A 33-year-old male with a left lower leg mass.

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Special Interest: Surgical pathology and Cytopathology

Clinical history and findings: The patient noticed a small nodule about the size of a cherry along the left leg in January 2014. This was no pain and erythema. But it had increased in size until it got to about the size of a small strawberry. Later MRI showed that the mass had a transverse diameter of 3.2 cm and anterior-posterior dimension of 1.7 cm. The mass was described as being subcutaneous and did not involve the deep fascia and did not invade directly into the skin. The tumor was removed on on April 18, 2014.

Gross examination: A circumscribed nodule measuring 2.9 x 2.9 x 2.1 cm was identified. The cut surface revealed a firm, white to tan mass with a whorled appearance.

Microscopy and Immunohistochemistry (4 images):

Fig.1: spindle cells arranged in fascicles.

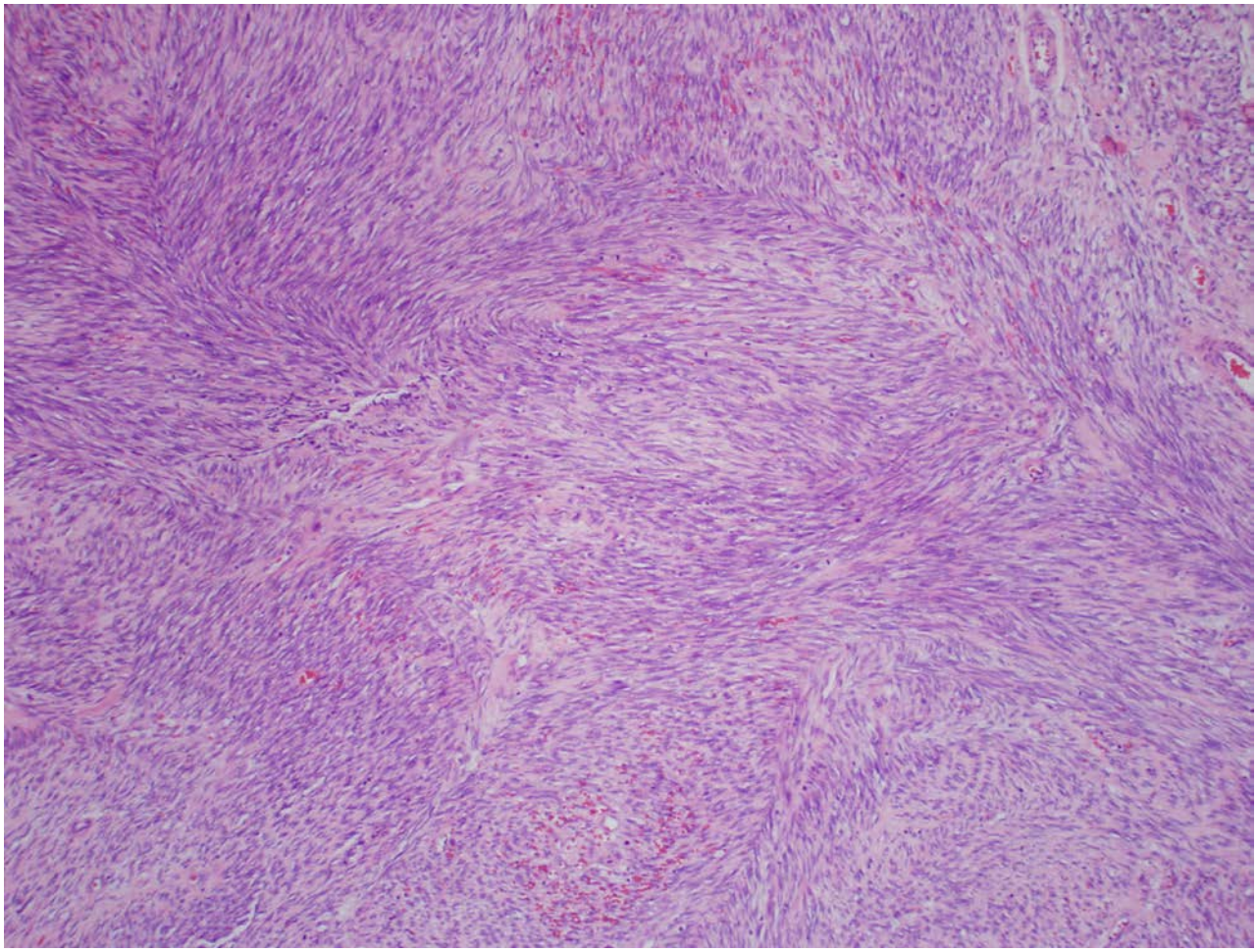


Fig. 2: elongated nuclei with atypia, small or inconspicuous nucleoli.

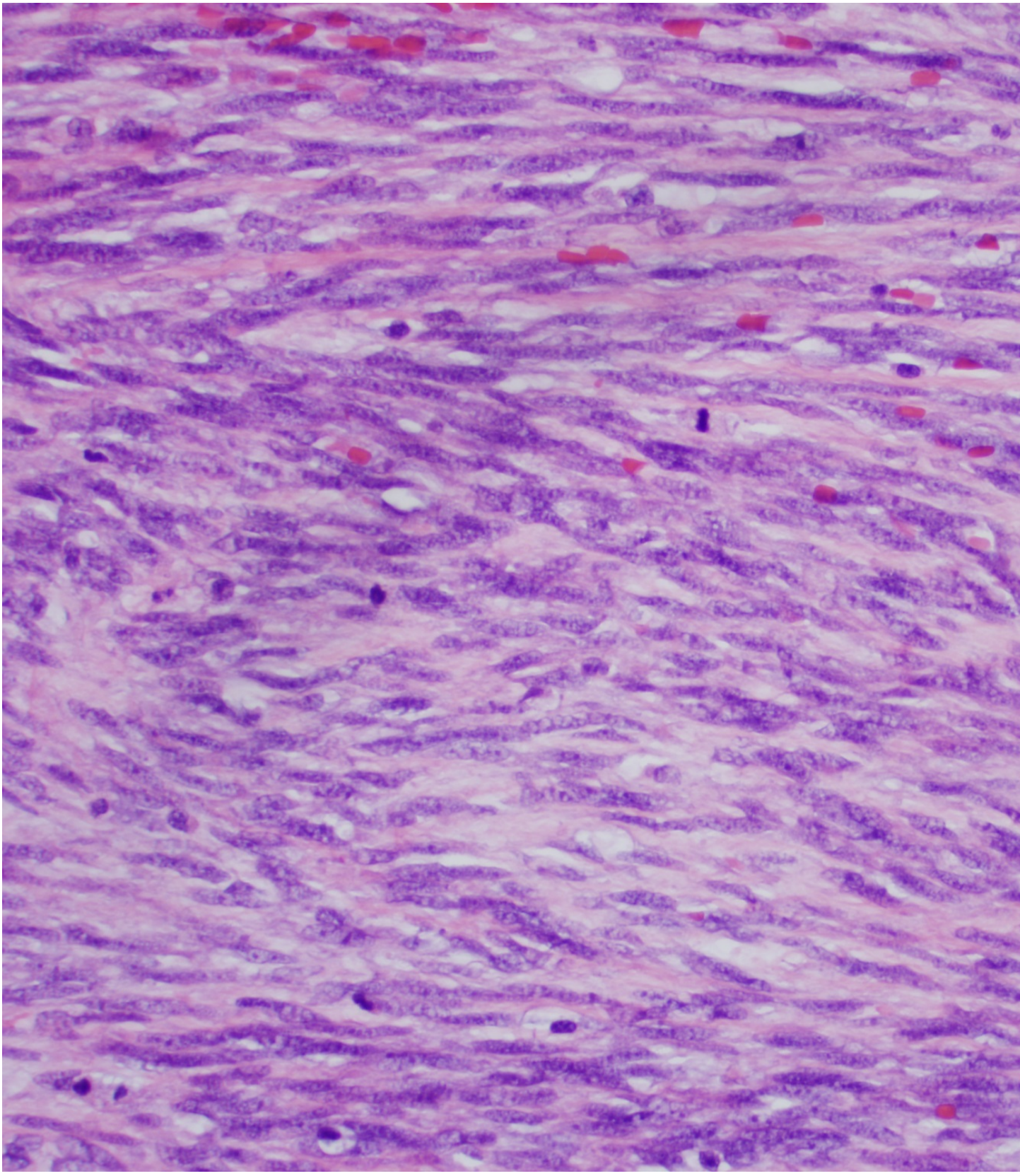


Fig. 3: SMA stain

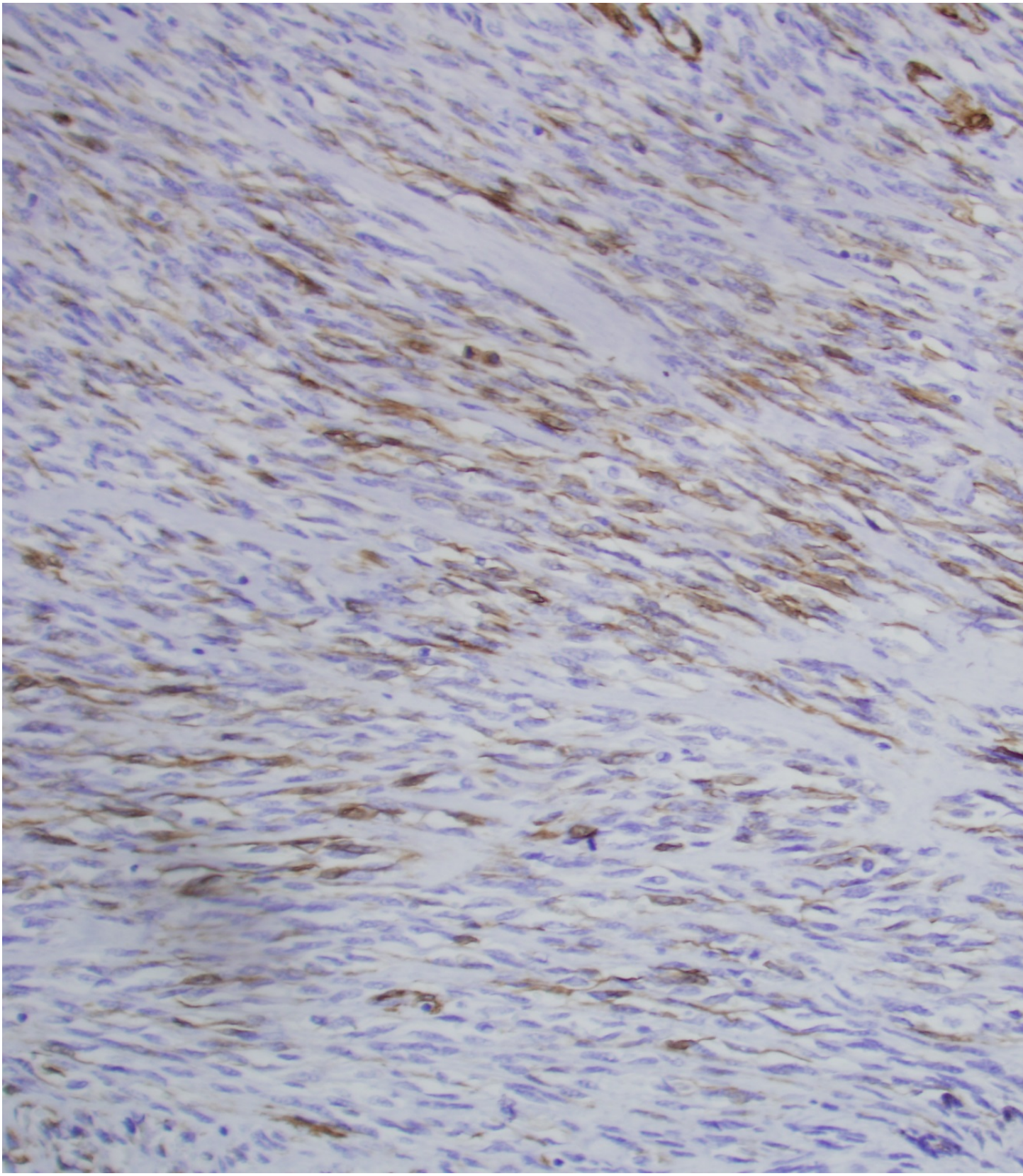
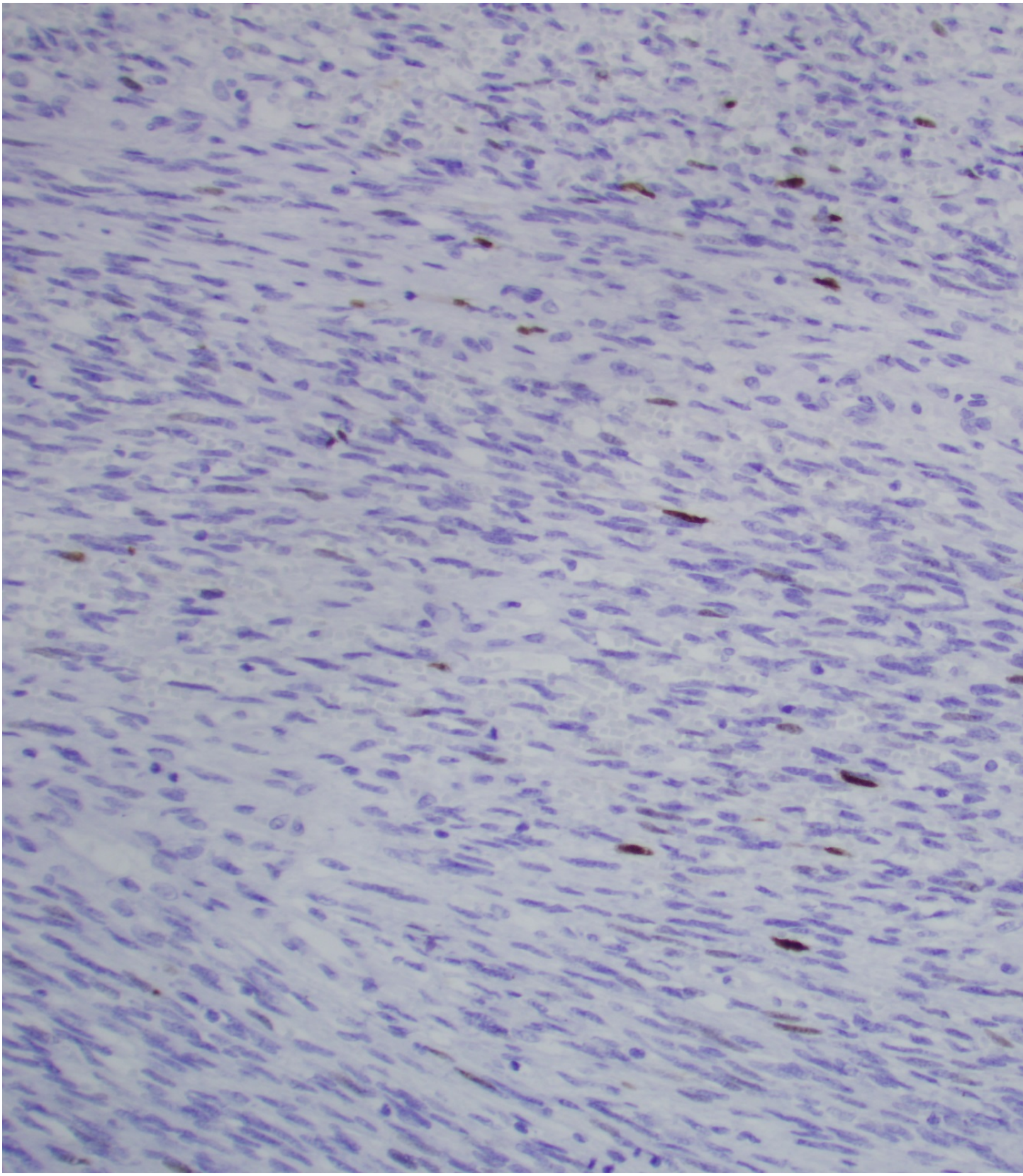


Fig. 4: Myogenin stain



Final diagnosis:

Adult spindle cell rhabdomyosarcoma:

Discussion: Spindle cell rhabdomyosarcoma (RMS) was first reported in the pediatric population in 1992 by the German-Italian Cooperative Sarcoma Study. It affects mainly young males (mean age approximately 7 years) and arises mainly in the paratesticular region, followed by head and neck region. In adults, the tumor is commonly located in the head and neck area with a minority of cases occurring in subcutaneous and deep soft tissues of the extremities and visceral organs. Clinically, the patients present with a rapidly growing and painless soft tissue mass. Clinical symptoms are related to the location and infringement on surrounding structures, which can lead to urinary retention, diplopia, unilateral deafness, proptosis, and sinusitis. The tumor varies in size significantly, with a range of a few centimeters to 35 cm. Tumors in the paratesticular region, head/neck and extremities can be detected earlier when they are small. But tumors are detected late and larger in the deep location. Gross appearance can mimic leiomyoma or leiomyosarcoma. Tumors can be either well or poorly circumscribed.

Microscopic examination shows relatively uniform spindle cell proliferation arranged in fascicles (Fig. 1) or whorls demonstrating a herringbone growth pattern. The tumor cells have elongated nuclei with blunted or fusiform ends, small to inconspicuous or prominent nucleoli (Fig. 2), and eosinophilic fibrillar cytoplasm. Mitotic figures are easily found, including atypical forms. Immature rhabdomyoblasts can be focally appreciated in the tumor and have eccentric nuclei and bright cytoplasmic eosinophilia. Cytoplasmic cross-striations can be observed occasionally. The presence of immature rhabdomyoblasts is a diagnostic clue. Some tumors are collagen–rich, while others are collagen-poor. Collagen fibers alternate with spindle cells. In the collagen-poor form, the tumor cells are arranged in bundles or fascicles with little stroma and morphologically mimic smooth muscle cells.

Spindle cell RMS, a rare variant of embryonal RMS, shows positivity for myogenic markers such as SMA (Fig. 3), desmin, titin, troponin D, MyoD1 and myf-4 (myogenin, Fig. 4). The proportion of desmin-positive cells may vary from case to case. In this case, rare scattered cells are strongly positive for desmin (data not shown). It is

worth mentioning that myofibroblasts, smooth muscle tumor, desmoplastic small round cell tumor, etc are also positive for desmin. Desmin is not useful to distinguish spindle cell RMS from other spindle cell neoplasms. Myogenin and MyoD1 are myogenic nuclear transcription factors present early in skeletal muscle differentiation and are currently used as standard biomarkers for confirming a diagnosis, with sensitivity exceeding 95% and specificity of virtually 100%. Myogenin demonstrates no reactivity in other spindle cell lesions, such as leiomyosarcoma, myofibrosarcoma, and malignant peripheral nerve sheath tumor. The diagnostic utility of Myo-D1 could be limited by technical challenges with background and cytoplasmic nonspecific staining. There have been few molecular and/or cytogenetic studies on spindle cell RMS.

Spindle cell RMS can be confused with other spindle cell neoplasms, mostly of smooth muscle, myofibroblastic, nerve origin, etc. Differential diagnosis list includes leiomyosarcoma (LMS), low-grade myofibroblastic sarcoma, fibrosarcoma, malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation, desmoplastic melanoma, spindle cell squamous cell carcinoma, solitary fibrous tumor (SFT), and synovial sarcoma. Spindle cell RMS has overlapping morphologic features with LMS and was called in old literatures as ‘‘leiomyomatous’’ embryonal RMS. Presence of rhabdomyoblasts and positive myogenin immunostaining are helpful to distinguish these two entities. Adult and infantile fibrosarcoma will also consist of similar spindled cells, and both tumors can show herringbone pattern. However, spindle cells are negative for myogenin or MyoD1. In the adult population, desmoplastic melanoma and spindle cell (sarcomatoid) squamous cell carcinoma commonly occur in the head and neck region and should be ruled out first in this age group. Myofibroblastic lesions such as nodular fasciitis, low-grade myofibroblastic sarcoma, etc do not stain for myogenin. Malignant peripheral nerve sheath tumor (MPNST) and malignant triton tumor (MPNST with rhabdomyoblastic differentiation) arise often from a large peripheral nerve in patients with known history of neurofibromatosis. These tumors show focal positivity for S-100. SFT can show spindle cells alternating with collagen fibers. Spindle cells are positive for CD34 and STAT6. Monophasic synovial sarcoma shows spindle cell proliferation with short fascicle formation and wiry collagen. Spindle cells have relatively uniform nuclei and are positive for TLE1 (nuclear stain).

Pediatric spindle cell RMS has been demonstrated to have a highly favorable prognosis compared with other forms of RMS. In this population, paratesticular lesions appear to have an even better outcome in comparison to tumors of non-paratesticular sites because these lesions are detected and treated earlier. Major prognostic factors include resectability, tumor size, and tumor stage. Due to complex anatomy of the head and neck region and the local aggressiveness of the tumor, it is often difficult to obtain adequate free surgical margins. This compromises local control of the disease. In the adult population with spindle cell RMS, 40% of patients have experienced uncontrolled local disease, 25% developed metastases, and 17% died of the disease. Therefore, adult spindle cell RMS has a poorer prognosis. Staging of rhabdomyosarcomas is based on resection and clinical findings, which include site of origin, presence or absence of residual disease, lymph node involvement, and distant metastases. Spindle cell RMS are treated aggressively with similar protocols as for other RMS. The standard protocols include surgery, chemotherapy, and adjuvant radiation.

Reference:

1. Carroll SJ and Nodit L. Spindle Cell Rhabdomyosarcoma: A Brief Diagnostic Review and Differential Diagnosis. Arch Pathol Lab Med. 2013;137:1155–1158
2. Mentzel T and Kuhnen C. Spindle cell rhabdomyosarcoma in adults: clinicopathological and immunohistochemical analysis of seven new cases. Virchows Arch 2006; 449:554–560