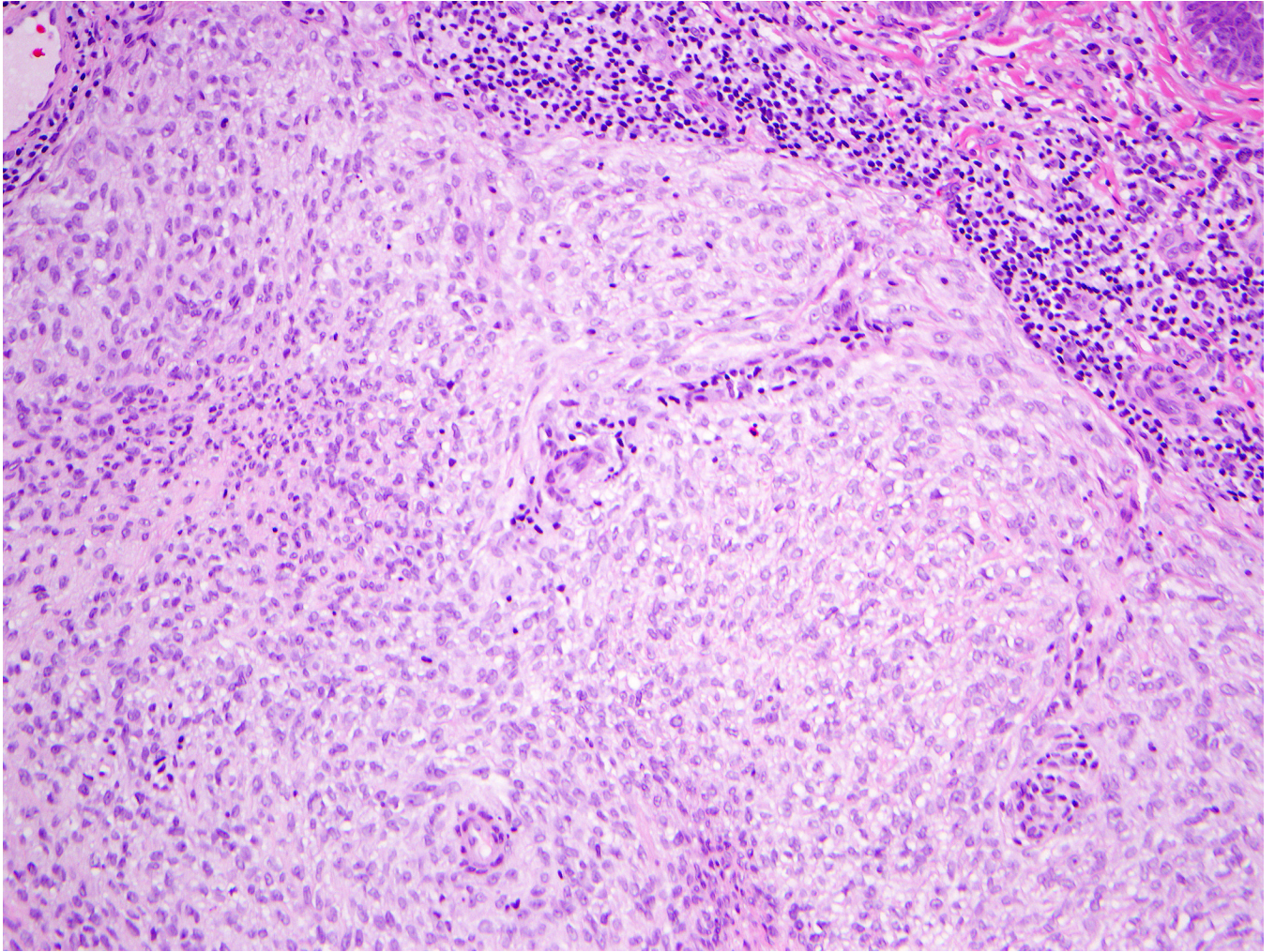
Figure 4.
A subset of tumors showed a minimal-to-moderate lymphoplasmacytic infiltrate, mostly at the periphery.
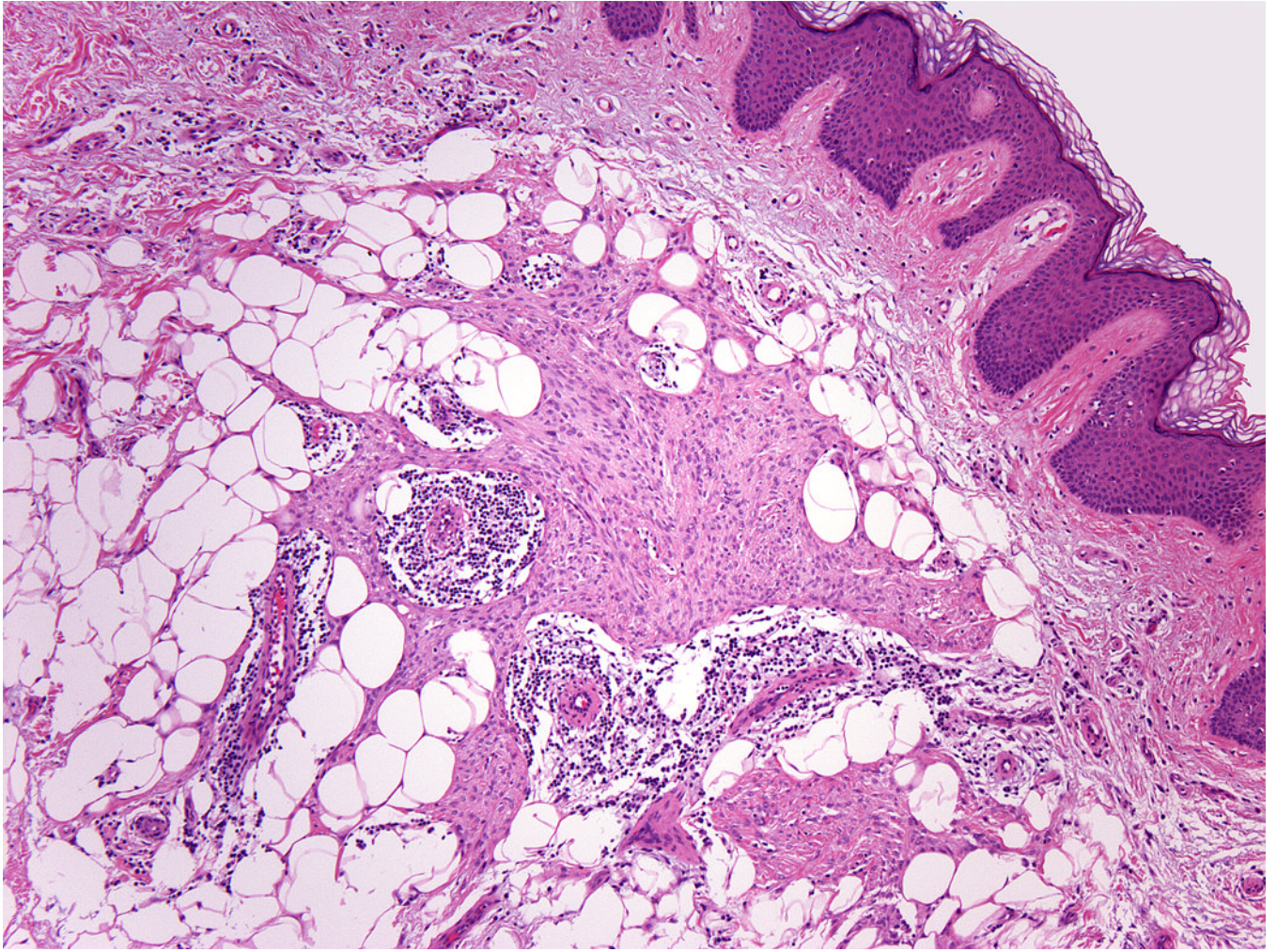
Figure 5.
Adipocytic metaplasia, appearing as superficial fat seemingly entrapped within the tumor, was observed in twelve cases.
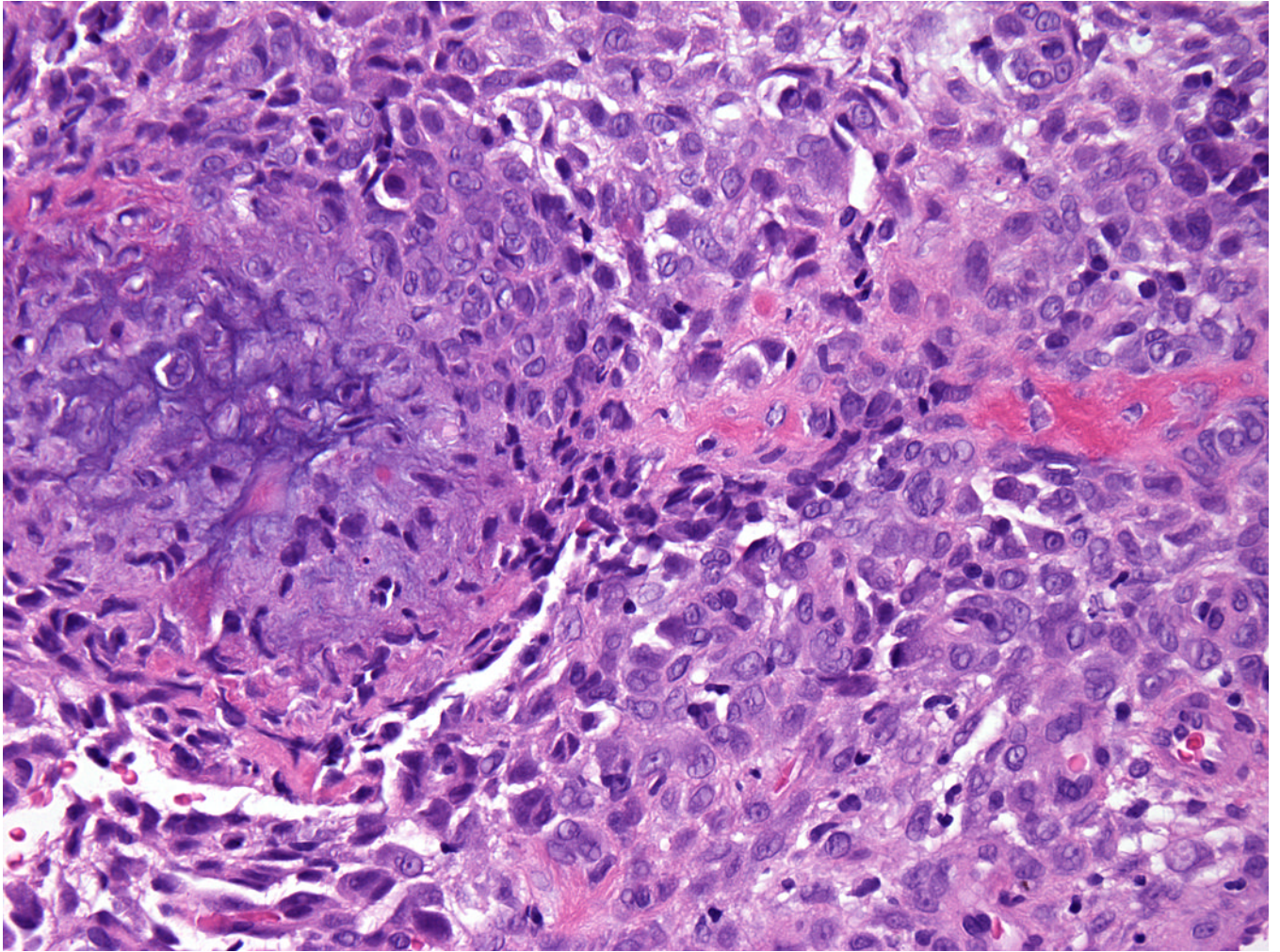
Figure 6.
Chondro-osseous differentiation was seen in one tumor.
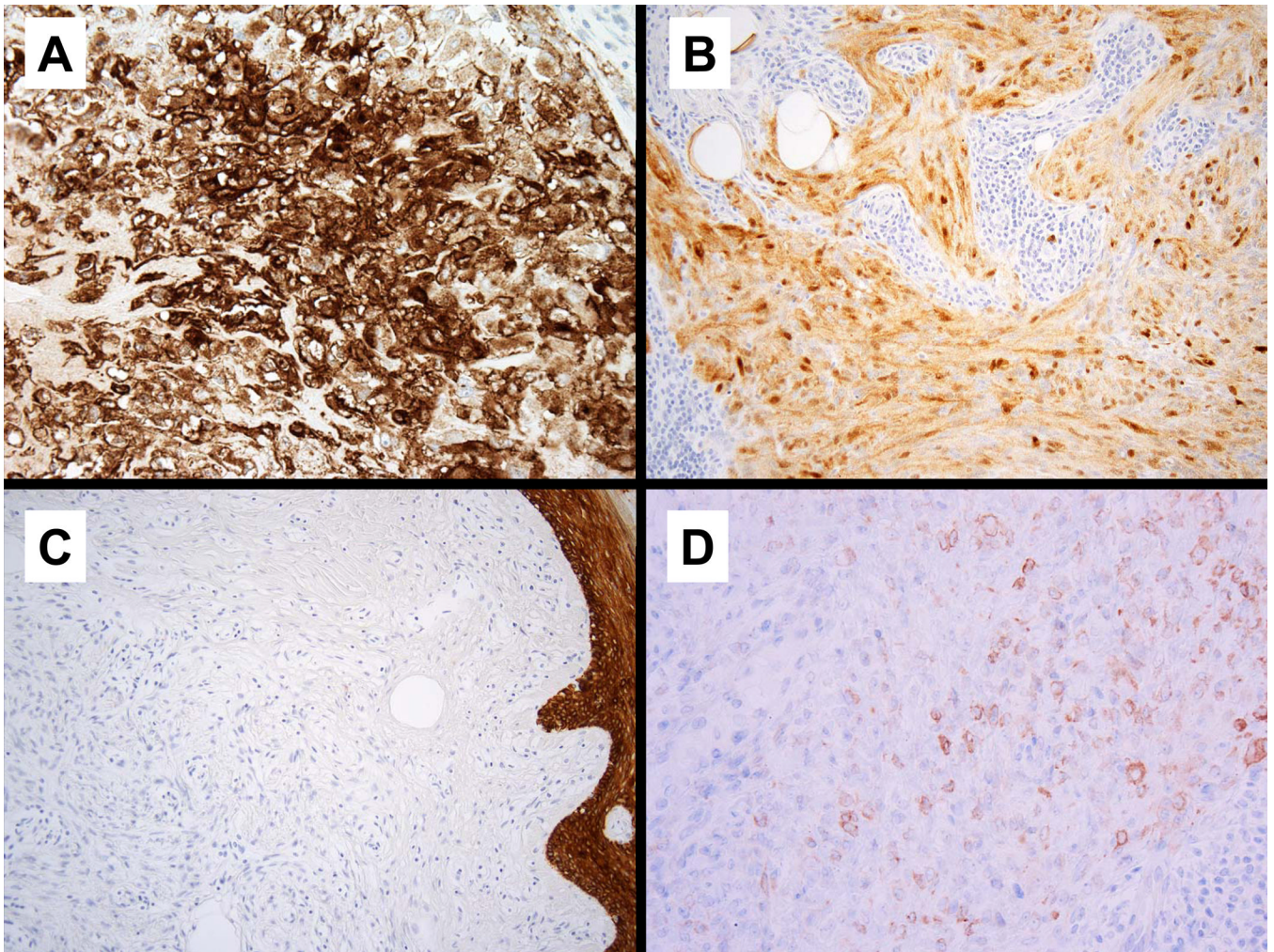
Figure 7.
Immunohistochemical findings. All tumors showed diffuse positivity for EMA (7a) and S100 (7b). The majority of tumors were negative for keratin expression (7c). GFAP staining, when positive, was typically weak and multifocal (7d).
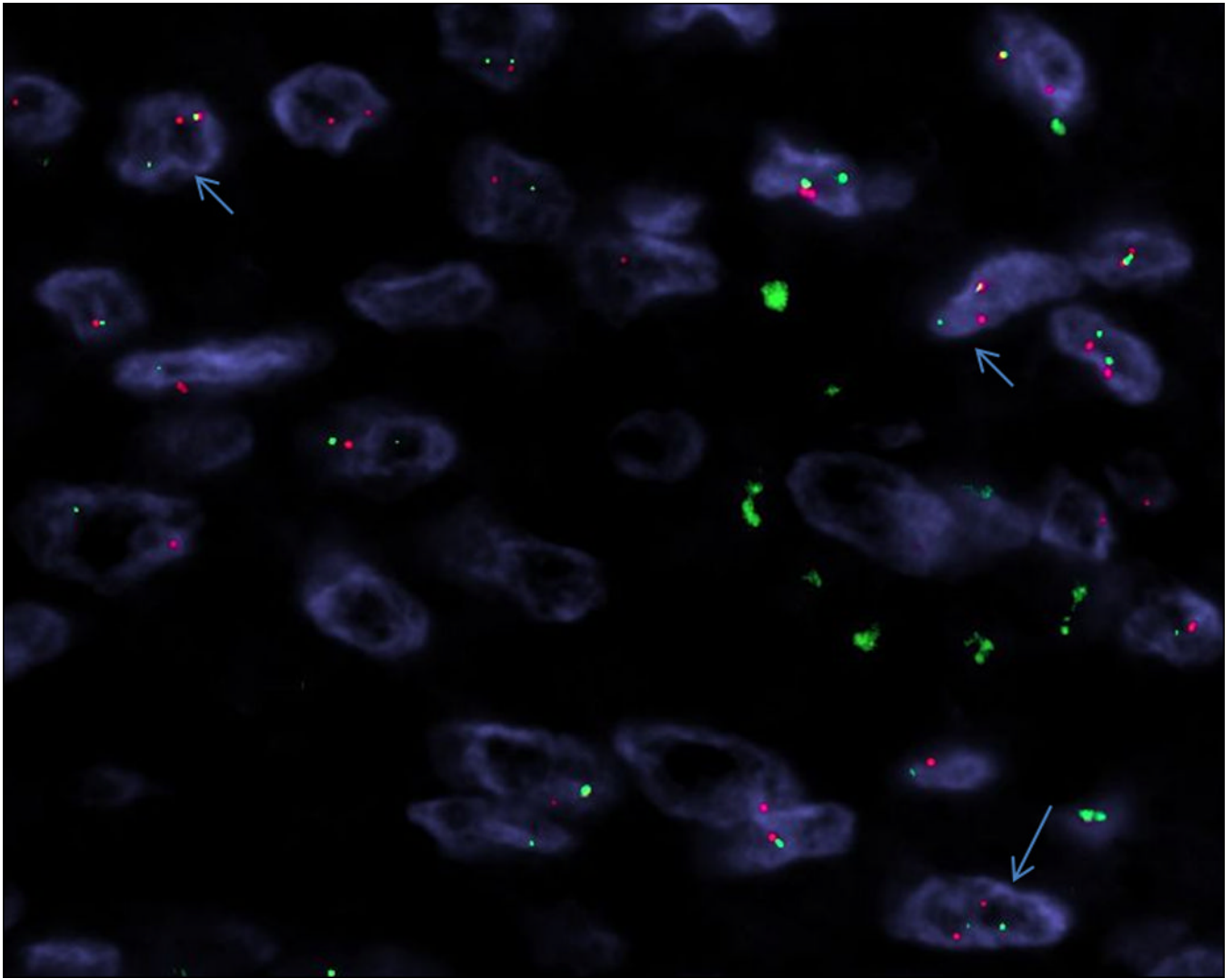
Figure 8.
Fluorescence in situ hybridization (FISH) for the *EWSR1* gene demonstrated a break-apart signal in 14 cases (arrows) (Case 10).

Table 1

Immunohistochemistry: Sources, Clones, Dilutions, and Pretreatment Conditions

| Antibody	Source	Clone	Dilution	Pretreatment
EMA	Dako (Carpinteria, CA	E29	1:200	None
S100 protein	Dako	Polyclonal	1:3000	None
CK (pankeratin)	Dako	MNF-116	1:700	10 min protease digestion
CK (AE1/AE3)	Dako	AE1 + AE3	1:200	10 min protease digestion
CK (CAM 5.2)	Dako	CAM5.2	1:50	10 min protease digestion
GFAP	Dako	Polyclonal	1:15,000	Citrate buffer, pressure cooker
p63	Neomarkers, (Fremont, CA)	4A4	1:600	Citrate buffer, microwave
SMA	Sigma (St. Louis, MO)	1A4	1:20,000	None

Abbreviations: EMA, epithelial membrane antigen; CK, cytokeratin; SMA, smooth muscle actin; GFAP, glial fibrillary acidic protein

Table 2

Clinical Features of 38 Cases of Cutaneous Syncytial Myoepithelioma

Case	Age (years)	Sex	Site, Laterality	Size (cm)	Duration (mo)	Biopsy/Treatment (Margin Status)	Follow-up Status (mo)
1	16	M	Thigh, L	0.7	4.5	Excision (wide)	NED (56)
2	41	M	Palm, L	0.8	240	Excisional bx (wide)	NA
3	52	M	"Digit", R	1.3	3	Excision (wide)	NED (28)
4	15	M	Back	0.5	NA	Bx (positive)	NA
5	20	M	Leg, L	0.5	6	Excision (wide)	NED (18)
6	45	F	Leg, L	0.8	12	Excision (wide)	NED (6)
7	29	M	Arm, R	0.6	NA	Bx (wide)	Lost to f/u
8	24	M	Shoulder, L	0.3	NA	Bx (wide)	NA
9	64	M	Back	0.3	NA	Bx (positive)	NA
10	29	M	Thigh, R	1.9	NA	Excisional bx (positive)	NA
11	45	M	Arm, L	0.6	NA	Bx and excision (positive)	Lost to f/u
12	59	M	Thigh, L	0.7	48	Bx and excision (wide)	NED (1)
13	50	M	Axilla, R	0.9	NA	Bx (positive)	NA
14	68	F	Toe, R	1.0	NA	Excisional bx (positive)	NED (7)
15	26	M	Cheek, L	0.4	NA	Bx (positive)	NA
16	35	M	Heel, L	0.9	24	Excision (wide)	NED (7)
17	26	M	Back	2.7	24	Excision (wide)	NED (36)
18	43	F	Buttock, R	1.0	12	Excision (positive)	NED (22)
19	74	F	Thigh, u/k	1.2	NA	Excisional bx (wide)	NED (4)
20	18	F	Thigh, L	0.5	NA	Excisional bx (wide)	NA
21	25	M	Thigh, R	1.4	NA	Excision (wide)	NED
22	2 mo.	M	Arm, R	2.5	2	Excision (marginal)	NED (30)
23	28	F	Arm, R	0.8	1	Bx and Excision (wide)	NED (9)
24	60	M	Arm, L	1.3	NA	Bx (positive)	NA
25	34	M	Shoulder, L	1.6	NA	Excisional bx (positive)	NED (15)
26	13	M	Arm, R	0.6	NA	Shave bx (positive)	Lost to f/u

Case	Age (years)	Sex	Site, Laterality	Size (cm)	Duration (mo)	Biopsy/Treatment (Margin Status)	Follow-up Status (mo)
27	36	F	Arm, L	1.5	2	Bx and Excision (wide)	NED (14)
28	51	M	Nose	0.5	3	Bx and Excision (wide)	NED (14)
29	50	F	Thigh, R	0.7	12	Excisional bx(wide)	NED (10)
30	39	M	Chest	0.3	NA	Bx (wide)	NA
31	29	M	Thigh, L	1.3	24	Excision (wide)	NA
32	47	F	Toe, R	0.7	NA	Bx (positive)	NA
33	8	M	Arm, R	0.7	NA	Shave bx (positive)	NED (NA)
34	49	F	Arm, L	1.0	NA	Shave bx (positive)	NED (NA)
35	47	F	Back	1.1	NA	Bx (positive)	NA
36	13	M	Back	0.6	NA	Shave bx (positive)	NED (1)
37	39	M	Leg, L	0.6	NA	Shave bx (positive)	Recurrence (51)
38	62	M	Back	0.9	24	Bx (positive)	NA

Abbreviations: Mo., months; L, left; R, right; NA, not available; F/U, follow up; Bx, biopsy; NED, no evidence of disease