Problem-Prone Soft Tissue Lesions with a Potential for Litigation

Sharon W. Weiss, MD
Professor of Pathology
Associate Dean

Emory University School of Medicine

BULLET POINTS

1. Understand the incidence of serious errors in soft tissue pathology and how the method of ascertainment affects one's perception of the problem.

2. Develop an awareness of the most common situations and/or lesions in soft tissue pathology that give rise to potentially litigious errors.

3. Understand the reasons that underlie these mistakes and develop a strategy or approach to avoid them.

INTRODUCTION

Although there are numerous problem-prone situations in soft tissue pathology, this lecture will focus on those in which a misdiagnosis significantly alters therapy or prognosis such that a malpractice claim could arguably ensue. How one identifies this group of lesions and assesses their relative importance is influenced by the method of ascertainment. In other words, the manner in which a misdiagnosed case comes to one's attention can influence our perception of which lesions are problem-prone. For example, a retrospective study of sarcomas referred to a northwest England regional cancer registry found that 22% of cases were not sarcomas following review of an expert panel.[1] On the other hand, a large review of referral material submitted on patients undergoing therapy at a large tertiary care center, found that in 1.4% (86 of 6171) the diagnosis was changed.[2] Of these 86 cases only 1% involved soft tissue lesions, an incidence that roughly paralleled the incidence of soft tissue lesions in the group as a whole. This could be construed as indicating that significant misdiagnoses in soft tissue are a minor problem.

More recently Troxel has analyzed "diagnostic pitfalls" in surgical pathology based on an review of actual malpractice claims submitted to The Doctors Company, a physician-owned professional liability insurer of approximately 10% of pathologists in this country. Although approximately one half of claim cases displayed no error pattern and were therefore considered "random errors," the other half fell into a number of "repetitive" patterns indicating "systematic cognitive error."[3] The most common systematic cognitive errors related to melanoma and breast biopsy diagnosis; each accounted for 15% of all claims. The diagnosis of sarcomas, also considered among systemic cognitive errors, accounted for about 5% of all malpractice claims and, therefore, are disproportionately represented relative to the rarity of the disease. Furthermore, litigation more often centered around the failure to diagnose malignancy (false negative diagnosis) than the over diagnosis of malignancy (false positive).

Claim cases, however, represent the end result of numerous failed opportunities to either diagnose the case correctly or to resolve the case short of a malpractice claim. The study by Arbiser et al, which analyzes soft tissue cases referred for expert consultation, gives a more balanced view of problematic lesions. The authors found that 25% of cases referred for consultation with an accompanying diagnosis underwent a diagnostic change. These could be broken down into the following categories: benign mesenchymal lesions diagnosed as sarcomas (45%), sarcomas

diagnosed as benign lesions (23%), non-mesenchymal lesions diagnosed as mesenchymal tumor (20%), and significant grading errors (12%). Interestingly, this study found that a relatively few number of lesions led to a majority of major diagnostic discrepancies (e.g. nodular fasciitis, desmoplastic melanoma) suggesting that heightened awareness of a few lesions could significantly reduce diagnostic discrepancies.

PROBLEM PRONE SITUATIONS

The following problem-prone categories will be discussed and illustrated with cases:

Low grade spindle cell sarcomas

One of the most common situations that leads to litigation is the failure to recognize a low grade spindle cell sarcoma as a malignant. The best example is the **monophasic synovial sarcoma**. In fact, in the study by Troxel one third of all claims involving false negative diagnosis of sarcoma were monophasic synovial sarcomas. In its classic form the synovial sarcoma is a densely cellular spindle cell sarcoma having a fascicular growth pattern and expressing EMA and cytokeratin in about 90% and 60% of cases respectively. The principal reasons for false negative diagnoses are:

- Long clinical duration such that the clinician has prejudged the lesion to be benign
- The lesions appears hypocellular because it is myxoid, densely hyalinized, calcified, or infiltrates between tendinous connective tissue.
- Immunostains for keratin and/or EMA are not performed or the presence of S100 protein, which occurs in about one third of cases, is interpreted as evidence of benign nerve sheath tumor

The common non-malignant diagnoses that are rendered for monophasic synovial sarcoma are fibroma, calcifying aponeurotic fibroma, fibromatosis, and neurofibroma
The diagnosis of monophasic synovial sarcoma should be suspected in low grade spindle cell proliferations on the extremities of young adults, especially if calcified. The appropriate immunostains should be ordered and confirmed by molecular genetic testing for the unique and specific t(X;18) in questionable cases

Low grade fibromyxoid sarcoma (LGFMS) , a relatively recently described lesion, usually develops in the deep soft tissue of the extremities of young to middle aged patients.[5,6] Consisting of fibromatosis-like areas that merge with highly myxoid zones containing an arborizing vasculature they have a “mosaic” or marble-like appearance at low power. The cells vary from oval to spindled and in some cases encircle large nodules of collagen leading to the formation of giant collagen rosettes. Prior to the description of this tumor by Evans, the majority of LGFMS were probably diagnosed as fibromas or fibromatosis. The features that distinguish this tumor from fibromatosis are the mosaic architectural pattern, greater degree of nuclear atypia and hyperchromatism, and highly vascularized myxoid zones. Recently, a t(7;16)[7] has been identified in this tumor and can serve as a molecular test to distinguish this lesion from other myxoid and fibroblastic lesions.[8] Unlike fibromatosis which never metastasize, LGFMS metastasizes in about 10% of cases; therefore, failure to separate this lesion from fibromatosis may have untoward consequences.

Reactive Lesions

Reactive lesions are among the most common soft tissue lesions encountered in routine practice. They group include, nodular fasciitis and its numerous variants (cranial, intravascular, proliferative, ischemic) and bone-producing pseudotumors (myositis ossificans, panniculitis ossificans, reactive periostitis).[9] The prototype of all of these lesions, nodular fasciitis, is classically a small (<3 cm) and superficially located lesion that evolves relatively rapidly and then stabilizes. It has a variegated appearance at low power consisting of short fascicles of mitotically active myofibroblasts alternating with myxoid and microcystic areas. The myofibroblast, common to all these reactive lesions, is a plump spindled cells with vesicular nuclear chromatin pattern and an eosinophilic to amphophilic cytoplasm. Misdiagnosis of nodular fasciitis as a sarcoma usually results when undue emphasis is given to the presence of mitotic figures without noting the lack of nuclear atypia or hyperchromatism or in assuming that the presence of actin within myofibroblasts is reflective of smooth muscle differentiation—hence a leiomyosarcoma. However, other pitfalls in the diagnosis of reactive lesions can be ascribed to unfamiliarity with the unique features of some of the variants—for example the large size of ischemic fasciitis, the sheet like proliferation of ganglion-like cells in proliferative fasciitis, or the intravascular growth of intravascular fasciitis.

Although more reactive lesions are probably called sarcomas, the converse situation also occurs. It is important to make certain that the diagnosis of a reactive lesion makes sense in the context of the case. For example, the diagnosis of nodular fasciitis should be seriously reconsidered if the lesion is large, deep, or recurrent. Since degenerated tumors can display "breakdown" changes that mimick fasciitis, be careful of making this diagnosis in degenerated material. Osteoid in bone-producing sarcomas may appear very mature and, therefore, this is an unreliable feature to use in making the diagnosis of myositis ossificans. Rather it is the quality of the cells producing the bone and the location of the bone (central vs. peripheral) which are more important determinants.

Non Mesenchymal Lesions Mimicking a Soft Tissue Tumor

About one fifth of significant errors in soft tissue relate to non mesenchymal lesions misdiagnosed as a sarcoma.[4] The common scenarios are pleomorphic carcinomas interpreted as pleomorphic sarcomas (malignant fibrous histiocytoma), lymphoblastic or large cell lymphoma interpreted as round cell sarcomas (e.g. Ewing sarcoma, rhabdomyosarcoma, round cell liposarcoma), and desmoplastic malignant melanoma interpreted as a scar, fibromatosis, or neurofibroma. It is useful to keep in mind that pleomorphic tumors presenting in sites where carcinomas are known to occur should always be evaluated with that thought in mind. For example, it is reasonable to consider the diagnosis of a sarcoma and carcinoma for a retroperitoneal mass and to perform the appropriate immunostains, whereas it is less reasonable in the case of a deep thigh mass. Likewise, the differential diagnosis of round cell lesions should include in some instances lymphoid markers.

Desmoplastic melanoma is probably the most common non mesenchymal tumor that leads to litigation in the area of soft tissue pathology. The reasons for this are manifold. They are

uncommon variants of melanoma and present in a manner different from classic melanoma.[10] White and scar-like in appearance they typically do not produce melanin or express melanin-associated markers. They may be biopsied with a superficial shave that reveals only a subtle desmoplasia of the papillary dermis. Alternatively, they may be pleomorphic lesions that resemble an atypical fibroxanthoma. Since the majority are associated with a precursor lesion, usually lentigo maligna, good clinical practice considers the diagnosis in all cases of lentigo maligna or in actinic-damaged skin having an underlying scar or desmoplasia.[11] Since S100 protein is strongly expressed by these lesions, it is wise to perform this stain on unusual cutaneous scar-like lesions of the head and neck of adults, particularly if accompanied by a prominent lymphocytic infiltrate, as well as lesions in which the diagnosis of atypical fibroxanthoma is being considered. However, since ordinary scars may occasionally contain small numbers of S100 protein positive cells,[12] one needs to evaluate the character of the cells in conjunction with the stain.

Summary

The foregoing discussion has focused on problem prone situations in soft tissue pathology with the potential to lead to litigation. However, it should be borne in mind that significant errors do not necessarily lead to litigation. Some errors are simply not preventable and therefore the actions of the pathologist or consultant do not fall below the "standard of practice." It is also important to remember that serious errors are far easier to defend if accepted practices have been followed.[3] This implies that difficult cases undergo peer review at consensus conferences, that the final report reflect this review, and that in cases of non-consensus an expert consultation be considered.

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