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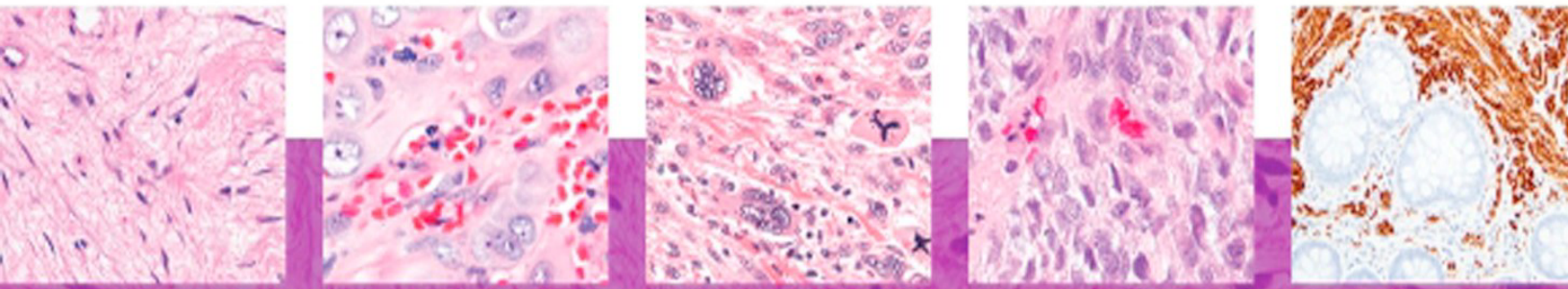
Practical Soft Tissue Pathology

A Diagnostic Approach

Second Edition



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Practical Soft Tissue Pathology

A Diagnostic Approach

A Volume in the Pattern Recognition Series

Edition 2

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This book is dedicated to Beryle-Gay Hornick and Jordana Hornick

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Series Preface

It is often stated that anatomic pathologists come in two forms: "Gestalt"-based individuals, who recognize visual scenes as a whole, matching them unconsciously with memorialized archives; and criterion-oriented people, who work through images systematically in segments, tabulating the results—internally, mentally, and quickly—as they go along in examining a visual target. These approaches can be equally effective, and they are probably not as dissimilar as their descriptions would suggest. In reality, even "Gestaltists" subliminally examine details of an image, and, if asked specifically about particular features of it, they are able to say whether one characteristic or another is important diagnostically.

In accordance with these concepts, in 2004 we published a textbook entitled *Practical Pulmonary Pathology: A Diagnostic Approach* (PPPDA). That monograph was designed around a *pattern-based* method, wherein diseases of the lung were divided into six categories on the basis of their general image profiles. Using that technique, one can successfully segregate pathologic conditions into diagnostically and clinically useful groupings.

The merits of such a procedure have been validated empirically by the enthusiastic feedback we have received from users of our book. In addition, following the old adage that "imitation is the sincerest form of flattery," since our book came out, other publications and presentations have appeared in our specialty with the same approach.

After publication of the PPPDA text, representatives at Elsevier, most notably William Schmitt, were enthusiastic about building a *series* of texts around pattern-based diagnosis in pathology. To this end we have recruited a distinguished group of authors and editors to accomplish that task. Because a panoply of patterns is difficult to approach mentally from a practical perspective, we have asked our contributors to be complete and yet to discuss only principal interpretative images. Our goal is eventually to provide a series of monographs that, in combination with one another, will allow trainees and practitioners in pathology to use salient morphological patterns to reach with confidence final diagnoses in all organ systems.

As stated in the introduction to the PPPDA text, the evaluation of dominant patterns is aided secondarily by the analysis of cellular composition and other distinctive findings. Therefore within the context of each pattern, editors have been asked to use such data to refer the reader to appropriate specific chapters in their respective texts.

We have also stated previously that some overlap is expected between pathologic patterns in any given anatomic site; in addition, specific disease states may potentially manifest themselves with more than one pattern. At first, those facts may seem to militate against the value of pattern-based interpretation. However, pragmatically, they do not. One often can narrow diagnostic possibilities to a very few entities using the pattern method, and sometimes a single interpretation will be obvious. Both of those outcomes are useful to clinical physicians caring for a given patient.

It is hoped that the expertise of our authors and editors, together with the high quality of morphologic images they present in this Elsevier series, will be beneficial to our reader-colleagues.

Kevin O. Leslie, MD
Mark R. Wick, MD

Preface to the First Edition

With its diversity of histologic appearances and the rarity of many types of mesenchymal tumors, soft tissue tumor pathology can be intimidating for pathologists in training and practicing pathologists alike. The current classification system informs the organization of the majority of soft tissue tumor textbooks, emphasizing the line of differentiation exhibited by the tumor cells. Pathologists can relatively easily recognize some mesenchymal tumors as fibroblastic/myofibroblastic, "fibrohistiocytic," smooth muscle, skeletal muscle, vascular, or adipocytic, but for many other soft tissue tumors, the lineage is not intuitively obvious. Immunohistochemistry therefore plays a major role in demonstrating such lineages. However, for some mesenchymal neoplasms, there is no apparent normal cellular counterpart; such tumors (which are both histologically and clinically diverse) are often found in textbooks lumped together in a separate chapter with tumors of uncertain lineage. Despite teaching junior residents to describe tumors based on cytologic findings and histologic patterns, our specialty features surprisingly few pathology textbooks wherein soft tissue tumors are presented in the same manner in which pathologists approach them in daily practice—with tumor cell appearance, architectural arrangements, and stromal characteristics as organizing principles.

This textbook addresses this gap in our literature by taking a pattern-based approach to soft tissue tumor pathology, with chapters devoted to the dominant cytology of the tumor cells (spindle cell tumors, epithelioid tumors, round cell tumors, pleomorphic sarcomas, biphasic tumors, and tumors with mixed patterns), the quality of the extracellular matrix (tumors with myxoid stroma), and other distinguishing features (giant cell–rich tumors, soft tissue tumors with prominent inflammatory cells). Because recognition of many adipocytic, vascular, cartilaginous, and osseous neoplasms is relatively straightforward on histologic grounds alone, separate chapters are devoted to these groups of lesions. Cutaneous, gastrointestinal, and lower genital mesenchymal tumors are also presented in separate chapters, because many distinctive tumor types arise exclusively or predominantly in those anatomic compartments. Because many soft tissue tumors have more than one distinguishing feature (e.g., epithelioid cytology and myxoid stroma, spindle cell morphology and prominent inflammatory cells), quite a few tumors are discussed in multiple chapters to emphasize approaches to differential diagnosis. Although molecular findings are included throughout the textbook when relevant, the final chapter is devoted to molecular testing in soft tissue tumor pathology, both to provide an overview of the methods used (and relative merits of the various techniques) and to give examples of how the application of molecular testing can aid in differential diagnosis.

The main patterns are included in table form in the front of the textbook. This section also includes additional distinguishing findings that can narrow down the differential diagnosis, specific diagnostic considerations within each category, and a reference to the chapter and page number where the particular tumor type can be found. The reader may choose either to use these tables to identify specific tumors in the book based on the dominant pattern and other particular features or to go directly to the chapter or chapters containing tumors with the histologic features recognized. Although these tables are relatively comprehensive, they do not include most vascular, adipocytic, cartilaginous, and osseous tumors, which can be studied in the chapters devoted to those groups of neoplasms.

Jason L. Hornick, MD, PhD

Preface

In the 5 years since the publication of the first edition of *Practical Soft Tissue Pathology* and the most recent World Health Organization classification, we have seen remarkable advances in diagnostic soft tissue tumor pathology; the second edition of this book incorporates these changes. New defining molecular genetic alterations continue to be discovered at an astonishing rate. In turn, these findings lead (also with increasing speed) to new diagnostic tests, not only molecular assays but also using immunohistochemistry. In many cases, single-antibody immunohistochemical tests serve as excellent surrogate markers for particular molecular genetic alterations. These novel diagnostic markers have proven to be extremely valuable tools for differential diagnosis, especially in limited biopsy material, such as core needle biopsies and fine needle aspirations, which we encounter every day in clinical practice. In the past, it could be challenging, if not impossible, to render a specific diagnosis in such limited samples; now accurate diagnosis is often possible with the aid of these powerful new markers. These markers have changed our diagnostic approach to both relatively common and rare tumor types, including major histologic categories of soft tissue tumors, such as spindle cell tumors, epithelioid tumors, and round cell sarcomas.

In sarcoma classification, among the most significant recent advances is the emergence of discrete tumor types within the previous category of "undifferentiated round cell sarcomas" based on molecular genetics. After Ewing sarcoma and other well-defined round cell sarcomas were excluded by immunohistochemistry and fluorescence in situ hybridization (FISH), we had no real options beyond this wastebasket category. Now, round cell sarcomas with *CIC* gene rearrangements (most with *CIC-DUX4*) and *BCOR* genetic alterations (most often *BCOR-CCNB3*) are recognized diagnostic categories, with important prognostic implications and, we hope in the near term, distinct systemic therapies. In rapid succession, pathologists have introduced immunohistochemical markers that correlate with these rearrangements, some based on the gene fusions per se (e.g., *CCNB3* and *BCOR*) and others reflecting downstream consequences of these fusions, often discovered by gene expression profiling (such as *ETV4*).

These genetic alterations and emerging diagnostic markers, which have been integrated into the second edition, should improve the accuracy and reproducibility of mesenchymal tumor diagnosis. I hope you find this book useful in your daily clinical practice.

Jason L. Hornick, MD, PhD

Acknowledgment

Many individuals have had a significant impact on my development as a diagnostic pathologist and on the creation of this textbook. I would first like to acknowledge my colleague and friend Christopher Fletcher, without whom I would not have become a surgical pathologist. Without his mentorship and support, this textbook would not exist. Chris generously allowed me to photograph his consult cases, which have greatly enhanced many of the chapters throughout the book. I would like to thank my colleagues and friends who devoted considerable time and effort working on the excellent chapters that they contributed to this project. Their research, writing, and teaching in this field will continue to advance our understanding (and improve the diagnosis) of mesenchymal tumors for a new generation of pathologists and our clinical collaborators.

The residents, fellows, and my colleagues in the pathology department at Brigham and Women's Hospital are an exceptional team of trainees and friends, and I am fortunate to share my passion for surgical pathology with them. My first introduction to monoclonal antibodies was during my doctoral work; I am grateful to Alan Epstein and Clive Taylor for this and for encouraging me to consider a pathology residency. Finally, my wife, Harmony Wu, has provided support and insights during the long journey toward the completion of this textbook, and our children, Hazel and Oscar, have been a source of inspiration and humility and have been (relatively) patient with me along the way.

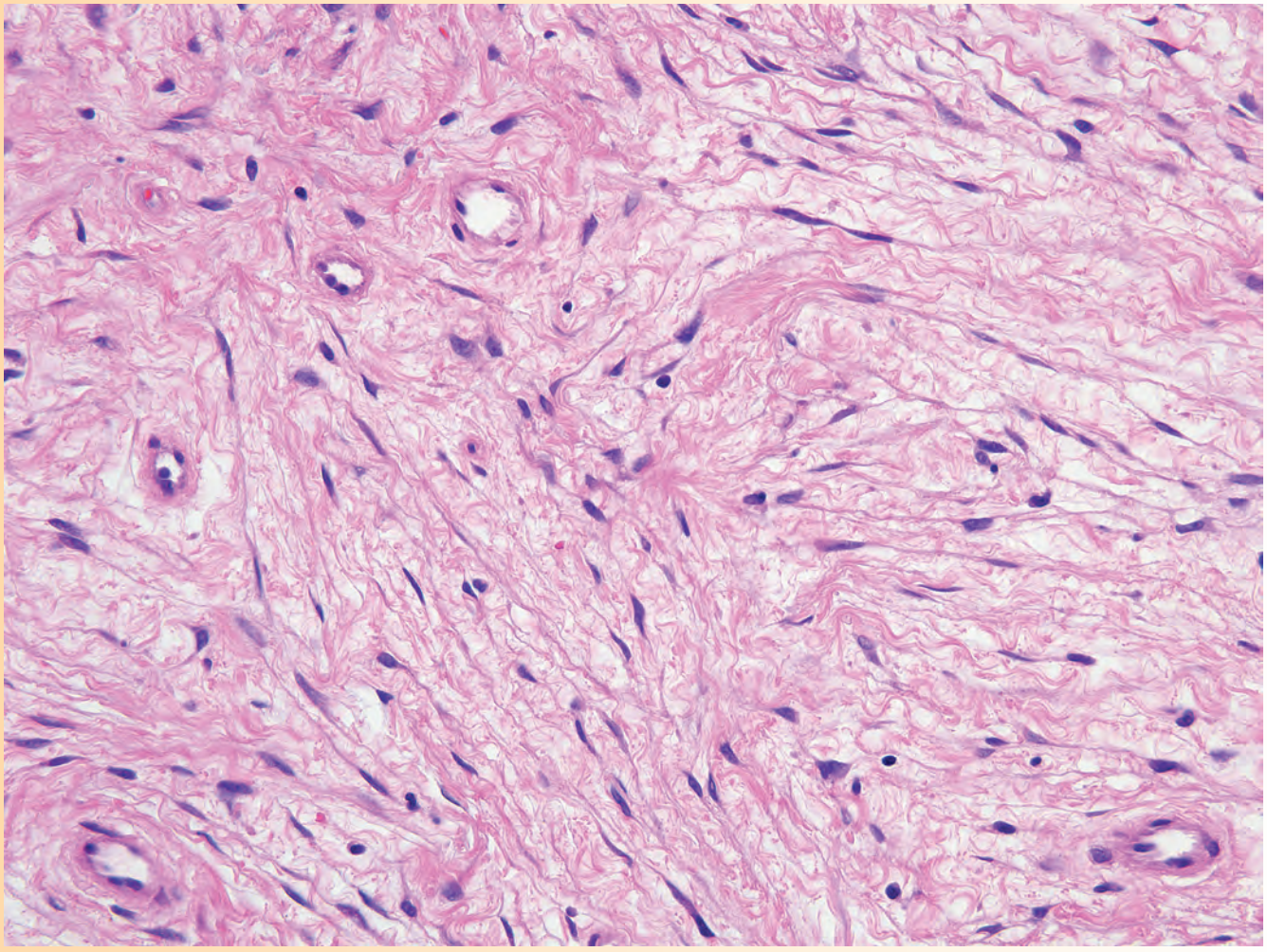
Jason L. Hornick, MD, PhD

Pattern-Based Approach to Diagnosis

Pattern	Selected Diseases to Be Considered
Spindle cell	Nodular fasciitis Myofibroma/myopericytoma Cellular benign fibrous histiocytoma Dermatofibrosarcoma protuberans Superficial or desmoid fibromatosis Neurofibroma Schwannoma Leiomyoma Leiomyosarcoma Gastrointestinal stromal tumor Solitary fibrous tumor Spindle cell lipoma Atypical spindle cell lipomatous tumor Soft tissue perineurioma Low-grade fibromyxoid sarcoma Monophasic synovial sarcoma Malignant peripheral nerve sheath tumor Biphenotypic sinonasal sarcoma Dedifferentiated liposarcoma Clear cell sarcoma Nodular Kaposi sarcoma Pseudomyogenic hemangioendothelioma
Epithelioid	Epithelioid hemangioma Epithelioid hemangioendothelioma Epithelioid angiosarcoma Glomus tumor Granular cell tumor Cellular neurothekeoma Myoepithelioma/myoepithelial carcinoma Epithelioid schwannoma Epithelioid malignant peripheral nerve sheath tumor Gastrointestinal stromal tumor Perivascular epithelioid cell tumor (PEComa) Epithelioid sarcoma SMARCA4-deficient thoracic sarcoma Malignant rhabdoid tumor Alveolar soft part sarcoma Clear cell sarcoma Sclerosing epithelioid fibrosarcoma
Pleomorphic	Atypical fibrous histiocytoma Atypical fibroxanthoma "Ancient" schwannoma Dedifferentiated liposarcoma

Pattern	Selected Diseases to Be Considered
Pleomorphic—*cont'd*	Pleomorphic liposarcoma Pleomorphic leiomyosarcoma Pleomorphic rhabdomyosarcoma Myxofibrosarcoma Myxoinflammatory fibroblastic sarcoma Extraskeletal osteosarcoma Undifferentiated pleomorphic sarcoma
Round cell	Ewing sarcoma Embryonal rhabdomyosarcoma Alveolar rhabdomyosarcoma Round cell (high-grade myxoid) liposarcoma Poorly differentiated synovial sarcoma Desmoplastic small round cell tumor Mesenchymal chondrosarcoma *CIC*-rearranged sarcomas *BCOR*-rearranged sarcomas
Biphasic or mixed	Biphasic synovial sarcoma Mixed tumor Glandular malignant peripheral nerve sheath tumor Myoepithelioma/myoepithelial carcinoma Gastrointestinal stromal tumor Ectopic hamartomatous thymoma Dedifferentiated liposarcoma
Myxoid	Intramuscular/cellular myxoma Dermal nerve sheath myxoma Superficial acral fibromyxoma Superficial angiomyxoma Deep angiomyxoma Ossifying fibromyxoid tumor Myoepithelioma/myoepithelial carcinoma Myxofibrosarcoma Pleomorphic liposarcoma Myxoid liposarcoma Extraskeletal myxoid chondrosarcoma Low-grade fibromyxoid sarcoma Myxoinflammatory fibroblastic sarcoma Neurofibroma Soft tissue or reticular perineurioma Malignant peripheral nerve sheath tumor Spindle cell lipoma

Pattern 1 Spindle Cell



Elements of the pattern: The tumor cells contain pointed or tapering ends.

Pattern 1 Spindle Cell

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	Cellular benign fibrous histiocytoma	Ch. 15:410
	Dermatomyofibroma	Ch. 15:412
	Superficial fibromatosis	Ch. 3:46
	Desmoid fibromatosis	Ch. 3:47; Ch. 4:109; Ch. 16:481
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	Inflammatory myofibroblastic tumor	Ch. 4:118; Ch. 10:269; Ch. 16:479
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	Monophasic synovial sarcoma	Ch. 3:72
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Pattern 1 Spindle Cell—*cont'd*

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	Dedifferentiated liposarcoma	Ch. 7:225; Ch. 12:328
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	Myxoinflammatory fibroblastic sarcoma	Ch. 5:155; Ch. 7:217; Ch. 10:286
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	Atypical fibrous histiocytoma	Ch. 15:411
	Atypical fibroxanthoma	Ch. 15:449
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	Myxoinflammatory fibroblastic sarcoma	Ch. 5:155; Ch. 7:217; Ch. 10:286
	Myxofibrosarcoma	Ch. 5:148; Ch. 7:218
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	Extraskeletal myxoid chondrosarcoma	Ch. 5:151

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	Calcifying fibrous tumor	Ch. 3:37
	Solitary fibrous tumor	Ch. 3:40
	Mammary-type myofibroblastoma	Ch. 3:31; Ch. 17:506
	Hyaline fibromatosis	Ch. 4:118
	Storiform collagenoma	Ch. 15:415
	Superficial fibromatosis	Ch. 3:46
	Desmoid fibromatosis	Ch. 3:47; Ch. 4:109; Ch. 16:481
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Pattern 1 Spindle Cell—*cont'd*

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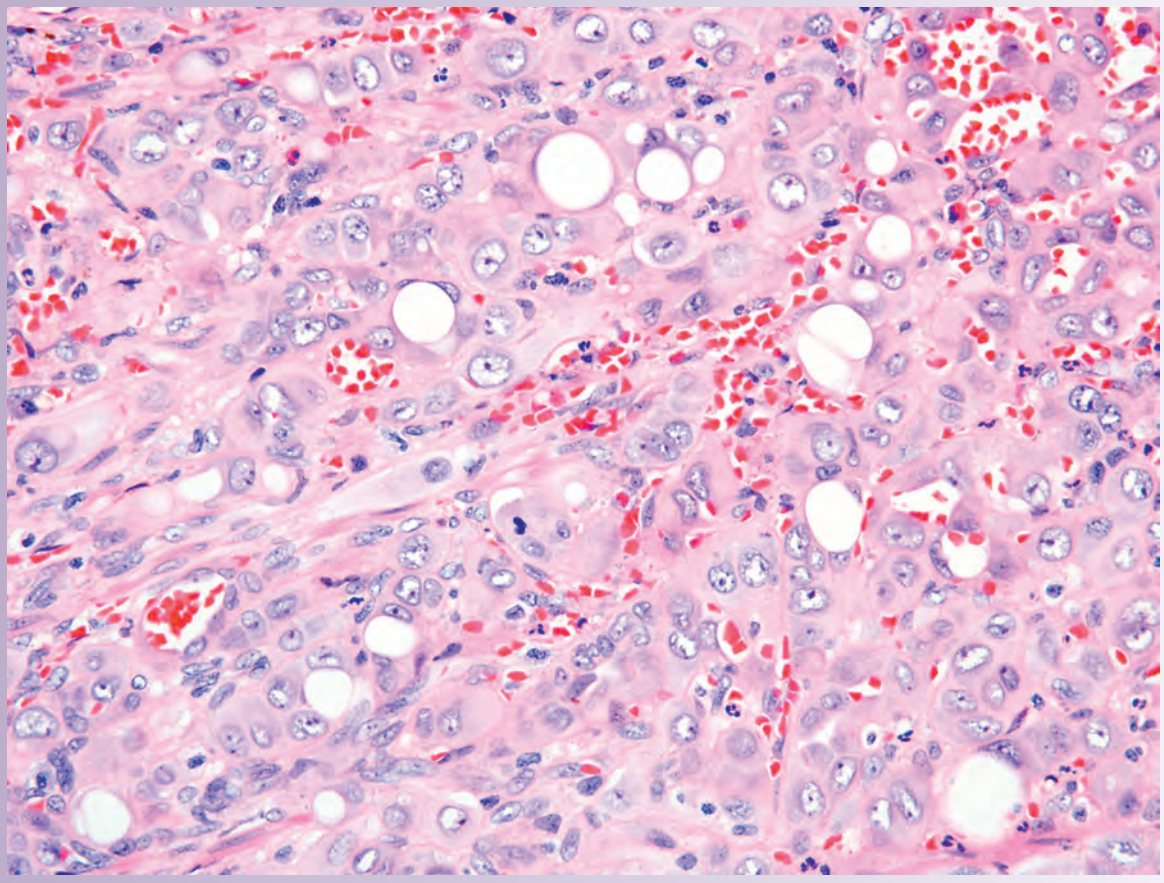
	Lipoblastoma	Ch. 12:319
	Myxoid liposarcoma	Ch. 5:150; Ch. 12:332
	Myolipoma	Ch. 3:64; Ch. 12:321
	Mammary-type myofibroblastoma (subset)	Ch. 3:31; Ch. 17:506
	Hemosiderotic fibrolipomatous tumor	Ch. 12:319
	Solitary fibrous tumor (subset)	Ch. 3:44
Calcifications, cartilage, and/or bone/osteoid	Phosphaturic mesenchymal tumor (calcifications, osteoid)	Ch. 3:30
	Calcifying fibrous tumor (calcifications)	Ch. 3:37
	Melanotic schwannoma (calcifications; subset)	Ch. 3:55
	Calcifying aponeurotic fibroma (calcifications)	Ch. 4:114
	Myositis ossificans (bone/osteoid)	Ch. 14:391
	Fasciitis ossificans (bone/osteoid)	Ch. 3:23
	Fibro-osseous pseudotumor (bone/osteoid)	Ch. 14:392
	Soft tissue aneurysmal bone cyst (bone/osteoid; subset)	Ch. 14:397
	Malignant peripheral nerve sheath tumor (cartilage and/or bone; subset)	Ch. 3:76
	Dedifferentiated liposarcoma (cartilage and/or bone; subset)	Ch. 7:225; Ch. 12:328
	Extraskeletal osteosarcoma (bone/osteoid)	Ch. 14:400
Prominent or distinctive blood vessels	Nodular fasciitis (plexiform)	Ch. 3:20; Ch. 4:102; Ch. 5:158
	Myofibroma/myofibromatosis/myopericytoma (dilated, branching)	Ch. 3:27; Ch. 4:107
	Fibroma of tendon sheath (slit-like)	Ch. 3:33
	Nasopharyngeal angiofibroma (dilated, irregular, thin-walled)	Ch. 4:117
	Angiofibroma of soft tissue (small, branching)	Ch. 3:37
	Spindle cell hemangioma (dilated)	Ch. 13:379
	Solitary fibrous tumor (rounded, hyalinized; dilated, branching)	Ch. 3:40
	Monophasic synovial sarcoma (dilated, branching; subset)	Ch. 3:72
	Schwannoma (rounded, hyalinized)	Ch. 3:51
	Angioleiomyoma (thick-walled)	Ch. 3:66
	Lymphangiomyoma (dilated lymphatics)	Ch. 3:68
	Superficial angiomyxoma (elongated)	Ch. 5:141; Ch. 15:428
	Deep angiomyxoma (rounded, medium-sized)	Ch. 5:141; Ch. 17:499
	Cellular angiofibroma (thick-walled, hyalinized, medium-sized)	Ch. 17:504
	Low-grade fibromyxoid sarcoma (elongated)	Ch. 3:81; Ch. 4:124; Ch. 5:153
	Myxoid liposarcoma (plexiform)	Ch. 5:148; Ch. 12:332
	Myxofibrosarcoma (curvilinear)	Ch. 5:148; Ch. 7:218
	Inflammatory fibroid polyp (rounded, small)	Ch. 16:482
	Plexiform fibromyxoma (branching, small)	Ch. 16:484

Pattern 2 Epithelioid



Elements of the pattern: The tumor cells resemble epithelial cells with a rounded or polygonal appearance and at least moderate amounts of cytoplasm.

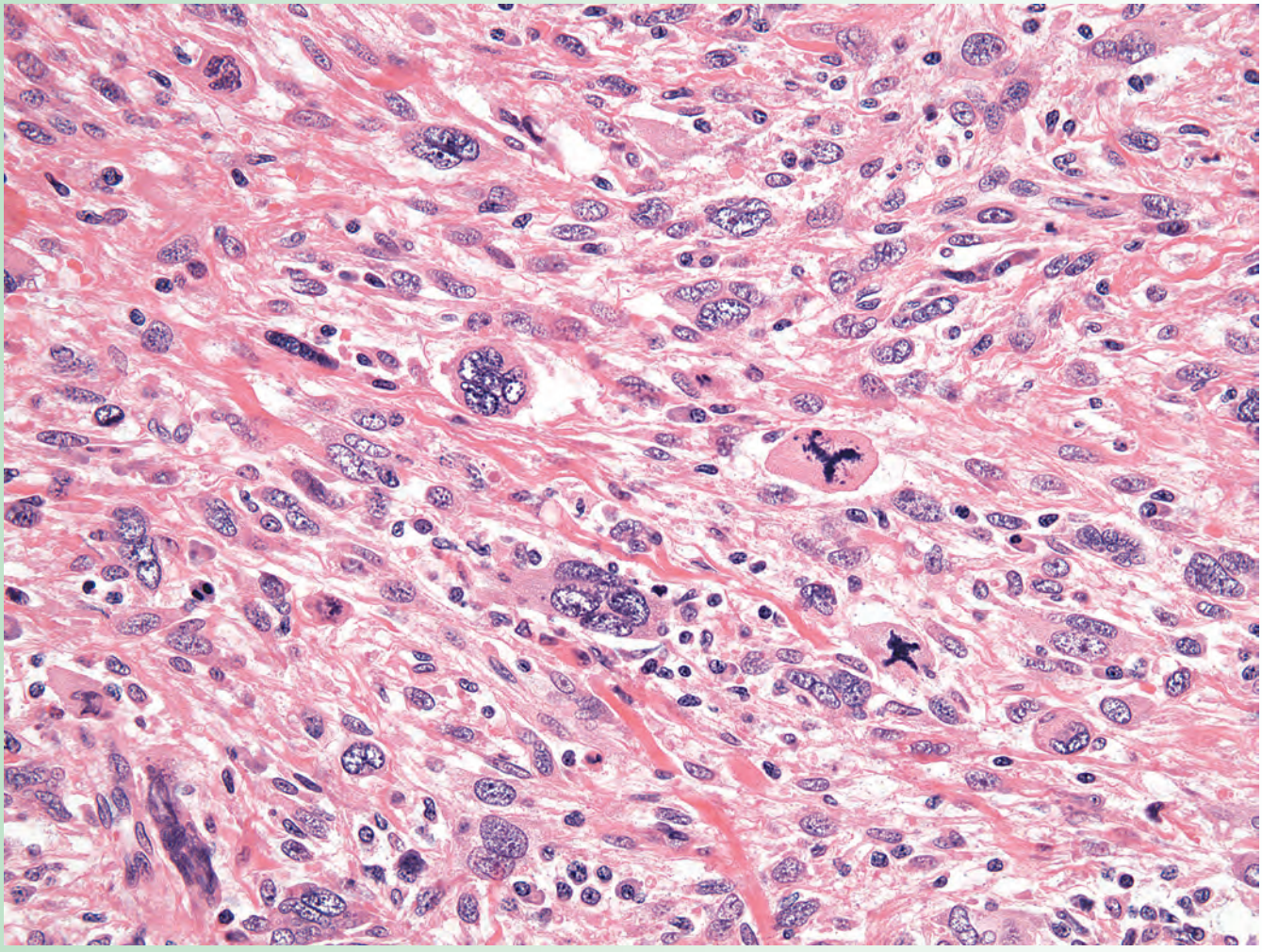
Pattern 2 Epithelioid

Additional Findings	Diagnostic Considerations	Chapter:Page
Lobulated architecture	Epithelioid hemangioma	Ch. 6:168; Ch. 13:372
	Giant cell tumor of soft tissue	Ch. 11:306
	Myoepithelioma/myoepithelial carcinoma	Ch. 5:145; Ch. 6:173
	Epithelioid schwannoma	Ch. 15:441
	Epithelioid malignant peripheral nerve sheath tumor	Ch. 6:201
	Ossifying fibromyxoid tumor	Ch. 5:143; Ch. 6:185
	Gastrointestinal stromal tumor (subset)	Ch. 16:460
	Ependymoma of soft tissue	Ch. 6:185
	Epithelioid myxofibrosarcoma	Ch. 6:202
Nested architecture	Perivascular epithelioid cell tumor (PEComa)	Ch. 6:177; Ch. 15:439; Ch. 16:485
	Cellular neurothekeoma	Ch. 15:437
	Extracranial meningioma	Ch. 6:184; Ch. 15:443
	Alveolar soft part sarcoma	Ch. 6:186
	Clear cell sarcoma	Ch. 3:87
Trabecular or cord-like architecture	Myoepithelioma/myoepithelial carcinoma (subset)	Ch. 5:145; Ch. 6:173
	Sclerosing PEComa	Ch. 6:178
	Sclerosing perineurioma	Ch. 3:63; Ch. 15:442
	Epithelioid schwannoma (subset)	Ch. 15:441
	Ossifying fibromyxoid tumor	Ch. 5:143; Ch. 6:185
	Extraskeletal myxoid chondrosarcoma	Ch. 5:151
	Epithelioid hemangioendothelioma	Ch. 6:188; Ch. 13:374
	Sclerosing epithelioid fibrosarcoma	Ch. 6:197
Sheet-like architecture	Epithelioid angiomatous nodule	Ch. 13:374
	Epithelioid fibrous histiocytoma	Ch. 15:434
	Cutaneous myoepithelioma	Ch. 15:435
	Reticulohistiocytoma	Ch. 15:446
	Juvenile xanthogranuloma	Ch. 15:444
	Extranodal Rosai-Dorfman disease	Ch. 10:283; Ch. 15:448
	Tenosynovial giant cell tumors	Ch. 11:298
	Glomus tumor	Ch. 6:171; Ch. 16:488
	Adult-type rhabdomyoma	Ch. 6:181
	Granular cell tumor	Ch. 6:182; Ch. 15:432; Ch. 16:490
	Epithelioid sarcoma	Ch. 6:192
	Malignant rhabdoid tumor	Ch. 6:195
	Epithelioid angiosarcoma	Ch. 6:199; Ch. 13:378
	Gastrointestinal stromal tumor	Ch. 16:460
	Gastrointestinal clear cell sarcoma–like tumor (gastrointestinal neuroectodermal tumor)	Ch. 16:477
	Epithelioid inflammatory myofibroblastic sarcoma	Ch. 10:270; Ch. 16:480
	Epithelioid myxofibrosarcoma	Ch. 6:202
	Pleomorphic liposarcoma, epithelioid variant	Ch. 6:202; Ch. 12:334
	Dedifferentiated liposarcoma	Ch. 6:204
Clear cell morphology	Myoepithelioma/myoepithelial carcinoma (subset)	Ch. 5:145; Ch. 6:173
	PEComa	Ch. 6:175; Ch. 15:439; Ch. 16:485
	Distinctive dermal clear cell tumor	Ch. 15:441
	Gastrointestinal stromal tumor (subset)	Ch. 16:460
	Clear cell sarcoma (subset)	Ch. 6:204
	Alveolar rhabdomyosarcoma (rare)	Ch. 8:239
Nuclear pleomorphism	PEComa (subset)	Ch. 6:175; Ch. 16:485
	Epithelioid myxofibrosarcoma	Ch. 6:202
	Pleomorphic liposarcoma, epithelioid variant	Ch. 6:202; Ch. 12:334
Myxoid stroma	Myoepithelioma/myoepithelial carcinoma	Ch. 5:145; Ch. 6:173
	Extraskeletal myxoid chondrosarcoma	Ch. 5:151
	Epithelioid schwannoma (subset)	Ch. 15:441
	Ependymoma of soft tissue	Ch. 6:185
	Ossifying fibromyxoid tumor	Ch. 5:143; Ch. 6:185
	Epithelioid inflammatory myofibroblastic sarcoma	Ch. 10:270; Ch. 16:480
	Epithelioid myxofibrosarcoma	Ch. 6:202

Pattern 2 Epithelioid—*cont'd*

Additional Findings	Diagnostic Considerations	Chapter:Page
Collagenous stroma	Myoepithelioma/myoepithelial carcinoma (subset)	Ch. 6:173
	Granular cell tumor	Ch. 6:182; Ch. 15:432; Ch. 16:490
	Cellular neurothekeoma	Ch. 15:437
	Sclerosing perineurioma	Ch. 3:63; Ch. 15:442
	Sclerosing PEComa	Ch. 6:178
	Sclerosing epithelioid fibrosarcoma	Ch. 6:197
Prominent inflammatory cells	Epithelioid hemangioma (lymphocytes, eosinophils; subset)	Ch. 6:168; Ch. 13:372
	Langerhans cell histiocytosis (eosinophils)	Ch. 10:280
	Indeterminate cell histiocytosis (lymphocytes)	Ch. 10:282
	Extranodal Rosai-Dorfman disease (various)	Ch. 10:283; Ch. 15:448
	Histiocytic sarcoma (lymphocytes, neutrophils)	Ch. 10:283
	Epithelioid inflammatory myofibroblastic sarcoma (neutrophils)	Ch. 10:270; Ch. 16:480
Prominent or distinctive giant cells	Clear cell sarcoma (wreath-like)	Ch. 3:87
	Tenosynovial giant cell tumors (osteoclast-like)	Ch. 11:298
	Giant cell tumor of soft tissue (osteoclast-like)	Ch. 11:306
	Juvenile xanthogranuloma (Touton)	Ch. 15:444
	Reticulohistiocytoma (glassy cytoplasm)	Ch. 15:446
	Gastrointestinal clear cell sarcoma–like tumor (gastrointestinal neuroectodermal tumor) (osteoclast-like; subset)	Ch. 16:477
Prominent or distinctive blood vessels	Epithelioid hemangioma (small- to medium-sized)	Ch. 6:168; Ch. 13:372
	Glomus tumor (capillary-sized; dilated, branching)	Ch. 6:171; Ch. 16:488
	Angiomyofibroblastoma (delicate, thin-walled)	Ch. 17:502
	Epithelioid myxofibrosarcoma (curvilinear)	Ch. 6:202

Pattern 3 Pleomorphic

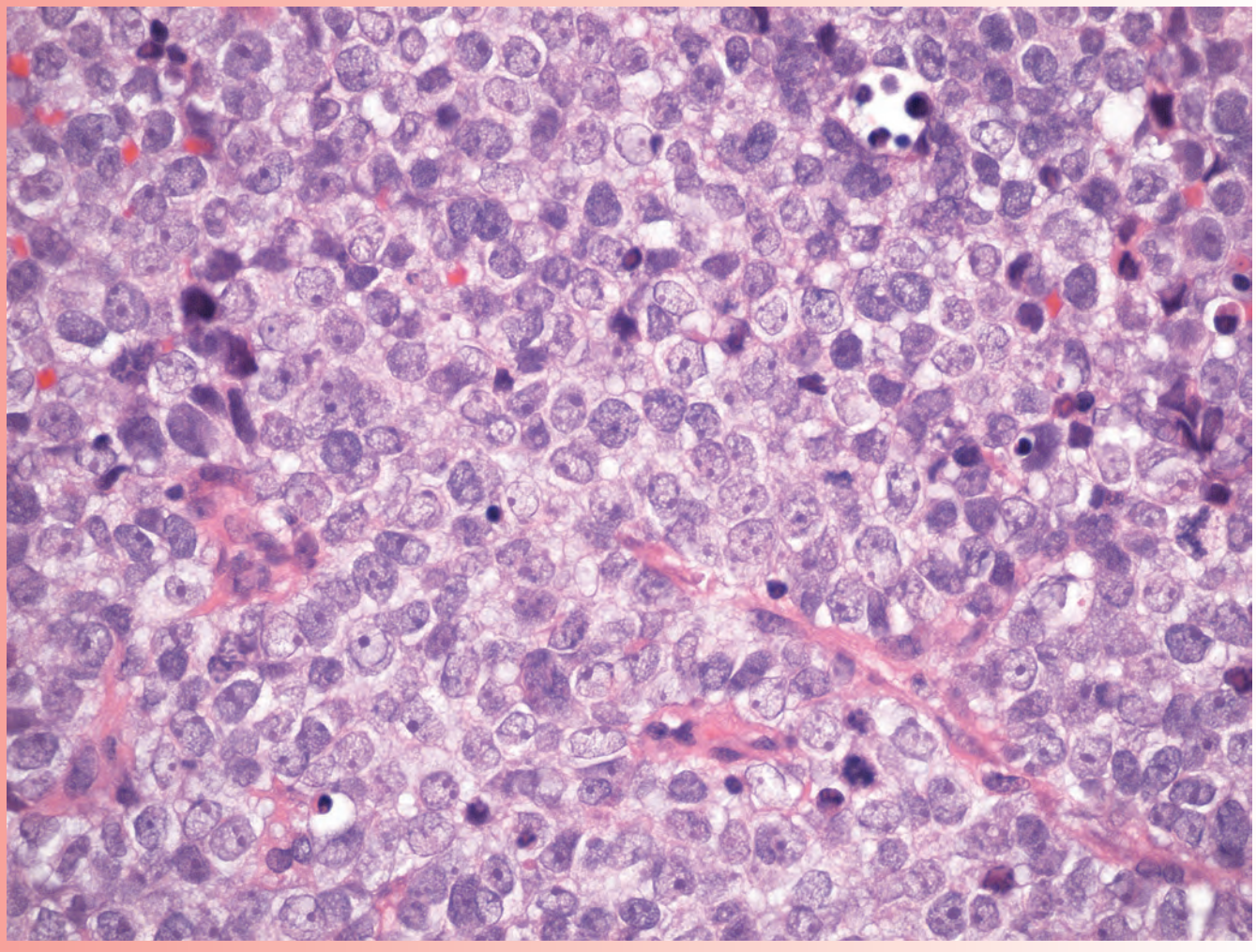


Elements of the pattern: The tumor cells show marked variation in size and shape, often including very large and bizarre forms.

Pattern 3 Pleomorphic

Additional Findings	Diagnostic Considerations	Chapter:Page
Abundant eosinophilic cytoplasm	Pleomorphic leiomyosarcoma	Ch. 7:221
	Pleomorphic rhabdomyosarcoma	Ch. 7:221
	Undifferentiated pleomorphic sarcoma (subset)	Ch. 7:212
Cutaneous	Pleomorphic fibroma	Ch. 15:452
	Atypical fibrous histiocytoma	Ch. 15:411
	Atypical fibroxanthoma	Ch. 7:210; Ch. 15:449
	Pleomorphic dermal sarcoma	Ch. 15:451
Myxoid stroma	Myxofibrosarcoma	Ch. 5:148; Ch. 7:218
	Pleomorphic liposarcoma (subset)	Ch. 7:223; Ch. 12:334
	Dedifferentiated liposarcoma (subset)	Ch. 7:225; Ch. 12:328
	Myxoinflammatory fibroblastic sarcoma	Ch. 5:155; Ch. 7:217; Ch. 10:286
Prominent or distinctive giant cells	Pleomorphic leiomyosarcoma (osteoclast-like; subset)	Ch. 11:309
	Giant cell–rich extraskeletal osteosarcoma (osteoclast-like; subset)	Ch. 11:308
	Undifferentiated pleomorphic sarcoma (osteoclast-like; subset)	Ch. 11:307
Prominent or distinctive blood vessels	Pleomorphic hyalinizing angiectatic tumor (hyalinized, dilated, thin-walled)	Ch. 7:216
	"Ancient" schwannoma (hyalinized)	Ch. 3:52
	Myxofibrosarcoma (curvilinear)	Ch. 5:148; Ch. 7:218
Prominent inflammation	Dedifferentiated liposarcoma (neutrophils, histiocytes; subset)	Ch. 7:225; Ch. 10:288
	Undifferentiated pleomorphic sarcoma (various; subset)	Ch. 7:212
	Myxoinflammatory fibroblastic sarcoma (neutrophils, lymphocytes)	Ch. 5:155; Ch. 7:217; Ch. 10:286
Adipocytic component or lipoblasts	Pleomorphic lipoma	Ch. 12:316
	Pleomorphic liposarcoma	Ch. 7:223; Ch. 12:334
	Dedifferentiated liposarcoma	Ch. 7:225; Ch. 12:328
Osteoid/bone	Extraskeletal osteosarcoma	Ch. 7:226; Ch. 14:400
	Dedifferentiated liposarcoma (subset)	Ch. 7:225; Ch. 12:328

Pattern 4 Round Cell

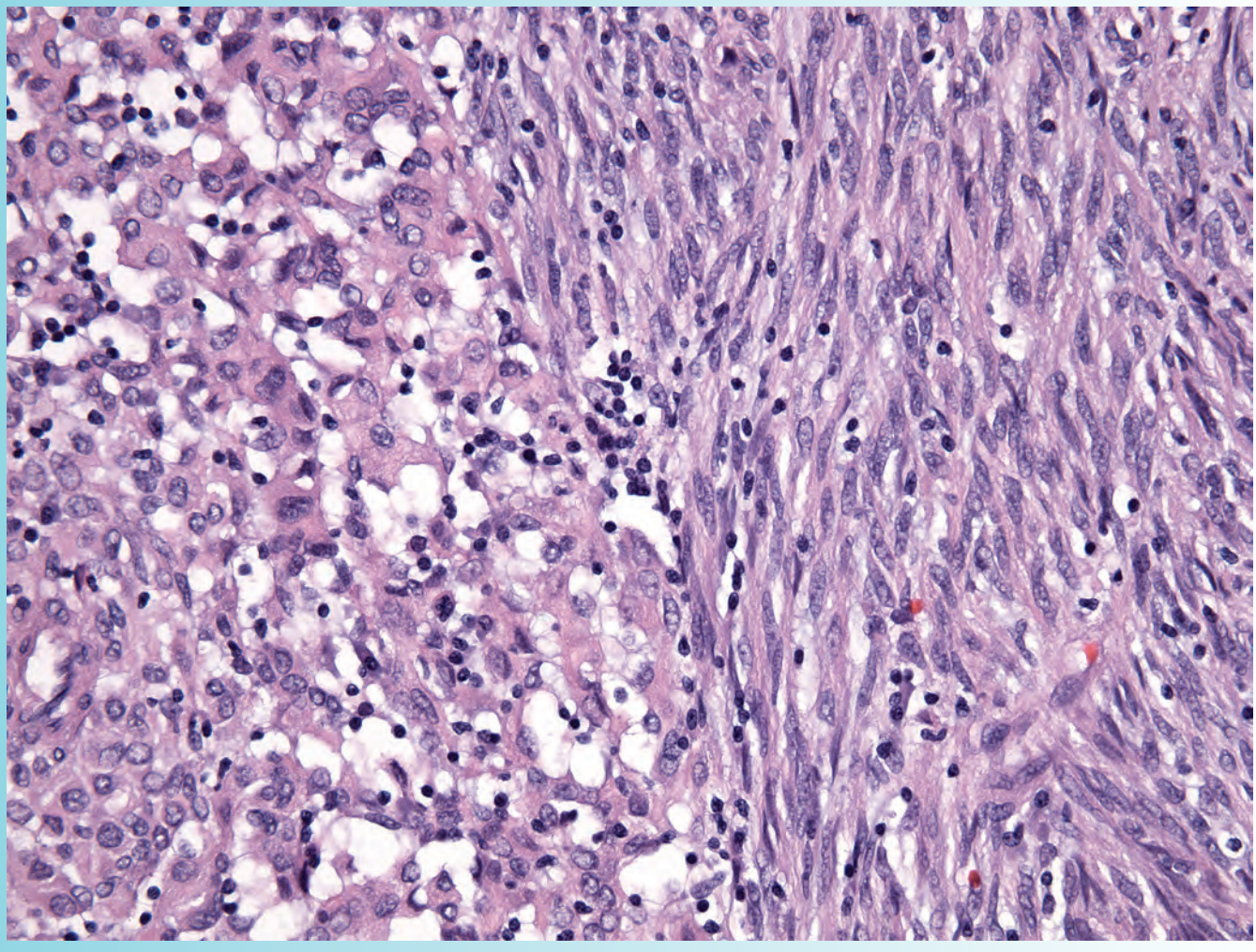


Elements of the pattern: The tumor cells contain round, often uniform nuclei and minimal cytoplasm.

Pattern 4 Round Cell

Additional Findings	Diagnostic Considerations	Chapter:Page
Nested architecture	Alveolar rhabdomyosarcoma (subset)	Ch. 8:239
	Desmoplastic small round cell tumor	Ch. 8:243
Sheet-like architecture	Ewing sarcoma	Ch. 8:235
	Alveolar rhabdomyosarcoma (subset)	Ch. 8:239
	Embryonal rhabdomyosarcoma	Ch. 8:242
	Round cell (high-grade myxoid) liposarcoma (subset)	Ch. 8:243; Ch. 12:332
	Poorly differentiated synovial sarcoma	Ch. 8:244
	Mesenchymal chondrosarcoma	Ch. 14:398
	Gastrointestinal clear cell sarcoma–like tumor (gastrointestinal neuroectodermal tumor)	Ch. 16:477
	CIC-rearranged sarcomas	Ch. 8:245
	BCOR-rearranged sarcomas	Ch. 8:246
Myxoid stroma	Embryonal rhabdomyosarcoma (subset)	Ch. 8:242
	Round cell (high-grade myxoid) liposarcoma (subset)	Ch. 8:243; Ch. 12:332
Collagenous stroma	Desmoplastic small round cell tumor	Ch. 8:243
	Poorly differentiated synovial sarcoma (focal; subset)	Ch. 8:244
Prominent or distinctive blood vessels	Round cell (high-grade myxoid) liposarcoma (plexiform)	Ch. 8:243; Ch. 12:332
	Poorly differentiated synovial sarcoma (dilated, branching; subset)	Ch. 8:244
Prominent or distinctive giant cells	Alveolar rhabdomyosarcoma (wreath-like)	Ch. 8:239
Cartilage	Mesenchymal chondrosarcoma	Ch. 14:398

Pattern 5 Biphasic or Mixed



Elements of the pattern: The tumor contains two or more types of cells with distinct morphology, such as spindle cells and epithelioid cells. Some tumors show variation in architecture and stromal composition.