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## **A 75 year old female with a palpable mass on the left leg**

Contributed by

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### **Clinical history:**

The patient is a 78 year old female, who presented with biliary colic and an incidental subcutaneous left leg (calf) mass. She had a normal range of motion and no pedal edema.

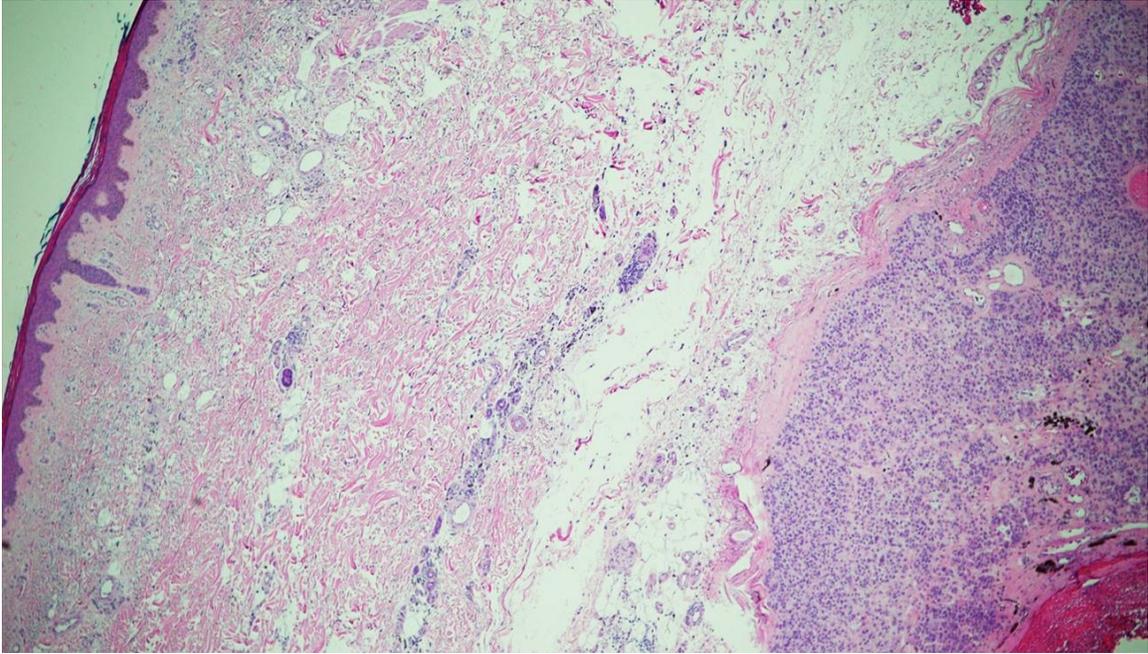
### **Gross examination:**

A 3.8 x 2.0 x 1.5 cm pale tan skin ellipse with a 2.7 x 1.6 x 1.2 cm gray-tan to red rubbery, well-circumscribed centrally hemorrhagic nodule abutting the inked surgical margin.

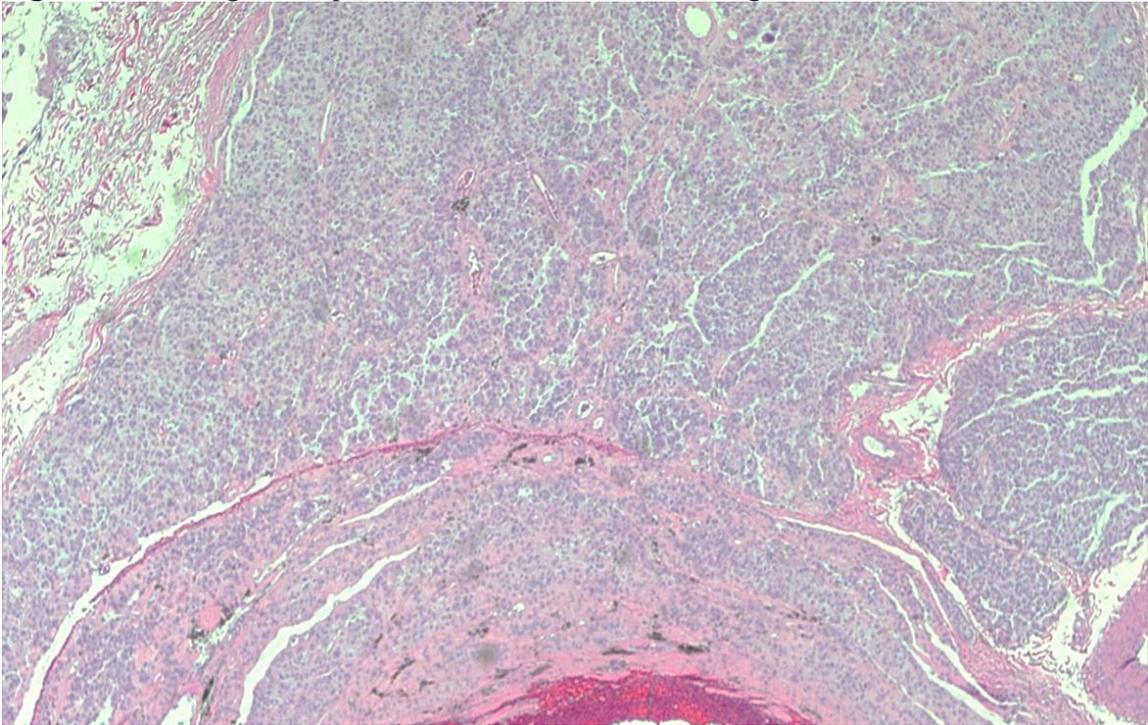
### **Microscopic examination:**

Sections of the mass show a dermal plexiform encapsulated lesion with a central hemorrhagic area. The cellular nodules of the lesion are comprised of monomorphic epithelioid cells in a myxoid background with numerous small hyalinized blood vessels. The cells possess eosinophilic cytoplasm, round to oval nuclei with prominent nucleoli. The cells show uniform nuclear and cytoplasmic staining with S-100. Collagen IV shows cytoplasmic staining with peripheral membrane enhancement. CD34 highlights the blood vessels but is negative in the tumor cells. The tumor cells do not show immunostaining with AE1/AE3, Melan A, actin, DOG1, desmin and EMA.

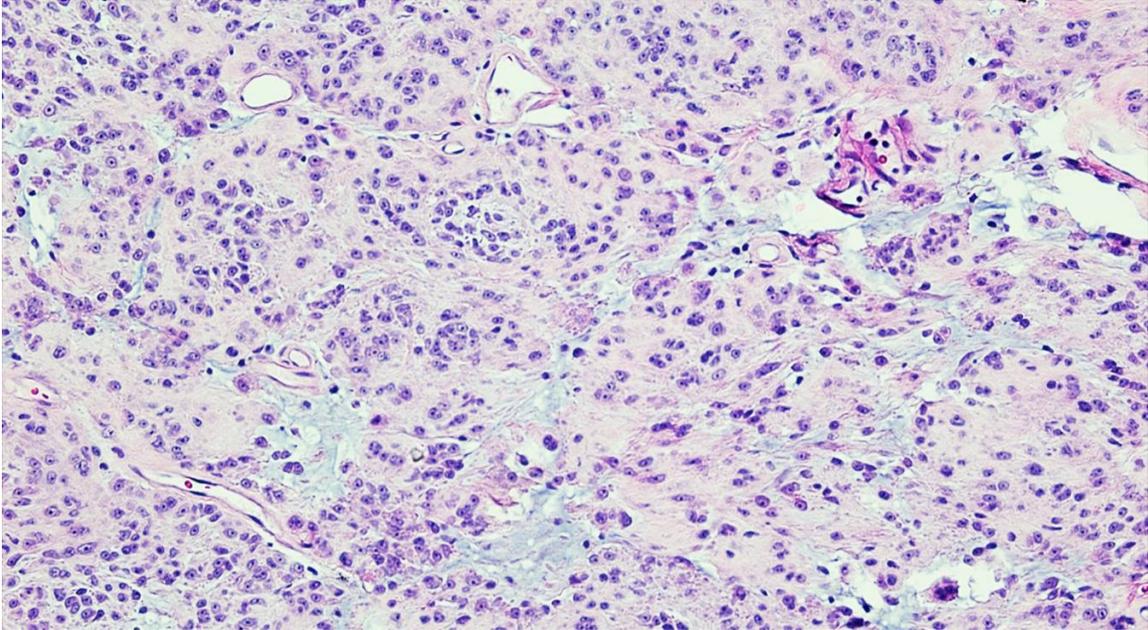
**Fig. 1:** Well circumscribed encapsulated subcutaneous nodule



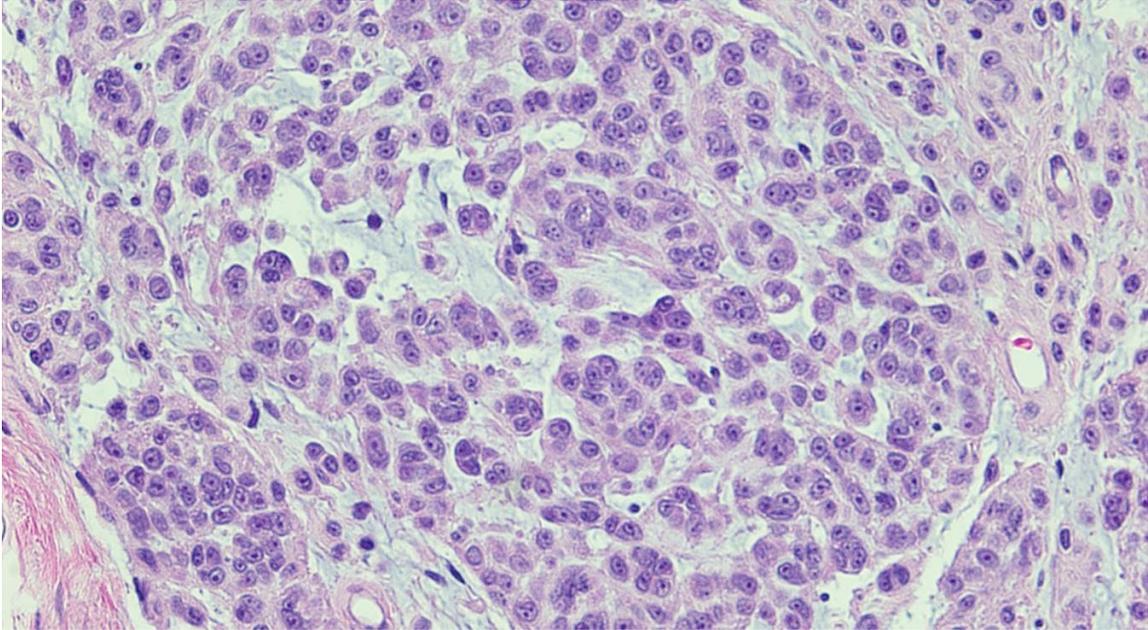
**Fig 2.** Plexiform growth pattern with central hemorrhagic area



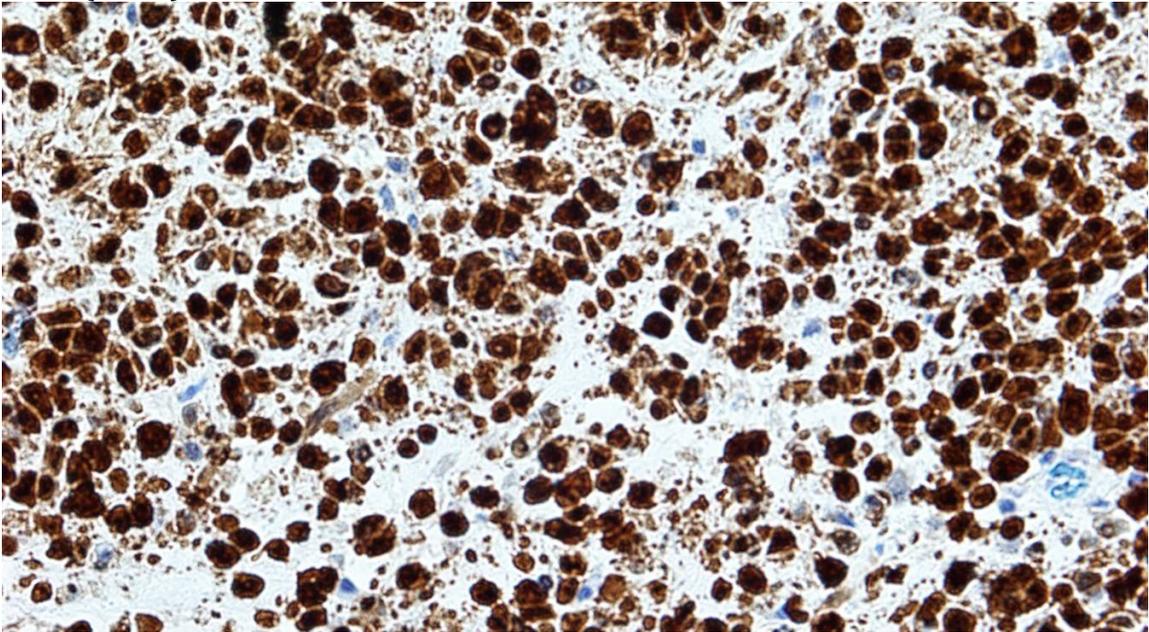
**Fig 3.** Myxoid background



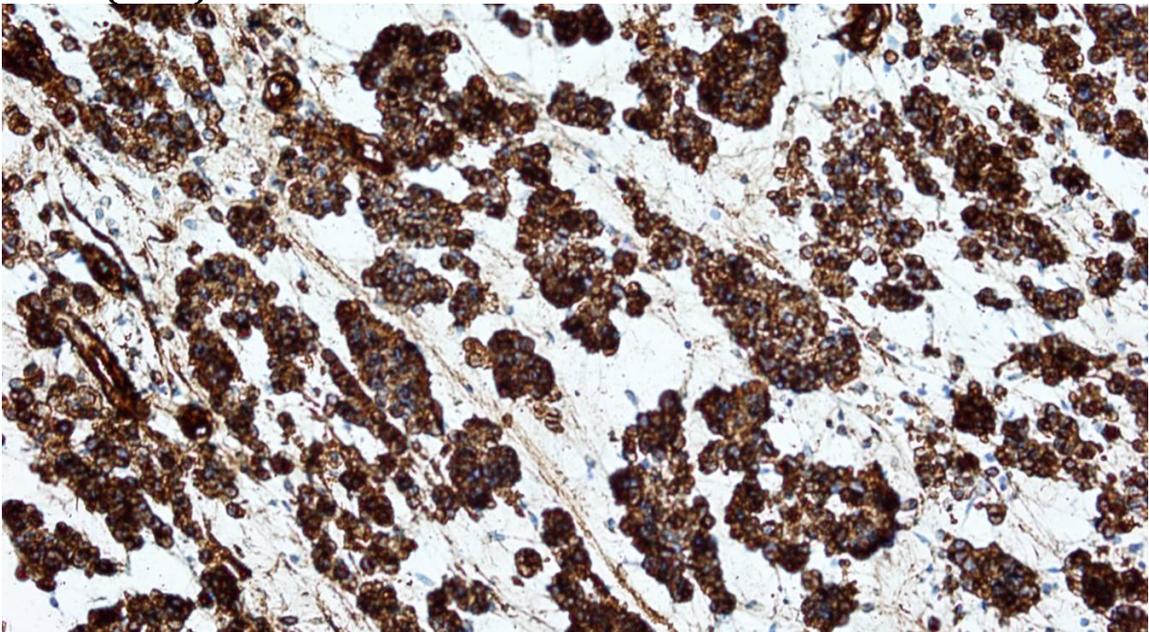
**Fig 4.** Epithelioid cells with low grade cytologic atypia



**S100 (X400)**



**COL IV (X200)**



## Final Diagnosis

### *Plexiform epithelioid schwannoma*

#### **Discussion:**

Benign peripheral nerve sheath tumors possess spindle cells and a myxoid stroma. Variants with epithelioid foci may be present. However, pure epithelioid variant of benign schwannoma is a rare entity. A few cases have been published till date<sup>1</sup>.

Majority of these lesions have been described in females. The age range varies from 23-73 years. The most common location of presentation is head and neck followed by back. The reported lesions vary from 1.5- 6.8 cm in size. Surgical excision with conservative margins is the accepted standard of care<sup>2</sup>.

Plexiform or multinodular growth pattern is not commonly observed in schwannoma and such tumors may show conventional, cellular, epithelioid or mixed appearance. The tumor is most commonly seen in the extremities but can also arise in the viscera. The age of presentation varies from 2-67 years. They are frequently associated with hyperchromatic nuclei and increased mitoses. The congenital plexiform schwannomas of childhood may be cellular and mitotically active. They display recurrent behavior but no metastatic potential. Deep plexiform schwannomas have a predilection for females, can occur in congenital settings and can show necrosis and myxoid change. They are known to recur. Plexiform schwannomas are typically not associated with neurofibromatosis. A single case of plexiform epithelioid schwannoma has been reported in English Language Medical Literature before.<sup>1</sup> Epithelioid schwannoma has been classified as benign peripheral nerve sheath tumor of intermediate histogenesis. by Laskin et al.<sup>3</sup> The cytologic features are usually low-grade with mild nuclear atypia and a low mitotic rate (<1/10 HPF).<sup>1</sup> Schwannomas show diffuse and uniform staining for S-100 protein, laminin and collagen type IV. EMA highlights peripheral perineurium. The other Schwann cell related markers include nerve growth factor receptor p75, CD57 and GFAP. The subcapsular areas show positivity for neurofilament protein<sup>1,2,4</sup>.

The differential diagnoses include epithelial neoplasms, epithelioid malignant peripheral nerve sheath tumor, plexiform neurofibroma, palisaded encapsulated neuroma, epithelioid leiomyoma, myoepithelial tumors, GIST, epithelioid fibromyxoid tumor of soft tissue, MPNST and melanocytic lesions.

Epithelial neoplasms would show positive immunostaining with Cytokeratin and negative immunostaining with S100.

Plexiform neurofibroma is a commonly occurring plexiform neural tumor, in association with neurofibromatosis (NF) 1. Morphologically it is a hypocellular lesion with myxoid background and well-defined nodules. Some of these lesions may show cellular areas with Schwannian nodules, including palisading. This tumor has a known malignant potential, thereby making it imperative to differentiate it from plexiform schwannoma<sup>4</sup>. Epithelioid neurofibroma is defined by presence of

epithelioid Schwann cell elements in association with a conventional neurofibroma. Neurofibromas show patchy positivity for S-100 and positivity for neurofilament within the tumor nodules<sup>2,4,5</sup>.

Cellular neurothekeoma shows a multinodular growth pattern, increased cellularity and pleomorphism, similar to plexiform schwannoma. Absence of S100 staining and positivity of melanoma specific antigen NKI/C3 in cellular neurothekeoma can be helpful in differentiation.

Epithelioid schwannoma shows negative immunostaining for HMB45, melan-A and CD34. A melanoma, in contrast would be positive for HMB45, melan-A and S100. In addition, a primary melanoma would have an in-situ component as well.

Myoepithelioma of soft tissue may sometimes be comprised predominantly of epithelioid cells. The tumor cells express S100, cytokeratins, p63 and smooth muscle markers<sup>2,4,5</sup>.

Epithelioid malignant peripheral nerve sheath tumors exhibit frank malignant cytologic features, necrosis and mitoses. The tumor consists of round to polygonal neoplastic cells with ample cytoplasm, atypical nuclei, coarse chromatin and prominent nucleoli. The staining pattern for S100 is patchy. The rare "glandular" malignant schwannoma possesses a minor component of true epithelial cells that form gland like structures. Superficially located benign schwannomas may also contain entrapped adnexal glands. <sup>1</sup>

Other less likely differential diagnoses include cutaneous mixed tumors, epithelioid variant of mesenchymal tumors such as fibrohistiocytic (epithelioid cell histiocytoma), smooth muscle and vascular (epithelioid hemangioendothelioma) lesions. Ossifying fibromyxoid tumor of soft tissue, usually presents in extremities and is more frequent in men. This tumor may have epithelioid features but S100 immunostaining is focal and less intense. Epithelioid leiomyosarcoma and leiomyoma often have vacuolar and/or clear cell cytoplasm. They express actin and/or desmin.

Palisaded encapsulated neuroma usually presents on the face and has no gender predilection. It differs from epithelioid schwannoma due to lack of myxoid background and hyalinization. Also, in palisaded encapsulated neuroma axons are present in close association with Schwann cells. Contrarily, the axons are located peripherally in the subcapsular area in epithelioid schwannoma<sup>2</sup>.

It is important to identify plexiform epithelioid schwannoma and differentiate it from the more aggressive tumors.

### References:

1. Zhenqiang Gao, Susan M. Palleschi, Shen Chen. Plexiform epithelioid schwannoma: A case report. *Am J Dermatopathol* 2007;29:56-58.
2. Aly G. Saad, George K Mutema, Diya F. Mutasim. Benign cutaneous epithelioid schwannoma. Case Report and Review of the Literature. *Am J Dermatopathol* 2005; 27: 45-47.

3. Laskin WB, Fetsch JF, Lasota J, et al. Benign epithelioid peripheral nerve sheath tumors of the soft tissues: clinicopathologic spectrum of 33 cases. *Am J Surg Pathol*. 2005; 27: 45-47.
4. Narasimhan P. Agram, Sonam Prakash, Cristina R. Antonescu. Deep-Seated Plexiform Schwannoma. A Pathologic study of 16 cases and Comparative Analysis With the superficial Variety. *Am J Surg Pathol* 2005;29: 1042-1048.
5. William B. Laskin, John F. Fetsch, Jerzy Lasota, Marku Miettinen. Benign epithelioid Peripheral nerve sheath tumors of the soft tissues. Clinicopathologic spectrum of 33 cases. *Am J Surg Pathol* 2005;29: 39-51.