Critical Concepts in Soft Tissue Pathology

1

1.1 General Principles of Classification

Soft tissue pathology is a subspecialty that involves the diagnosis of lesions that are neither epithelial nor skeletal and do not originate from the central nervous system. This includes neoplasms of muscle, connective fascia, vasculature, and the peripheral nervous system [1]. With such an ambitious definition, the scope of this subspecialty is broad and encompasses a formidable number of entities with specific histologic, genetic, and clinical features.

When encountering such an abundance of terms and neoplasms, one can be tempted to view soft tissue tumors simply by histologic grade. Although this approach simplifies several hundred neoplasms into low-, intermediate-, or high-grade sarcoma, it overgeneralizes and is incompatible with increasingly individualized treatment regimens. By classifying soft tissue neoplasms to a particular histologic entity, pathologists have been able to attribute unique clinical behaviors to specific tumors and establish a conceptual framework for future advances in soft tissue oncology [2]. Consequently, clinicians who frequently treat sarcoma patients can benefit from understanding the diagnostic terms and approach of soft tissue pathologists.

In order to maintain consistency, the diagnostic nomenclature of soft tissue pathology is determined by a consensus of international experts. Every few years, this terminology is edited to reflect the addition of newly discovered neoplasms or reassignment of entities to different categories. These efforts are published as a volume in the World Health Organization Classification of Tumours book series, titled *Pathology and Genetics of Tumours of Soft Tissue and Bone* [3].

Unlike carcinomas that are often classified by site of occurrence (e.g. colorectal adenocarcinoma, gastric adenocarcinoma), a soft tissue tumor can arise in multiple areas and is not amenable to description by anatomic location. Instead, these neoplasms are described according to the connective tissue that they most closely

K. Perry, *Soft Tissue Pathology for Clinicians*, Pathology for Clinicians,
DOI 10.1007/978-3-319-55654-3_1

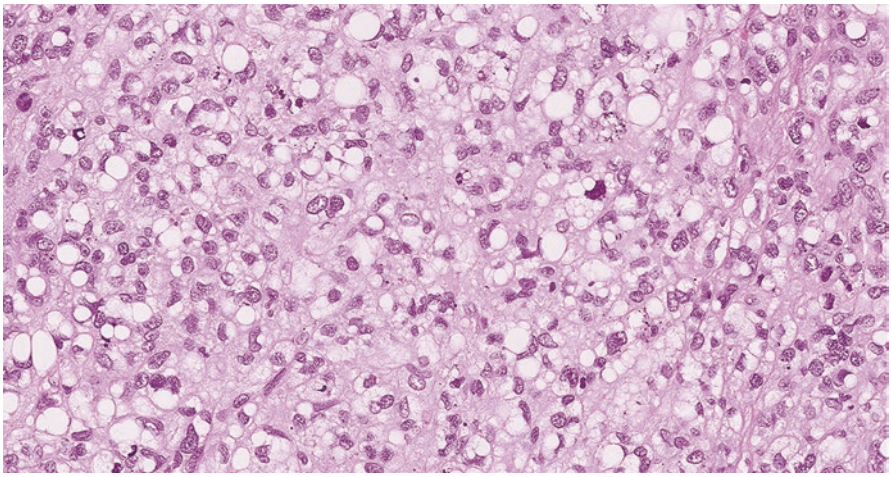

Fig. 1.1 Pleomorphic liposarcoma with lipoblasts

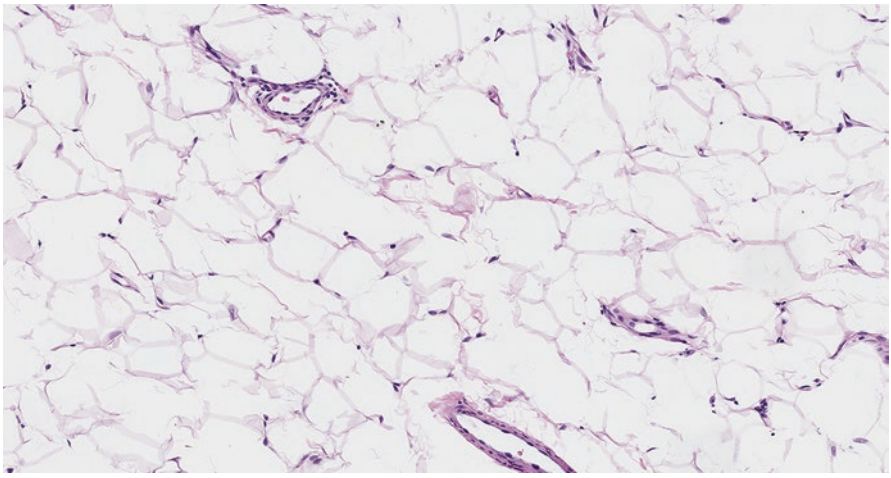

Fig. 1.2 Normal adipose tissue

resemble. Such entities include pleomorphic liposarcoma (Fig. 1.1) that resembles fat (Fig. 1.2) or leiomyosarcoma (Fig. 1.3) that resembles smooth muscle (Fig. 1.4). Many soft tissue tumors do not resemble any specific mesenchymal tissue and are simply designated as "tumors of uncertain differentiation" [3].

Following primary histologic classification, soft tissue tumors are further subdivided into clinical categories of benign, intermediate (locally aggressive), intermediate (rarely metastasizing), and malignant. Most benign lesions do not recur, and rare instances of recurrence are easily cured by complete local excision. Intermediate

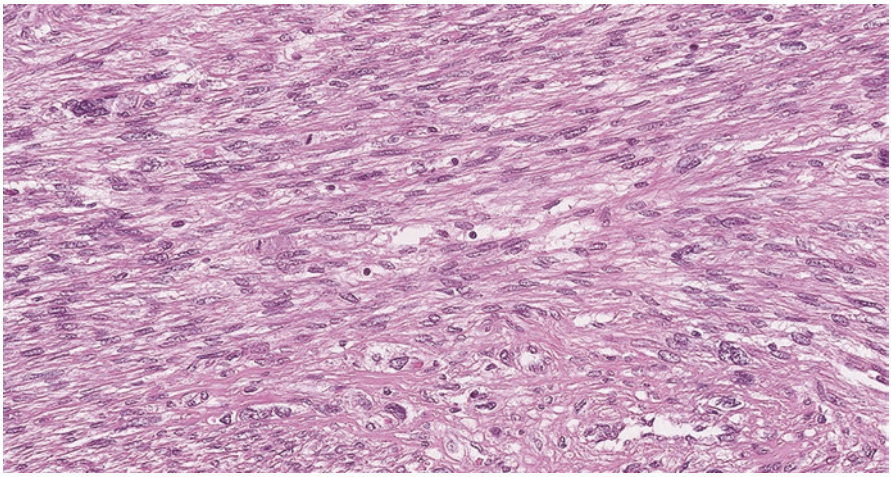

Fig. 1.3 Leiomyosarcoma with neoplastic muscle cells showing mitoses and nuclear atypia

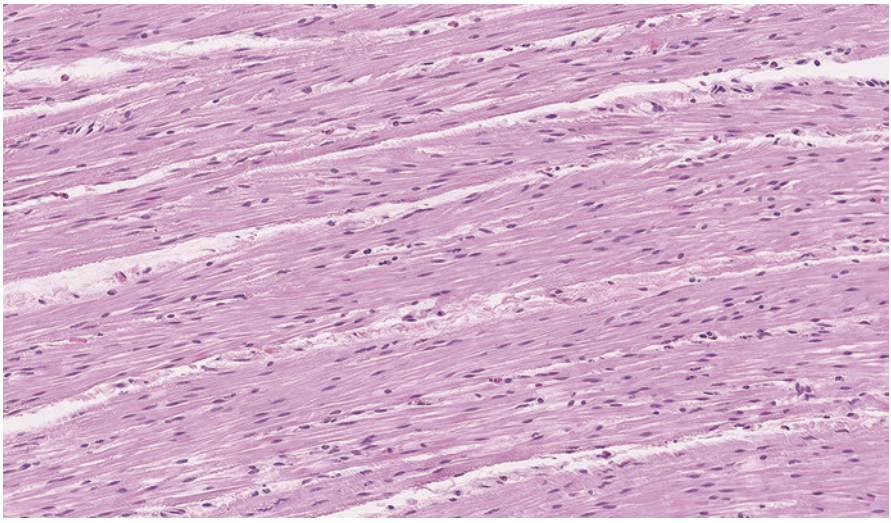

Fig. 1.4 Normal smooth muscle

(locally aggressive) tumors will not metastasize but are prone to recurrence and require wide excision given their infiltrative growth pattern. Intermediate (rarely metastasizing) soft tissue tumors are typically locally aggressive, but demonstrate the capability to occasionally metastasize (less than 2% risk). Malignant tumors are locally destructive and often metastasize. Generally, high-grade tumors tend to metastasize more frequently than low-grade tumors [3].

1.2 Acquisition, Handling, and Processing of Soft Tissue Specimens

Ultrasound or computed tomography (CT)-guided needle core biopsies have become the preferred procedure for diagnosing soft tissue neoplasms, as they are minimally invasive and less prone to surgical complications. Histologic interpretation of these biopsies is both sensitive (99.4%) and specific (98.7%) when distinguishing benign from malignant tumors [5]. The accuracy of needle core biopsies for a specific histologic diagnosis is also impressive (approximately 95% correct) [6]. Assessment of tumor grade in biopsies (low vs. intermediate vs. high) is helpful but slightly less accurate (approximately 85% correct) [7]. The interpretation of a needle core biopsy often represents a critical juncture in the care of a patient with a soft tissue neoplasm. A benign lesion might be monitored or undergo simple excision. A low-grade sarcoma is resected without neoadjuvant therapy, and an intermediate- or high-grade sarcoma often receives presurgical adjuvant treatment.

Following a biopsy or resection, the tissue is submitted to the pathology laboratory for evaluation. In order to prevent tissue degradation, many hospitals or clinics will place the biopsies directly into formalin in the operating suite. However, if a clinician or pathologist has an interest in culturing or freezing a representative part of the biopsy for possible cytogenetic or molecular studies, then at least some of the tissue must be maintained in a fresh, viable state and transported in cell culture media. Close communication with the pathologist is helpful in assuring the tissue is appropriately handled.

Upon arrival to the laboratory, the specimen must pass through a standardized process prior to visualization as a glass slide under the microscope. The tissue initially arrives in a labeled container with an accompanying requisition form that is reviewed by lab personnel (Fig. 1.5a). Including critical information on this form about the history of the patient or nature of the lesion facilitates a timely and accurate diagnosis. Awareness of the site and size of the mass helps the pathologist formulate a differential diagnosis based on anatomic location. Knowledge of previous malignancies (including prior diagnosis of carcinoma, melanoma, or hematolymphoid neoplasm) alerts the pathologist to recurrent or metastatic tumors that might mimic a sarcoma. Communication of familial syndromes, such as neurofibromatosis, helps raise a suspicion of certain malignant neoplasms like malignant peripheral nerve sheath tumor [4].

After reviewing the requisition and confirming the specimen is appropriately labeled, the pathologist or pathology assistant will typically describe the appearance of the tissue received (i.e. gross examination). For needle core biopsies, the number and size of the biopsies are documented. With resection specimens, the pathologist describes the location and size of the mass, as well as the distance from the surgical resection margin. The surgeon will often designate multiple anatomically specific margins by orienting the specimen with sutures (e.g., long suture, superior margin; short suture, medial margin). To preserve this orientation, the pathologist will typically paint the corresponding margins with an ink that can be seen under the microscope after processing. If there is a particular area of concern for margin involvement,

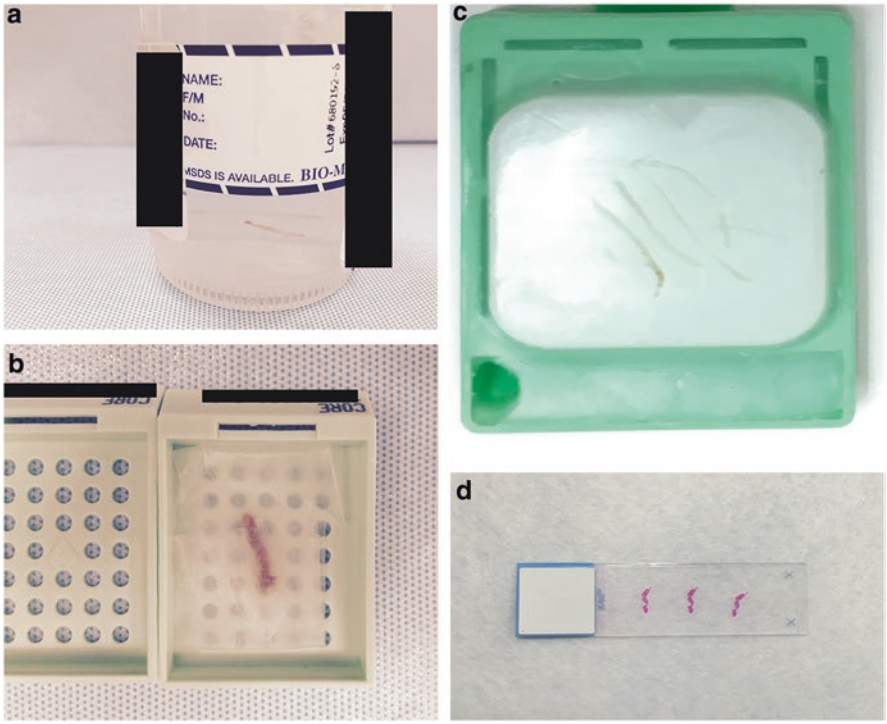

Fig. 1.5 (**a**) Specimen container with a needle core biopsy, (**b**) needle core biopsy wrapped in tissue paper for processing, (**c**) needle core biopsy embedded in paraffin wax after tissue processing, (**d**) needle core biopsy after being processed, cut and stained with hematoxylin and eosin

specific designation by the surgeon can assure this focus is appropriately examined and referenced in the report. Moreover, if the margin has become artificially ruptured, proactively notifying the pathologist can help avoid an erroneous report.

Once gross examination is complete, the tissue is submitted for processing. For needle core biopsies, the objective is to have sufficient tissue for diagnosis and grading. Consequently, many pathology laboratories will submit all of the received biopsies in a formalin fixative solution that suspends enzymatic processes and halts tissue degradation (Fig. 1.5b). Following formalin fixation, the biopsy is processed and ultimately immersed in paraffin wax, termed a "paraffin block" (Fig. 1.5c). A thin slice of this biopsy is then cut, placed on a glass slide and stained for microscopic examination (Fig. 1.5d).

For resection specimens, the pathologist must select which tissue fragments to submit for microscopic examination. Generally, multiple sections of tumor (often one per centimeter) are submitted to confirm the diagnosis or assess for treatment effect. Other sections are typically submitted to evaluate the relation of the tumor with various surgical margins. Following submission, the tissue is processed for microscopic examination similar to a needle core biopsy.

Facts to Remember

1. Soft tissue tumors are described according to the connective tissue they most resemble and are further categorized as benign, malignant, or intermediate in clinical behavior.
2. The needle core biopsy has become the primary specimen for diagnosis of soft tissue neoplasms. Appropriate and timely handling of the tissue is critical for successful classification.
3. Documentation of key clinical features on the requisition form, such as the anatomic site and size of the mass, previous malignancies, familial syndromes, and previous therapy can be immensely helpful for accurate and efficient diagnosis.
4. Communication of specimen orientation or areas that are suspicious for tumor involvement can facilitate clear pathologic reporting.

References

1. Goldblum J, Weiss S, Folpe AL, editors. Enzinger and Weiss's soft tissue tumors. 6th ed. Philadelphia: Elsevier; 2013.
2. Fletcher CD. The evolving classification of soft tissue tumours – an update based on the new 2013 WHO classification. Histopathology. 2014;64(1):2–11.
3. Fletcher CDM, Bridge JA, Hogendoorn PC, Mertens F, editors. Pathology and genetics of tumours of soft tissue and bone. 4th ed. Lyon: World Health Organization; 2013.
4. Lester S. Manual of surgical pathology. 3rd ed. Philadelphia: Elsevier Saunders; 2010.
5. Hoeber I, Spillane AJ, Fisher C, Thomas JM. Accuracy of biopsy techniques for limb and limb girdle soft tissue tumors. Ann Surg Oncol. 2001;8(1):80–7.
6. Fisher C, Montgomery EA, Thway K. Biopsy interpretation series: biopsy interpretation of soft tissue tumors. 2nd ed. Philadelphia: Wolters Kluwer; 2016.
7. Deyrup AT, Weiss SW. Grading of soft tissue sarcomas: the challenge of providing precise information in an imprecise world. Histopathology. 2006;48(1):42–50.