Distinctive clinicopathologic features of the common myxoid soft-tissue lesions

Meredith E Pittman

Elizabeth A Montgomery

Abstract

Myxoid change is a nonspecific finding in soft tissue tumours and can be encountered in sarcomas, benign soft tissue neoplasms, and even reactive lesions. For this reason, tumours that are intrinsically myxoid often present a diagnostic dilemma, especially if limited material is available for study. Here we provide a detailed description of four commonly encountered myxoid neoplasms: myxoma, myxoid liposarcoma, myxofibrosarcoma, and low grade fibromyxoid sarcoma. The accompanying differential diagnosis for each will aid the pathologist in the correct classification of myxoid soft tissue tumours.

Keywords low grade fibromyxoid sarcoma; myxofibrosarcoma; myxoid liposarcoma; myxoma; superficial angiomyxoma

Introduction

Soft tissue sarcomas are quite rare, estimated to comprise less than 1% of the malignant tumours encountered by pathologists each year.[1] Several of these soft tissue sarcomas are characterized by prominent myxoid stroma, a distinguishing feature that can aid in classification of the sarcoma. Benign soft tissue lesions may also have myxoid stroma, however, and the benign lesions are approximately 100-times more common than their malignant counterparts.[2] Unsurprisingly, many pathologists are uncomfortable with myxoid lesions.

Differentiating the myxoid soft tissue lesions requires knowledge of the clinical, radiologic, and histologic findings. Ancillary studies, including immunohistochemical stains and molecular tests, can be helpful when used in the appropriate setting. In this review, we describe how to distinguish between common benign and malignant myxoid soft tissue lesions so that practicing pathologists will have the tools to do the same.

Myxomas

Myxomas are characterized by abundant extracellular mucin in an otherwise hypocellular background of fibroblasts and myofibroblasts. Myxomas may occur in superficial, deep, and organ-based sites. While most are thought to be neoplastic, the juxta-articular variant may, in fact, be a reactive phenomenon related to injury.[3] The intramuscular and cutaneous variants are discussed here.

Intramuscular myxoma

Intramuscular myxomas are most commonly found in middle-aged women in the proximal extremities and limb girdle. They are poorly vascularized and have a water-like character (high T2 signal) on pre-operative MR imaging.[4] Although most are sporadic, a percentage of intramuscular myxoma are associated with Mazabraud syndrome (myxomas and fibrous dysplasia) or Mcune–Albright syndrome (myxomas, fibrous dysplasia, cutaneous hyperpigmentation, and endocrine abnormalities). Both sporadic and syndromic intramuscular myxomas have been found to have *GNAS* mutations.[5]

On gross examination, intramuscular myxomas are grey, myxoid, and relatively well demarcated. Microscopically, however, the myxoid matrix can infiltrate the surrounding atrophic and oedematous skeletal muscle. This infiltration can be in broad zones or thin strands of myxoid matrix. The lesion itself is classically paucicellular. (Figure 1) Scattered fibroblasts and myofibroblasts are seen in the myxoid matrix. Blood vessels are scant and consist of small capillaries or thicker walled vessels. Collagenous stroma may be focally present. Histiocytes are often numerous and can mimic lipoblasts if foamy; the myxoid matrix may also have "bubbles" that give the appearance of lipoblasts on low power.

A subtype of intramuscular myxomas have been termed "cellular myxomas" due to the increase in both cellularity and vascularity[6] In this subtype of myxoma, the majority of the lesion may be made up of spindled or stellate cells with only focal areas of paucicellular myxoid matrix. (Figure 2) Nevertheless, nuclear pleomorphism, hyperchromatic nuclei, and necrosis should be absent in any type of intramuscular myxoma. Mitotic figures are very rarely identified.[6]

The treatment for intramuscular myxoma is simple excision. There is no risk of metastasis, and a low risk of local recurrence even with the cellular variant.

The main differential diagnosis for intramuscular myxoma includes two sarcomas that do carry a risk of metastases: myxoid liposarcoma and low grade myxofibrosarcoma. Both of these entities will be described in detail later. Briefly, myxoid liposarcoma has a characteristic delicate capillary network that is lacking in myxoma, while low grade myxofibrosarcoma contains hyperchromatic and pleomorphic nuclei that should not be seen in myxoma. If immunohistochemical stains are used, myxomas show focal positivity for CD34 and SMA, but are nonreactive for S100 or desmin. Myxofibrosarcoma may also be positive for CD34. In contrast, myxoid liposarcomas have focal S100 reactivity and lack CD34.

Cutaneous myxoma/superficial angiomyxoma

Although histologically similar to intramuscular myxomas, cutaneous myxomas are otherwise different tumours. Often called superficial angiomyxoma, these lesions occur most commonly on the trunk and head and neck area. Sporadic lesions have a slight male predominance and occur in middle age, while syndromic lesions have no gender difference and arise in younger patients.

Meredith E Pittman *MD Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA. Conflicts of interest: none.*

Elizabeth A Montgomery *MD Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD, USA. Conflicts of interest: none.*

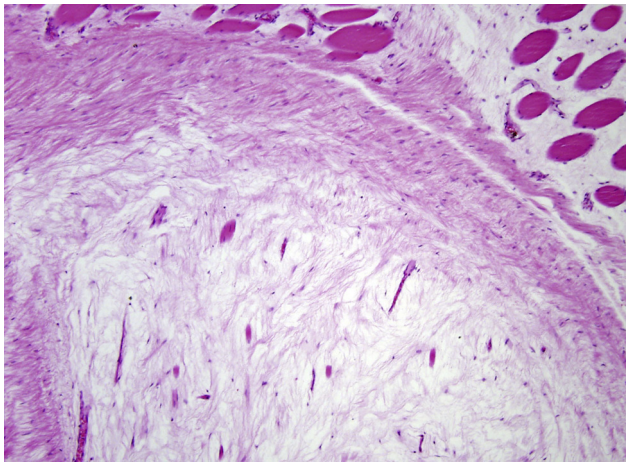

Figure 1 Intramuscular myxoma with lobules of paucicellular myxoid matrix, unremarkable blood vessels, and oedematous skeletal muscle at the edge of the lesion.

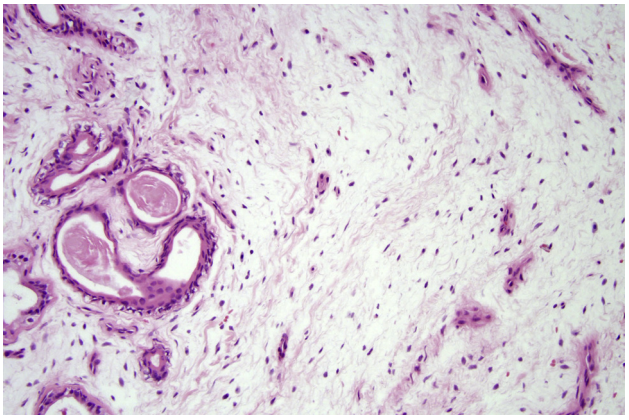

Figure 3 Cutaneous myxoma/Superficial angiomyxoma. This lesion has bland spindled cells, a variable number of blood vessels, and sometimes entrapped adnexal elements that can be mistaken for malignancy.

Cutaneous myxomas can be found in the dermis or in the subcutaneous tissues and should present as a painless mass. As with intramuscular myxoma, the histologic appearance is one of abundant extracellular mucin with bland spindled or stellate supporting cells and an increased number of blood vessels. Importantly, entrapped adnexal elements are found in this lesion up to 25% of the time[7] (Figure 3).

The diagnosis of a cutaneous myxoma will often prompt clinicians to consider Carney complex. The majority of families with Carney complex, which is transmitted in an autosomal dominant fashion, have been found to have mutations in the *PRKAR1A* gene on chromosome 17q.[7] Patients with Carney complex have both cutaneous and cardiac myxomas, characteristic skin pigmentation, and various endocrine abnormalities.[8]

The importance of making the syndromic diagnosis is in locating and monitoring cardiac myxomas, which may cause intracardiac obstruction or sudden embolization. Cutaneous myxomas, on the other hand, are merely an irritation to patients, and up to one-third of them locally recur after excision. There is no metastatic potential for these lesions.[3]

The differential diagnosis for cutaneous myxoma/superficial angiomyxoma is broader than for that of the deep intramuscular myxoma, although the list predominantly consists of other benign lesions. The superficial acral fibromyxoma is a painful lesion found on the palm, sole, or periungual region that also has myxoid matrix and stellate fibroblasts. Besides the characteristic site, microscopic clues to this diagnosis versus a myxoma are increased bland cellularity in a fascicular or storiform pattern, increased vascularity, and prominent mast cells. (Figure 4) The lesional cells are reactive for CD34, but negative for S100 and desmin. Local excision is the treatment, although up to a quarter of superficial acral fibromyxomas recur.[9]

Another cutaneous lesion with myxoid stroma is the myxoid neurothekeoma. These lesions usually arise in younger patients

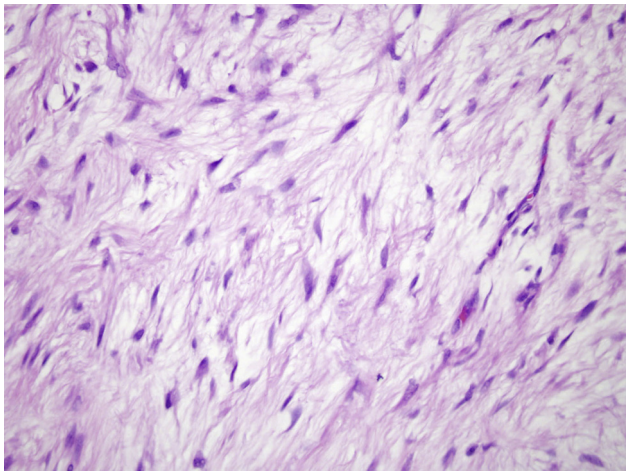

Figure 2 Cellular intramuscular myxoma. Although there is increased cellularity, the constituent fibroblasts and myofibroblasts have open chromatin with indistinct stellate or spindled cytoplasm. The blood vessels remain unremarkable, with the exception that the endothelial cells may be more hyperchromatic that the lesional cells (a reassuring finding).

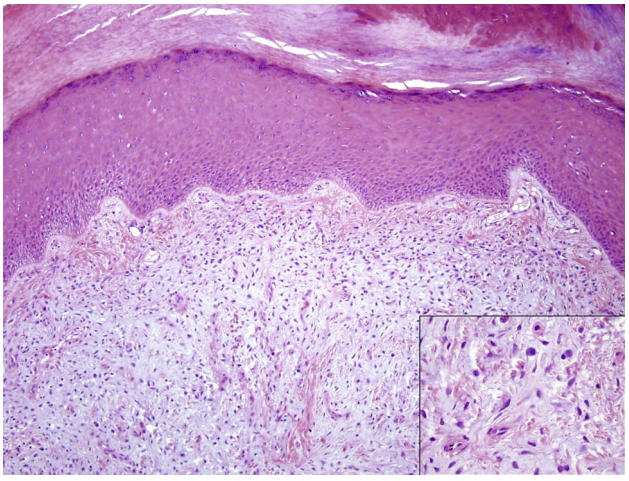

Figure 4 A superficial acral fibromyxoma has increased cellularity, including mast cells (inset), and numerous unremarkable vessels. The lesions are classically found around nails or on the palms/soles.