- Plantar: Common in young patients, unilateral and without contractures.
- Penile *(Peyronie disease):* Palpable induration or mass on the dorsolateral aspect of the penis. Eventually, it may cause abnormal curvature of the shaft, constriction of the urethra, or both.

In about 20% to 25% of cases, the palmar and plantar fibromatoses stabilize and do not progress, in some instances resolving spontaneously. Some recur after excision, particularly the plantar variant.

Deep Fibromatosis (Desmoid Tumors)

Deep fibromatoses are large, infiltrative masses that frequently recur but do not metastasize. They are most frequent in the teens to 30s, predominantly in women. Abdominal fibromatosis generally arises in the musculoaponeurotic structures of the anterior abdominal wall but tumors can arise in the limb girdles or the mesentery. Deep fibromatoses contain mutations in the *APC* or β-catenin genes, both of which lead to increased Wnt signaling. The majority of tumors are sporadic, but individuals with familial adenomatous polyposis (Gardner syndrome, Chapter 17) who have germline *APC* mutations are predisposed to deep fibromatosis.

MORPHOLOGY

Fibromatoses are gray-white, firm, poorly demarcated masses varying from 1 to 15 cm in greatest diameter. They are rubbery and tough, and have marked infiltration of surrounding muscle, nerve and fat. Cytologically bland fibroblasts arranged in broad sweeping fascicles amid dense collagen are the characteristic histologic pattern (Fig. 26-52). The histology resembles scar.

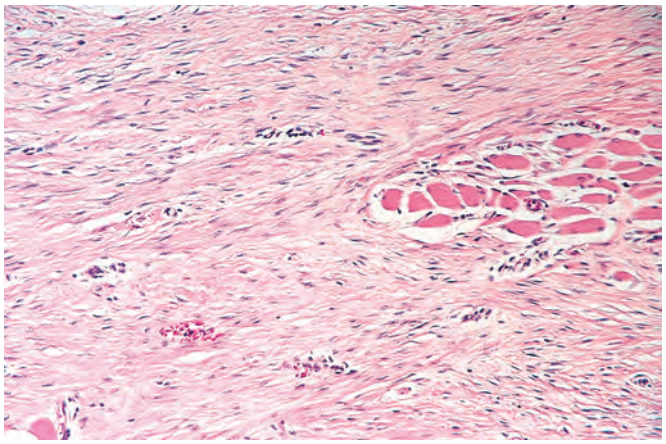

Figure 26-52 Fibromatosis infiltrating between skeletal muscle cells.

In addition to possibly being disfiguring or disabling, deep-seated fibromatosis is occasionally painful. Because of the extensively infiltrative nature, complete excision is often difficult. Recent efforts have concentrated on medical therapy with cyclooxygenase 2 inhibitors, tyrosine kinase inhibitors, or hormonal blockade (tamoxifen).

Skeletal Muscle Tumors

Skeletal muscle neoplasms, in contrast to other mesenchymal histotypes, are almost all malignant. The benign variant, rhabdomyoma, is frequent in individuals with tuberous sclerosis and is discussed in Chapter 28.

Rhabdomyosarcoma

Rhabdomyosarcoma is a malignant mesenchymal tumor with skeletal muscle differentiation. Three subtypes are recognized: *alveolar* (20%), *embryonal* (60%) and *pleomorphic* (20%). Rhabdomyosarcoma (alveolar and embryonal) is the most common soft tissue sarcoma of childhood and adolescence, usually appearing before age 20. Pleomorphic rhabdomyosarcoma is seen predominantly in adults. The pediatric forms often arise in the sinuses, head and neck and genitourinary tract, locations that do not normally contain much skeletal muscle, underscoring the notion that arcomas do not arise from mature, terminally differentiated muscle cells. The embryonal and pleomorphic subtypes are genetically heterogeneous. Alveolar rhabdomyosarcoma frequently contains fusions of the *FOXO1* gene to either the *PAX3* or the *PAX7* gene, rearrangements marked by the presence of (2;13) or(1;13) translocations, respectively. PAX3 is a transcription factor that initiates skeletal muscle differentiation, and it appears that the chimeric PAX3-FOXO1 fusion protein interferes with the gene expression program that drives differentiation, a mechanism similar to many of the transcription factor fusion proteins that are found in various forms of acute leukemia.

MORPHOLOGY

Embryonal rhabdomyosarcoma presents as soft gray infiltrative mass. The tumor cells mimic skeletal muscle at various stages of embryogenesis and consist of sheets of both primitive round and spindled cells in a myxoid stroma (Fig. 26-53*A*). Rhabdomyoblasts with visible cross-striations may be present. **Sarcoma botryoides**, described in Chapter 22, is a variant of embryonal rhabdomyosarcoma that develops in the walls of hollow, mucosal-lined structures, such as the nasopharynx, common bile duct, bladder, and vagina. Where the tumors abut the mucosa of an organ, they form a submucosal zone of hypercellularity called the **cambium layer.**

Alveolar rhabdomyosarcoma is traversed by a network of fibrous septae that divide the cells into clusters or aggregates, creating a crude resemblance to pulmonary alveoli. Those in the center of the aggregates are discohesive, while those at the periphery adhere to the septae. The tumor cells are uniform round, with little cytoplasm—cross striations are not a common feature (Fig. 26-53*B*).

Pleomorphic rhabdomyosarcoma is characterized by numerous large, sometimes multinucleated, bizarre eosinophilic tumor cells and can resemble other pleomorphic sarcomas histologically. Immunohistochemistry (e.g., myogenin) is usually necessary to confirm rhabdomyoblastic differentiation.

Rhabdomyosarcomas are aggressive neoplasms that are usually treated with surgery and chemotherapy, with or without radiation therapy. The histologic type and location of the tumor influence survival. The botryoid variant of embryonal rhabdomyosarcoma has the best prognosis, while the pleomorphic subtype is often fatal.