Solitary superficial angiomyxoma: an infrequent but distinct soft tissue tumor

Superficial angiomyxoma (SA) is a distinct soft tissue tumor characterized by a circumscribed collection of spindled and stellate fibroblasts that are admixed with thin-walled blood vessels and embedded in a mucinous stroma. Because of its relative infrequent occurrence, the purpose of this article was to present a classical example of an isolated superficial angiomyxoma and discuss the differential diagnosis.

Satter EK. Solitary superficial angiomyxoma: an infrequent but distinct soft tissue tumor.

J Cutan Pathol 2009; 36 (Suppl. 1): 56–59. © 2009 John Wiley & Sons A/S.

Superficial angiomyxoma (SA) is a distinct type of soft tissue myxoma characterized by increased numbers of stellate fibroblasts and thin-walled blood vessels admixed with a variable inflammatory infiltrate. Approximately 30% of lesions additionally contain an entrapped epithelial component consisting of keratin cysts or thin strands of squamous epithelium. Despite the fact that 20–30% of lesions recur, metastases have yet to be described.1–3 Because of its relative infrequent occurrence, the purpose of this article was to present a classical example of an isolated superficial angiomyxoma and discuss the differential diagnosis.

Case report

A 35-year-old African American man presented with a slowly enlarging asymptomatic nodule on his midback treated 9 months previously with liquid nitrogen and again 1 month later. The patient had no history of endocrine abnormalities, lentigines, blue nevi or other neoplasms. On examination, a soft 1-cm well-demarcated pedunculated nodule was noted (Fig. 1).

Histological evaluation of a shave biopsy revealed a dome-shaped lesion containing stellate and multinucleated fibroblasts admixed with numerous small thin-walled blood vessels surrounded by pools of mucin that formed cleft-like spaces (Fig. 2). Lymphocytes were scattered throughout the lesion, and centrally, an abortive follicular structure was appreciated. There was no evidence of epidermal effacement, dermal fibrosis or neovascularization suggestive of the prior treatment. Immunohistochemical stains showed strong labeling of the stellate cells with CD68 and factor XIIIa, but CD34 only labeled the blood vessels (Fig. 3A–C). To date, there is no evidence of recurrence after complete excision.

Discussion

Allan depicted SA as a specific entity in 1988; however, similar tumors had been previously described, albeit by different names, at least 30 years earlier.3 Originally proposed to be synonymous with cutaneous focal mucinosis, myxoid perifollicular fibroma, fibrofolliculomas, trichofolliculomas and trichodiscomas, Calonje et al.9 disagreed with this hypothesis concluding that SA was a distinct entity.2

SA has a slight male predilection, typically presenting between the ages of 20–40 years. Although they preferentially occur on the trunk, extremities and head and neck regions, they can arise in a variety of
The majority of lesions occur in isolation; however, multiple SA, especially those located on the external ear, are considered pathognomonic for Carney complex, an autosomal dominant disorder associated with multiple myxomas (cardiac, cutaneous and mammary), blue nevi, lentigines, psammomatous melanotic schwannoma and endocrine overactivity.\textsuperscript{1–4}

Although the exact incidence is unknown, in the index article, only 27 solitary tumors were identified among 4500 consults seen over 23 years.\textsuperscript{2} To evaluate the incidence at our institution, a Systematized Nomenclature of Medicine (SNOMED) word search engine using the descriptors myxoma, angiomyxoma and superficial cutaneous angiomyxoma was performed within the computerized archives of the

\begin{table}[h]
\centering
\begin{tabular}{llllll}
\hline
 & Age (years) & Gender & Most common location & Size & Associated conditions \\
\hline
Superficial angiomyxoma & 20–40 & 64\% males & 37\% trunk, 33\% lower extremities & Most < 5 cm & Carney’s complex \\
Intramuscular myxoma & 20–89 & 66\% females & 50\% thigh & 2–20 cm & Mazabraud and McCune-Albright’s syndromes \\
Juxta-articular myxoma & 16–83 & 72\% males & 88\% knee & 0.6–12 cm & Degenerative joint disease \\
Aggressive angiomyxoma & 20–50 & 95\% females & Pelvic and perineal regions & Most > 10 cm & None \\
Angiomyofibroblastoma & 25–60 & 99\% females & Pelvic and perineal regions & Most < 10 cm & None \\
Superficial acral fibromyxoma & 14–72 & 68\% males & Nail bed of the fingers and toes & 0.6–5 cm & None \\
Nerve sheath myxoma & 8–72 & 55\% males & 86\% extremities & 0.5–2.5 cm & None \\
\hline
\end{tabular}
\caption{Clinical features of various soft tissue myxomas*}
\end{table}

* Mazabraud syndrome: multiple intramuscular myxomas and fibrous dysplasia of bone. McCune-Albright’s syndrome: multiple intramuscular myxomas, polyostotic fibrous dysplasia, café au lait macules, precocious puberty and other endocrinopathies. Carney’s complex: multiple myxomas (cardiac, cutaneous and mammary), blue nevi, lentigines, psammomatous melanotic schwannoma and endocrine over activity.

\textsuperscript{57}
|                | Margin                              | Vascular pattern               | Cellularity                                 | Stroma                                                | Staining characteristics                         | Recurrence rate |
|----------------|-------------------------------------|--------------------------------|---------------------------------------------|-------------------------------------------------------|---------------------------------------------------|-----------------|
| Superficial angiomyxoma | Poor to moderately circumscribed, multilobular | Scattered thin-walled vessels | Moderately cellular, bland spindled and stellate cells, variable inflammatory cell infiltrate | Abundant mucin with clefts. Up to 30% have an associated epithelial component | Vimentin; variable staining with CD34, factor XIIa, SMA, MSA and S-100 | 20–30%          |
| Intramuscular myxoma | Poorly circumscribed merges with surrounding muscle | Hypovascular variant; hypervascular variant | Hypocellular variant; hyper cellular variant; bland spindle cells | Abundant mucin with cystic spaces. Hypercellular variant has strands of collagen | Vimentin; variable staining with actin, desmin, CD34 | None            |
| Juxta-articular myxoma | Poorly circumscribed infiltrates surrounding tissue | Focally vascular              | Focally hypercellular, peripheral spindle cells with occasional atypical cells and mitoses | Abundant mucin, 89% of cases contain cystic spaces lined by fibrin or collagen | Vimentin; variable staining with actin, desmin, CD34 | 34%             |
| Aggressive angiomyxoma | Infiltrative                        | Uniformly distributed medium-sized blood vessels often with prominent hyalinization | Low to moderately cellular, evenly distributed round, spindled or stellate cells | Loose myxoid to focally collagenous | Vimentin, desmin, SMA, MSA, estrogen and progesterone receptor | 36–72%          |
| Angiomyofibroblastoma | Well circumscribed                 | Abundant thin-walled blood vessels | Alternating hypercellular and hypocellular areas, perivascular condensations of spindled to epithelioid stromal cells | Collagenous to edematous with minimal mucin | Vimentin, desmin, CD34, estrogen and progesterone receptor | No recurrences reported, but rare cases of sarcomatous degeneration |                  |
| Superficial acral fibromyxoma | Pushing to infiltrative            | Mild to moderately accentuated vasculature | Moderately cellular, spindle and stellate cells with a storiform to fascicular pattern, variable mast cells | Myxoid to collagenous | CD34, EMA, CD99 | Recurrence rare and primarily for incompletely excised lesions |                  |
| Nerve sheath myxoma | Well circumscribed, multilobular   | Hypovascular                   | Moderately cellular, spindled cells in fascicles and whorls | Nests of cells separated by collagenous bundles | S-100, EMA | 47% if incompletely excised |                  |

EMA, epithelial membrane antigen; MSA, muscle-specific actin; SMA, smooth muscle actin.
Department of Pathology, Naval Medical Center San Diego. Over the past 10 years, approximately 180,000 surgical pathology cases were examined and only two cases, other than the one that is the subject of this article, were identified. Because our population is somewhat skewed, several other dermatopathologists at various institutes were queried, and SA represented approximately 0.0008% (14/1,680,000) of all specimens accessioned. Of the two soft tissue pathologists questioned, SA represented less than 0.3% (175/59,500) of all soft tissue neoplasms; therefore, SA is infrequently encountered in routine practice.

The differential diagnosis of SA is extensive; nevertheless, the most common benign neoplasms include intramuscular myxoma, juxta-articular myxoma, aggressive angiomyxoma, angiomyofibroblastoma, superficial acral fibromyxoma, and nerve sheath myxoma. While clinical and histological overlap exists among these entities, they are readily differentiated by characteristic clinicopathological findings (Tables 1 and 2). Other benign entities with extensive mucinous stroma include ganglion cysts, focal mucinosis, myxoid neurofibroma and angiomylipoma. Lastly, a few malignant myxomatous tumors should be included in the differential diagnosis, particularly with large lesions that extend deep, namely myxofibrosarcoma, fibromyxoid sarcoma, myxoid liposarcoma, myxid dermatofibrosarcoma protuberans and myxoid malignant peripheral nerve sheath tumor.

Almost all reported cases that have utilized immunohistochemical stains have been immunoreactive with vimentin and negative with desmin and cytokeratin. The staining results for CD34, smooth muscle actin, muscle-specific actin, S-100 and factor XIII A have been more variable. The case presented herein had a slightly different immunophenotype compared with previously reported cases. Although the spindled and multinucleated cells strongly labeled with factor XIII A, a finding reported in approximately 53% of cases that have utilized this stain, these cells failed to stain with CD34, which has been expressed in approximately 71% of cases. Furthermore, the lesion strongly expressed CD68, a finding that has not been previously reported. However, since the use of CD68 has been infrequently reported in the literature, the positive staining of the current case may not be unique and requires further investigation.

In conclusion, the features most useful to differentiate a SA from other myxoid tumors include its superficial location, lack of atypia, stromal inflammatory infiltrate and a frequent association with an entrapped epithelial component. It is essential that dermatopathologist be aware of this entity to avoid confusion with more aggressive myxoid tumors.

References

1. Allen PW. Myxoma is not a single entity: a review of the concept of myxoma. Ann Diagn Pathol 2000; 4: 99.
2. Allen PW, Dymock RB, MacCormac LB. Report of 30 tumors in 28 patients. Am J Surg Pathol 1998; 12: 519.
3. Calonje E, Guerin D, McCormick D, Fletcher CD. Superficial angiomyxoma: clinicopathologic analysis of a series of distinctive but poorly recognized cutaneous tumors with tendency for recurrence. Am J Surg Pathol 1999; 23: 910.
4. O’Connell JX, Nielsen GP. Benign myxoid fibroblastic tumors of soft tissue: the “Myxomas”. Pathol Case Rev 2002; 7: 146.
5. Fetsch JE, Laskin WB, Miettinen M. Superficial angiomyxoma (cutaneous myxoma): a clinicopathologic study of 17 cases arising in the genital region. Int J Gynecol Pathol 1997; 16: 325.
6. Fetsch JE, Laskin WB, Miettinen M. Superficial acral fibromyxoma: a clinical and immunohistochemical analysis of 37 cases of a distinctive soft tissue tumor with predilection for the fingers and toes. Hum Pathol 2001; 32: 704.
7. Steeper TA, Rosai J. Aggressive angiomyxoma of the female pelvis and perineum. Report of nine cases of a distinctive type of gynecologic soft-tissue neoplasm. Am J Surg Pathol 1983; 7: 463.
8. Fletcher CD, Tsang WY, Fisher C, Lee KC, Chan JK. Angiomylipoblastoma of the vulva. A benign neoplasm distinct from aggressive angiomyxoma. Am J Surg Pathol 1992; 16: 373.
9. Fetsch JE, Laskin WB, Miettinen M. Nerve sheath myxoma: a clinicopathologic and immunohistochemical analysis of 57 morphologically distinctive, S-100 protein and GFAP-positive, myxoid peripheral nerve sheath tumors with a predilection for the extremities and high local recurrence rate. Am J Surg Pathol 2005; 29: 1615.
10. Bedlow AJ, Sampson SA, Holden CA. Congenital superficial angiomymphoma. Clin Exp Dermatol 1997; 22: 237.
11. Yeun HK, Cheuk W, Lai FO, Wat CS, Auyeung KC, Lam DS. Solitary superficial angiomyxoma of the eyelid. Am J Ophthalmol 2003; 139: 1141.
12. Wilk M, Schmoeckel C, Kaiser HW, Hepple R, Kreysel HW. Cutaneous angiomyxoma: a benign neoplasm distinct from cutaneous mucinosis. J Am Acad Dermatol 1995; 33: 353.
13. Khandlikar UN, Khandlikar NF, Rao PS, Chakraborty S, Goel G. Superficial angiomyxoma of the external ear not associated with Carney’s complex: a case report Kathmandu Univ Med J 2007; 5: 546.
14. Nakayama H, Hiroi M, Kiyoku H, Naruse K, Enzan H. Superficial angiomyxoma of the right inguinal region: report of a case. Jpn J Clin Oncol 1997; 27: 200.
15. Hidayat AA, Flint A, Marenolette L, et al. Myxomas and angiomyxomas of the orbit. Ophthalmology 2007; 114: 1012.
16. Yu C, Cheuk W, Lai FO, Wat CS, Auyeung KC, Lam DS. Superficial angiomyxoma of the eyelid. Am J Ophthalmol 2003; 139: 1141.

Note added after online publication: conflicts of interest
None declared.