Non-mesenchymal Mimics of Sarcoma

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KEYWORDS

• Soft tissue • Tumor • Sarcoma • Melanoma • Sarcomatoid carcinoma • Immunohistochemistry • Molecular genetics

ABSTRACT

A variety of different non-mesenchymal neoplasms may mimic sarcoma, in particular sarcomatoid carcinoma and melanoma, but also mesothelioma and rarely some lymphomas. This article reviews the key clinical and histologic features of such neoplasms in different settings, along with the use of ancillary studies to help identify the tumor types most frequently misdiagnosed as sarcoma.

OVERVIEW

Soft tissue tumors encompass a broad group of clinically, histologically, and molecularly diverse tumor types. Many soft tissue tumors show significant histologic overlap with one another (eg, spindle cell sarcomas, pleomorphic sarcomas), and distinguishing different sarcoma types often requires clinical correlation along with ancillary diagnostic tests, most often immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH). However, many non-mesenchymal tumor types can also show significant histologic overlap with sarcomas, and should be considered in the differential diagnosis of many different soft tissue neoplasms. In most cases, distinction can be made with a combination of clinical correlation, identification of certain diagnostic histologic features, and a relatively limited panel of immunohistochemical stains. This article reviews some of the most commonly encountered situations in which non-mesenchymal neoplasms may show significant histologic overlap with sarcoma and provides a practical approach to such cases, incorporating the use of ancillary studies.

MALIGNANT MELANOMA

Malignant melanoma, both primary and metastatic, frequently mimics sarcoma. Most primary cutaneous melanomas are readily recognizable as such due to the presence of an in-situ component, with the exception of desmoplastic or spindle cell melanoma, which may be difficult to distinguish histologically from other intradermal spindle cell neoplasms, such as atypical fibroxanthoma/pleomorphic dermal sarcoma, and nerve sheath neoplasms. However, the diverse histologic features (epithelioid, spindled, round cell, pleomorphic, mixed) seen in metastatic melanoma accounts for the significant overlap with many different sarcoma types (**Fig. 1**). Although clinical history is clearly crucial, histologic clues to the diagnosis of metastatic melanoma include the presence of mixed architectural growth patterns, particularly a nested or theke-like growth pattern, cytologic pleomorphism, melanin pigmentation (often not present in metastatic tumors), and prominent "cherry-red" nucleoli. However, in many cases, and especially in small biopsy samples, IHC is needed to confirm the diagnosis and to exclude other entities. Most metastatic melanomas show at least focal nuclear and cytoplasmic S100 protein expression, but expression of secondary melanocytic markers, such as melan-A/MART-1, HMB45, tyrosinase, and MiTF is highly variable, and many metastatic tumors are negative for all these markers. In addition, melanomas with a spindled morphology, both primary and metastatic, are usually negative for secondary melanocytic markers. Quite recently, however, SOX10 has been described as a highly sensitive and relatively specific marker of neuroectodermal differentiation, and has proven to be very useful

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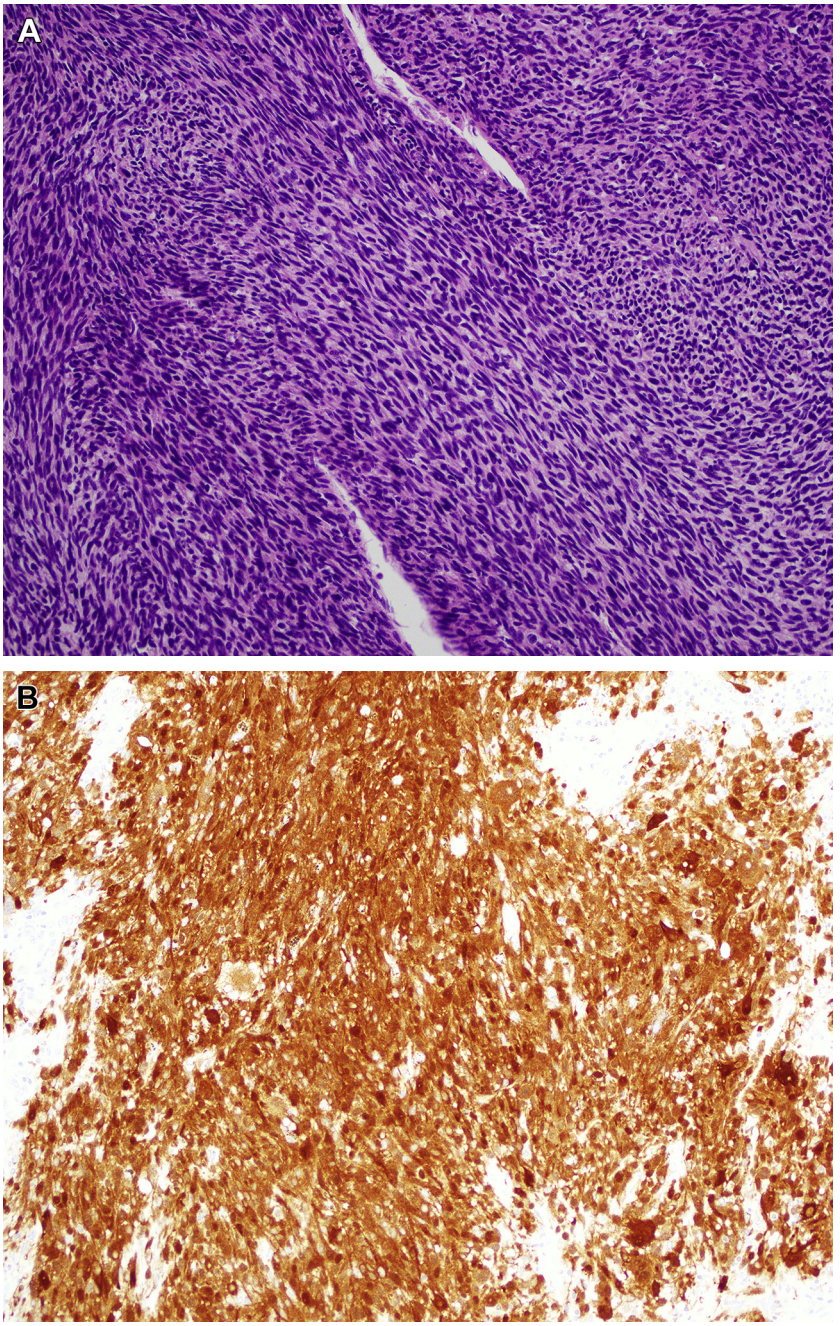

Fig. 1. Metastatic malignant melanoma involving bone and showing a fascicular growth pattern virtually indistinguishable from MPNST (*A*). The tumor cells show diffuse nuclear and cytoplasmic expression of S100 protein (*B*).

in clinical practice in the evaluation of melanocytic lesions, particularly those that lack expression of other secondary melanocytic markers (see **Fig. 1**D).[1] Expression of SOX10 is seen in more than 99% of melanocytic and nerve sheath neoplasms, as well as a subset of (usually benign) myoepithelial tumors.[2–4] Three relatively common scenarios in which melanoma may be mistaken for sarcoma are described in the following sections, and include the distinction of melanoma from malignant peripheral nerve sheath tumor (MPNST) and clear cell sarcoma, as well as the occurrence of metastatic melanoma in the absence of a known primary tumor.