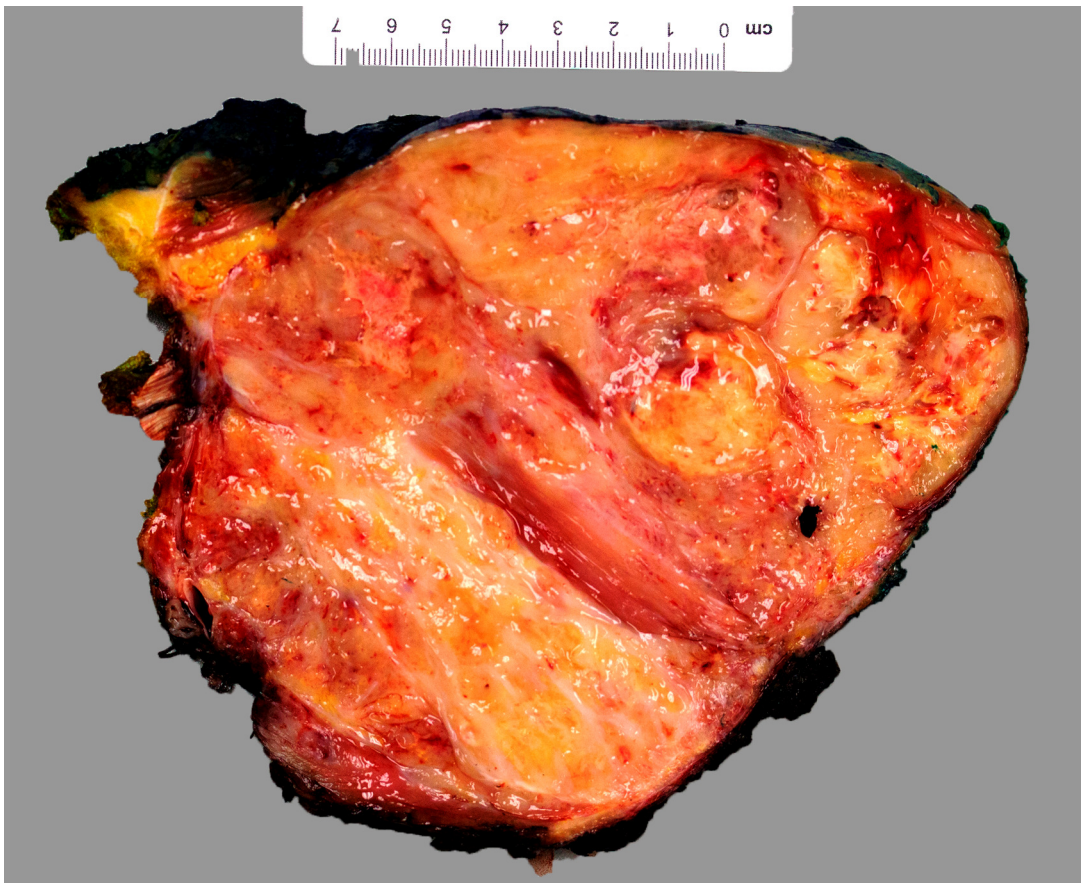
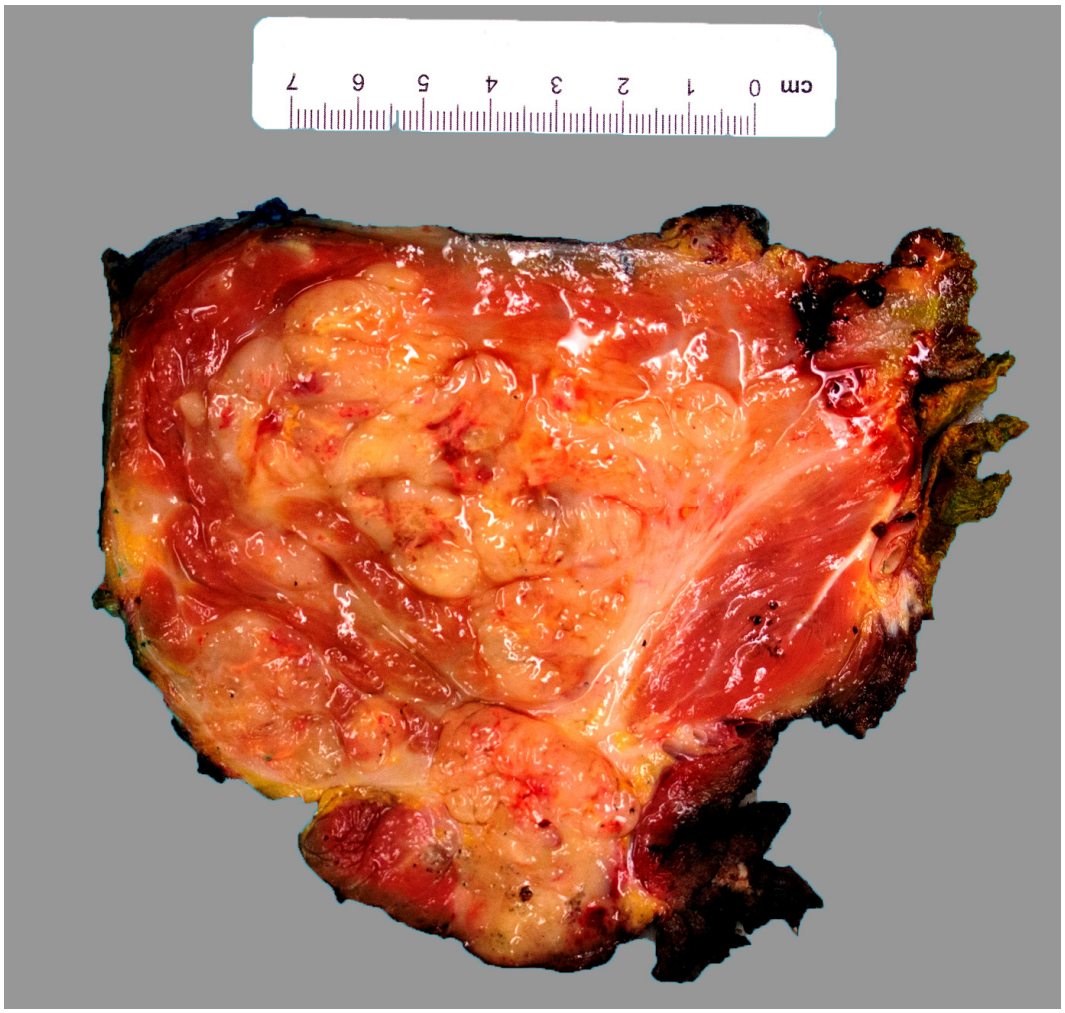
IAP case of the month (August, 2015) by Rasha Salama MD.

Clinical history:

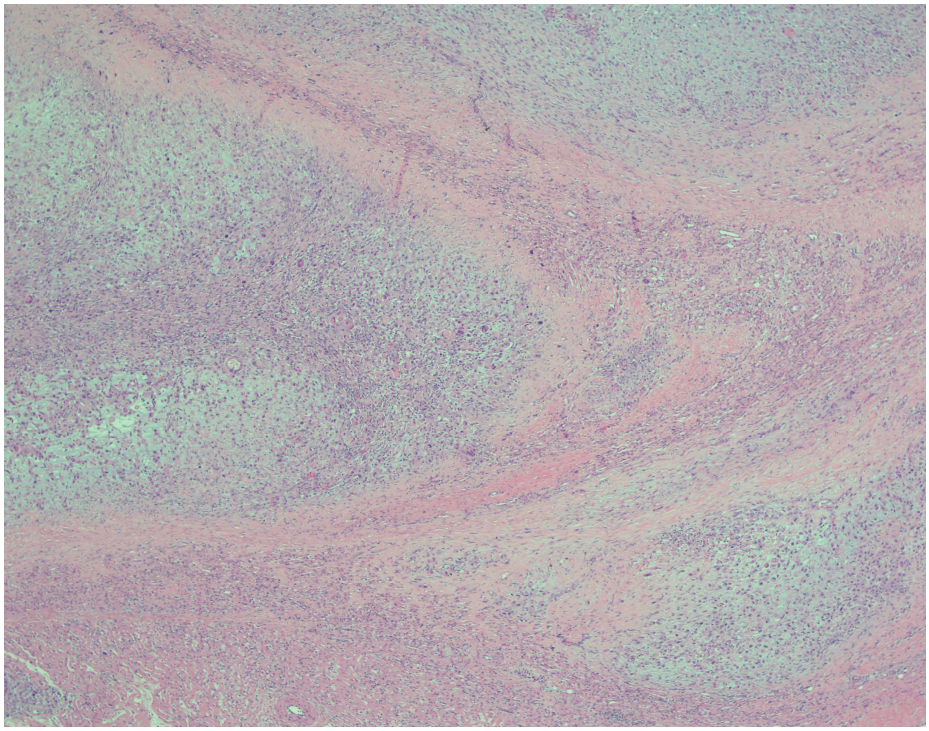
A 33-year-old male started feeling some discomfort in the posterior aspect of his left thigh back while sitting in 2013. He later developed a lump at the back of his thigh so he finally sought medical care in 2014. His primary care physician at first thought it was bursitis and recommended nonsteroidal anti-inflammatory drugs and physical therapies. However, the mass continued to increase in size and the pain became more significant. An MRI was ordered and showed 12.5 x 14.5 x 18.6 cm enhancing soft tissue mass with multiple septations and central necrosis. The bone did not appear to be involved. The patient also had a chest CT scan that showed several noncalcified subcentimeter lung nodules suspicious for metastatic disease. FNA was performed and diagnosis was rendered. The patient underwent chemotherapy prior to the surgical intervention; however, the treatment did not seem to work and it metastasized to the left inguinal lymph node, right shoulder, left back, and multiple abdominal subcutaneous locations.

Gross pictures from the thigh tumor resection:

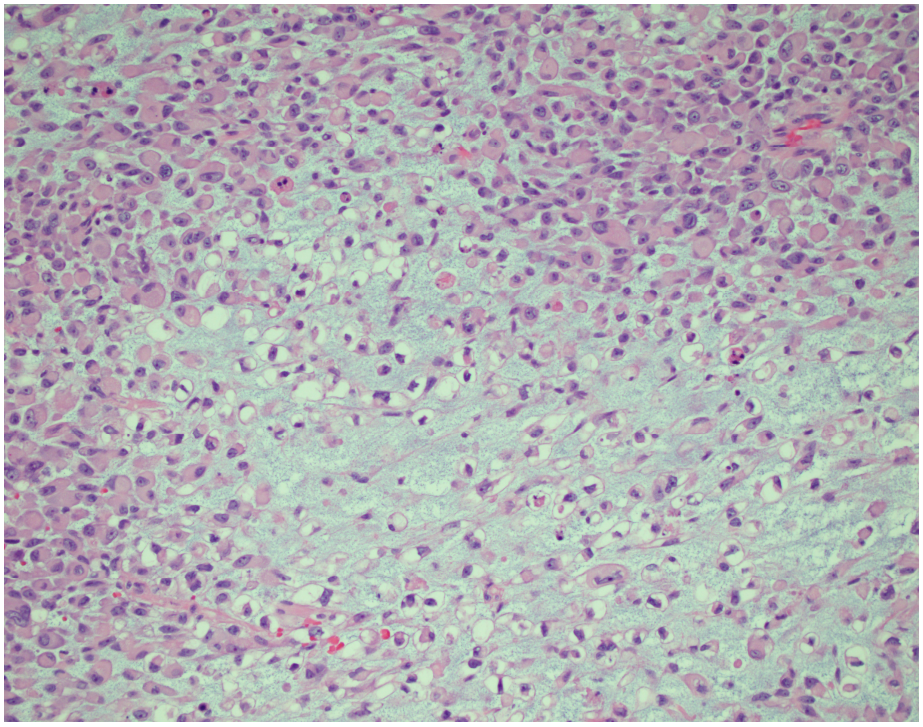



cm
0
1
2
3
4
5
6
7

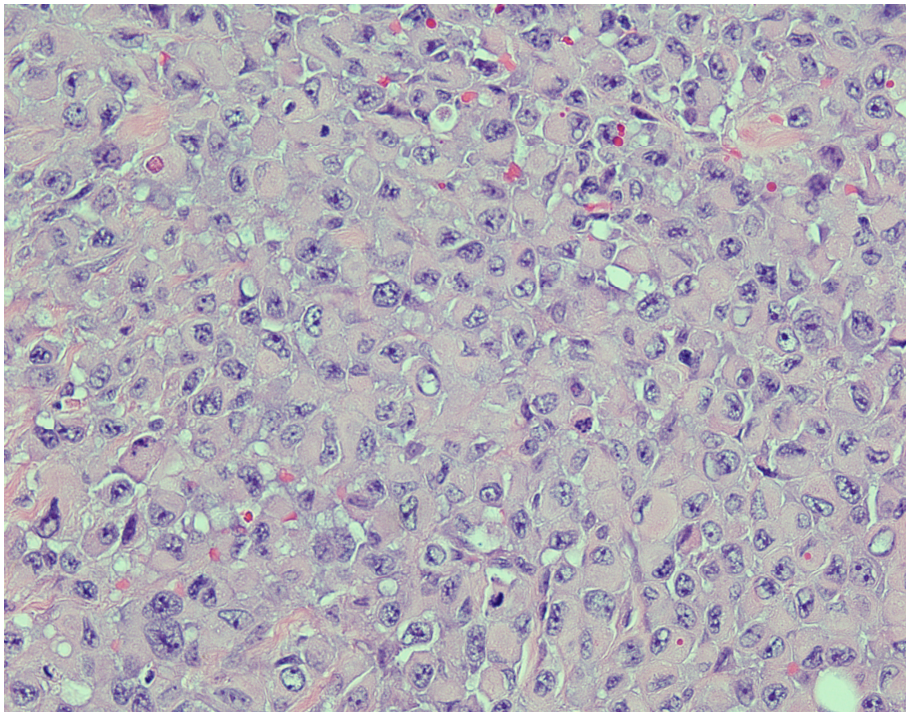
Histologic sections from the thigh tumor resection:



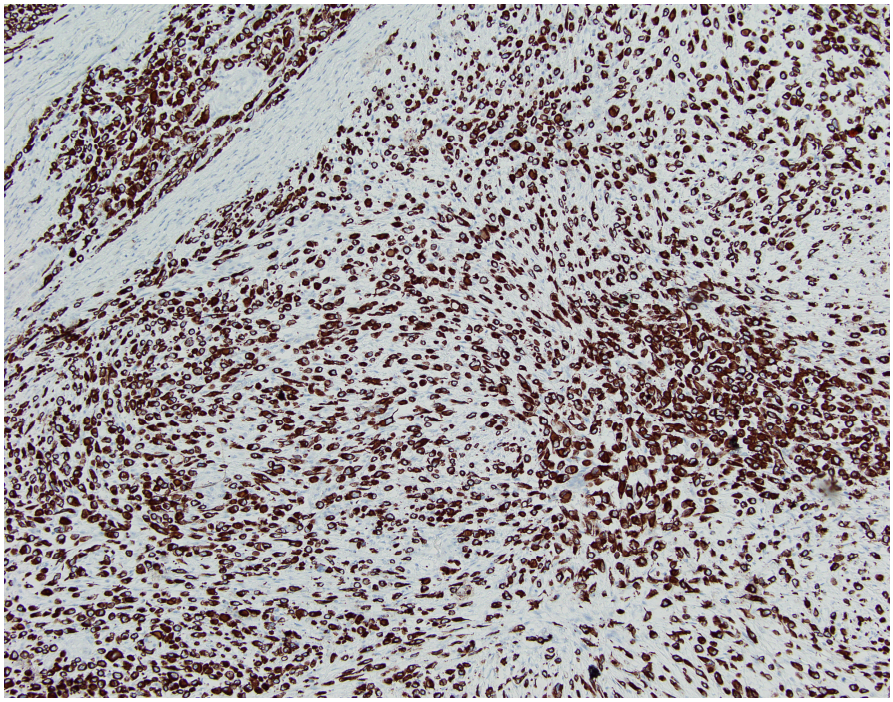
(Hematoxylin-eosin, original magnification _X40)



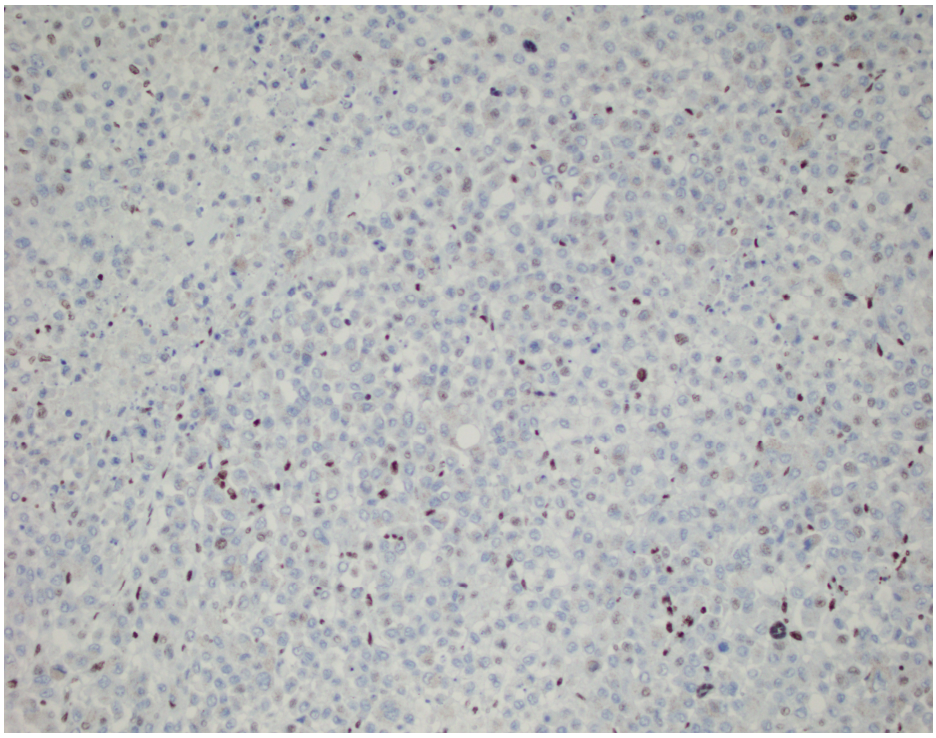
(Hematoxylin-eosin, original magnification _X200)



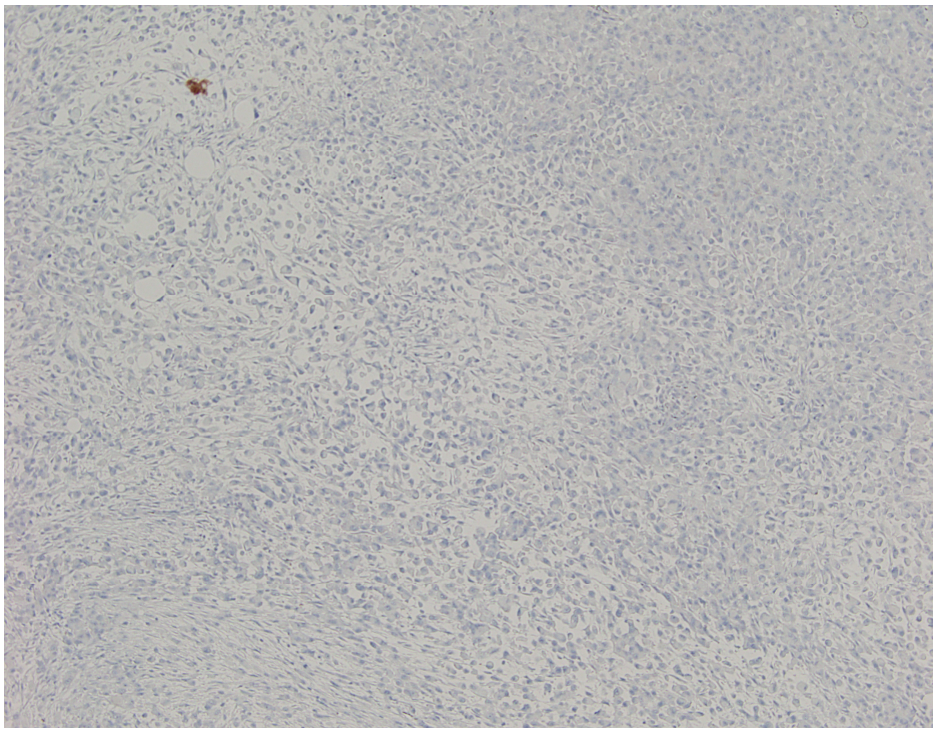
(Hematoxylin-eosin, original magnification _X400)



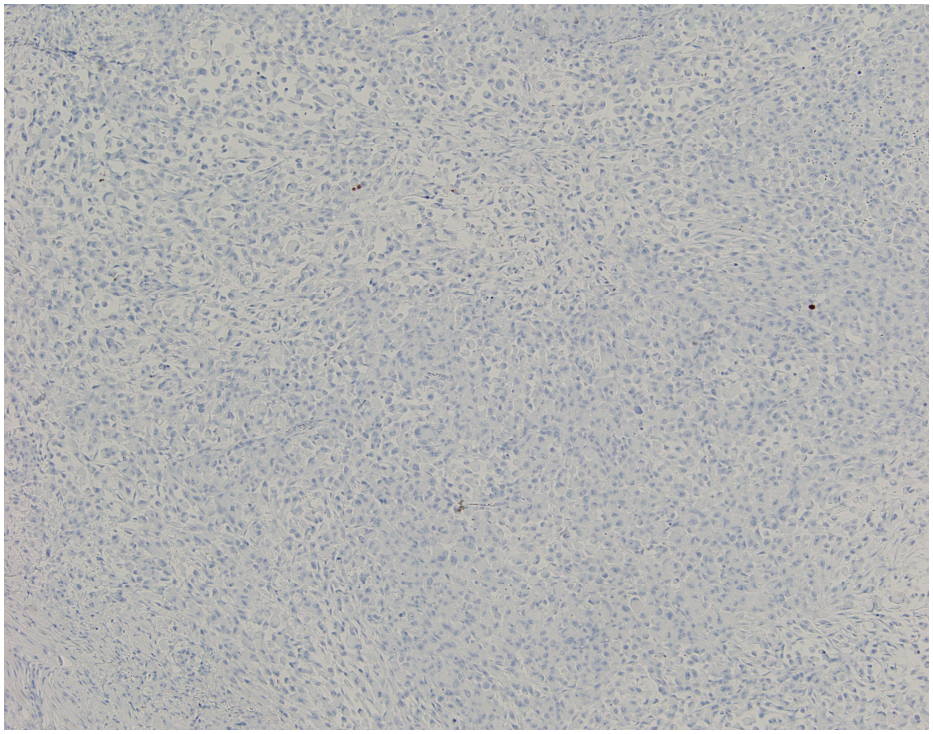
Pan cytokeratin immunostaining, AE1/AE3 *(immunoperoxidase, original magnification _X100)*



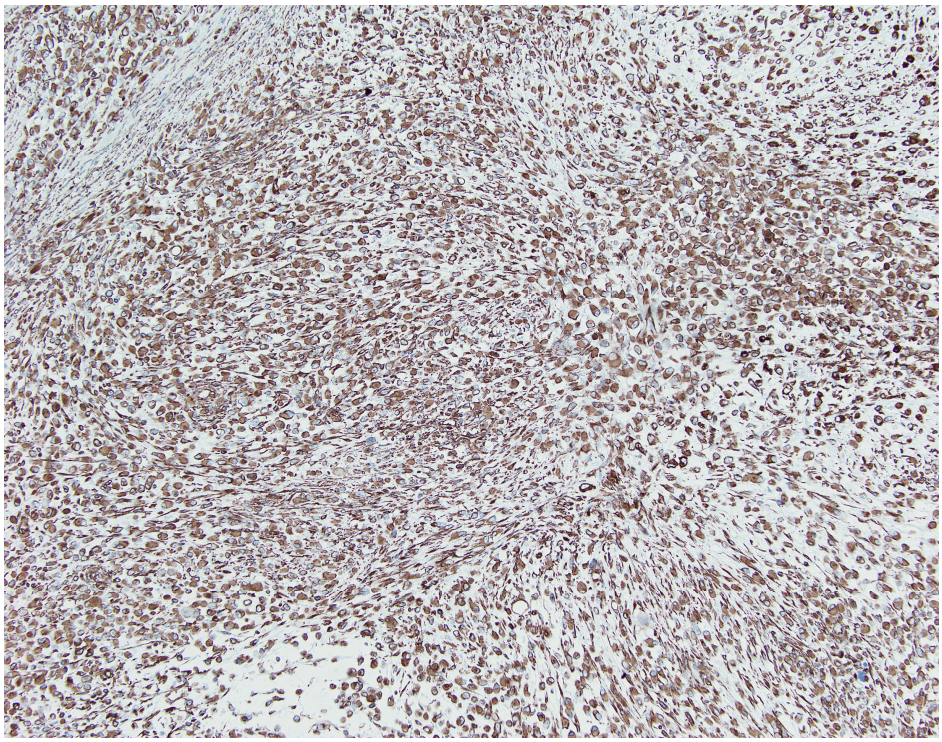
INI-1 immunostaining *(immunoperoxidase, original magnification _X40)*



Myogenin immunostaining *(immunoperoxidase, original magnification _X40)*



S100 immunostaining *(immunoperoxidase, original magnification _X40)*



Vimentin immunostaining *(immunoperoxidase, original magnification _X100)*

Choices:

A- Melanoma

B- Epithelioid malignant peripheral nerve sheath tumor

C- Epithelioid angiosarcoma

D Epithelioid rhabdomyosarcoma

E- Epithelioid monophasic synovial sarcoma

F- Extrarenal rhabdoid tumor

G- Undifferentiated carcinoma.

H- Epithelioid sarcoma, proximal type.

Your answer?

Epithelioid sarcomas affect mainly young adults (median age, 26 years) and have predilection for the distal extremities. They can be superficial and tend to ulcerate into the skin -- sometimes mistaken for a benign condition like granuloma annulare or a rheumatoid nodule. They also occur deeply, where they are usually attached to tendons and tend to move with the extremity.

Grossly, they usually present as multinodular masses with irregular outlines. The cut surface has a glistening gray-tan mottled surface with focal yellow or brown areas caused by focal necrosis or hemorrhage.

There are two types of epithelioid sarcoma: classic and proximal. The classic type has a nodular arrangement of tumor cells with central necrosis. The geographic lesion is usually formed by the fusion of multiple necrotized nodules. The proximal type (1, 2) usually occurs in older people, is more aggressive, and has the propensity to arise in axial locations (pelvis, perineum, or genital tract). It consists of large pleomorphic epithelioid cells with vesicular nuclei, prominent nucleoli, and intracytoplasmic hyaline inclusions. It usually does not have a granuloma-like pattern.

Both types have similar staining pattern. They stain positive with EMA, vimentin, low and high cytokeratin, and CD34 in about 50% of the cases (2). Both types are also proven to have loss of INI1 expression (3).

Epithelioid sarcoma has the tendency for local recurrence and distant metastasis. The most common sites of metastasis are the lung, regional lymph nodes, and skin.

Ok, now let us discuss the other options provided in the question:

Melanoma should be S100 positive.

Epithelioid malignant peripheral nerve sheath tumor might be positive for cytokeratin and EMA occasionally, but about 80% show diffuse and strong reactivity for S100 protein.

Epithelioid angiosarcoma shows vascular spaces lined directly by tumor cells, slit-like structures, vacuolated cells often containing red blood cells, and positive immunoreactivity with endothelial markers (e.g., CD31 and Factor VIII); cytokeratin (but not EMA) expression has also been observed in varying degrees.

Epithelioid rhabdomyosarcoma are positive for myogenin.

Monophasic epithelioid variant of synovial sarcoma is usually vimentin negative, EMA negative, and cytokeratin positive. It usually shows, at least focally, a biphasic pattern. The absence of t(X,18) is also a supporting feature in ruling this sarcoma out.

Extrarenal rhabdoid tumor: both tumors show immunohistochemical overlap with coexpression of epithelial markers and vimentin, and loss of INI-1 staining, but up to 60% of epithelioid sarcomas express CD34, a marker typically absent in rhabdoid tumors. In addition, extrarenal rhabdoid tumors affect a younger population (8-9 years) and a wide range of possible locations.

Undifferentiated carcinoma: the occurrence of tumors in the subcutis or deep soft tissues without any connection with the overlying epidermis, the absence of areas with typical differentiation, and the presence of CD34 reactivity in about 50% of the cases all favor the diagnosis of epithelioid sarcoma over undifferentiated carcinoma. The latter are negative for CD34 in most cases.

References:

1- *Guillou L1, Wadden C, Coindre JM, Krausz T, Fletcher CD. "Proximal-type" epithelioid sarcoma, a distinctive aggressive neoplasm showing rhabdoid features. Clinicopathologic, immunohistochemical, and ultrastructural study of a series. Am J Surg Pathol. 1997 Feb;21(2):130-46.*

2- *Tadashi Hasegawa, Yoshihiro Matsuno, Tadakazu Shimoda, Toru Umeda M.D.3, Ryohei Yokoyama and Setsuo Hirohashi. Proximal-Type Epithelioid Sarcoma: A Clinicopathologic Study of 20 Cases. Mod Pathol 2001;14(7):655–663*

3- *Hornick JL, Dal Cin P, Fletcher CD. Loss of INI1 expression is characteristic of both conventional and proximal-type epithelioid sarcoma. Am J Surg Pathol. 2009 Apr;33(4):542-50. doi: 10.1097/PAS.0b013e3181882c54.*

4- *Kohashi K, Izumi T, Oda Y, et al: Infrequent SMARCB1/INI1 gene alteration in epithelioid sarcoma: a useful tool in distinguishing epithelioid sarcoma from malignant rhabdoid tumor. Hum Pathol 2009; 40: pp. 349-355*