

# Epithelioid malignant peripheral nerve sheath tumor

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## CASE SUMMARY

A previously healthy 17-year-old male presented for evaluation of a left medial elbow soft tissue mass with associated burning radiating pain down into his volar forearm. He had reported slight increase in size of the mass over the past couple of months. The patient was initially evaluated by ultrasound and then by MRI. Patient underwent total surgical excision of the mass, which was submitted for histopathological evaluation. Pathology identified the mass as a  $3.0 \times 1.7 \times 1.5$  cm high-grade tumor with negative surgical margins that was surrounded by an intact capsule measuring less than 0.1 cm. Immunohistochemistry revealed S-100 protein, which was diffusely and strongly positive. To establish a wide negative margin, the patient underwent tumor bed re-excision.

## IMAGING FINDINGS

An ultrasound of the soft tissue mass was performed. Longitudinal and transverse-oriented images demon-

strated a solid heterogeneous ovoid mass in the medial forearm measuring  $29 \times 17 \times 15$  mm with no evidence of internal flow and mild posterior acoustic enhancement. The mass was well circumscribed and appeared to respect the soft tissue planes (Figure 1). On MR scanning the lesion demonstrated hypointense T1, and heterogeneous hyperintensity T2 mass with peripheral hyperintensity and central hypointensity, which likely reflects elements of necrosis and/or hemorrhagic products. Gadolinium enhanced T1-weighted images revealed peripheral enhancement (Figures 2 and 3).

## DIAGNOSIS

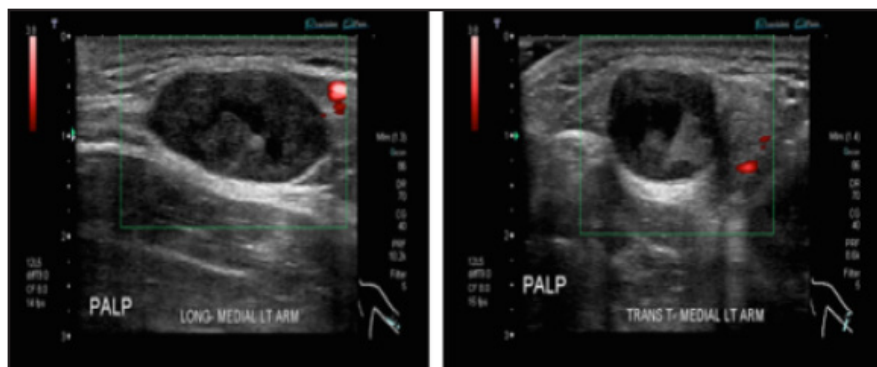
Epithelioid malignant peripheral nerve sheath tumor

## DISCUSSION

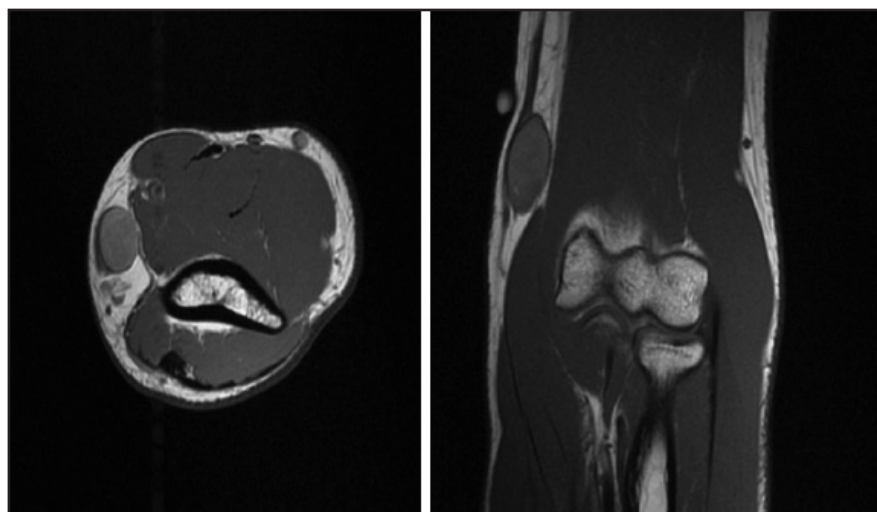
Malignant peripheral nerve sheath tumors (MPNST) are a group of neurogenic tumors that may be sporadic or coexist with neurofibromatosis. They originate from peripheral nerves

or from cells associated with the nerve sheath, such as Schwann cells or fibroblasts. They are considered rare neoplasms and affect 0.001 percent of the population.<sup>1</sup> The epithelioid subtype is more rare and represents a well-recognized entity comprising of about 5 percent of these tumors.<sup>2</sup> The clinical behavior of this variant is unclear and raises a completely separate differential diagnosis and is characterized by a predominance of large epithelioid cells. A definitive diagnosis of MPNST is obtained by histopathology and S-100 immunostaining. The epithelioid subtype is more common in superficial sites and in contrast to conventional MPNSTs, expresses S-100 protein strongly and typically, diffusely.<sup>3</sup> Our patient's immunohistochemistry demonstrated S-100 protein positivity and loss of INI1, consistent with EMPNST.

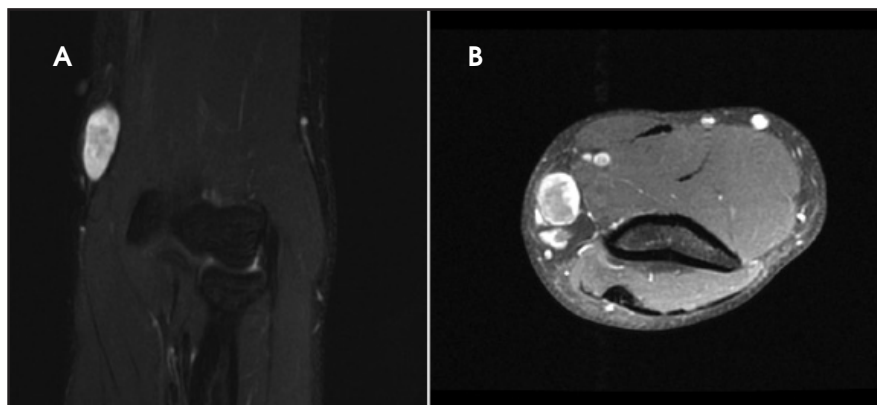
The biological behavior and prognosis of EMPNST is not clear and recent literature reports are not consistent. Malignant peripheral nerve sheath



**FIGURE 1.** Ultrasound evaluation of the left medial epicondyle region demonstrates a heterogeneous mixed echogenic ovoid lesion with no vascular flow.



**FIGURE 2.** Axial and coronal T1 sequences demonstrate an oval well-circumscribed relatively homogeneous hyperintense lesion along the medial cutaneous nerve of the forearm, which "splits" the subcutaneous fat.



**FIGURE 3.** T2 fat-saturated sequence demonstrates a heterogeneous hyperintense mass at the same area of concern within the medial epicondyle (A). T1 fat-saturated gadolinium enhanced MR sequence demonstrates a heterogeneous mass with peripheral enhancement (B).

tumors have a tendency to recur locally and to metastasize and are known to be highly malignant.<sup>4</sup>

Epithelioid MPNST has complex histopathological findings and histopathological features similar to other epithelioid tumors, especially malignant melanoma. This differential diagnosis is specially considered when, in an adult, a tumor is localized in the lower extremities; it is dermal based without an intraepidermal component, the patient has no previous history of malignant melanoma, and the tumor expresses S-100 protein. In broad terms, the differential diagnosis of epithelioid MPNST includes melanoma, clear cell sarcoma, epithelioid sarcoma and carcinoma. Lack of expression of melanocytic markers (eg MelanA, HMB45, MITF) is very helpful in the distinction of epithelioid MPNST from melanoma and clear cell sarcoma. Absent cytokeratin expression distinguishes them from carcinoma and epithelioid sarcoma.<sup>5,6</sup>

Adjacency to a big vessel or nerve trunk makes EMPNST unresectable and recurrence with distant metastasis make this tumor fatal. Therefore, the diagnosis of the EMPNST before surgery is important. Considering the overlap in clinical manifestation, distinguishing EMPNST from benign neurogenic tumor is difficult. Imaging plays an important role in diagnosis of malignant peripheral nerve sheath tumors. Ultrasound features that may suggest malignancy have been studied and these features are not consistent. They cannot be used reliably to differentiate malignant from benign peripheral nerve sheath tumors.<sup>7</sup> In our case, the ultrasound examination demonstrated smooth margined a well-circumscribed avascular mass (Figure 1), features that are not suspicious for malignancy.

Junji et al examined the MRI features of malignant nerve sheath tumors

and concluded that certain MRI features help to distinguish malignant peripheral nerve sheath tumors from neurofibromas. These features have been studied and include: increased largest dimension of the mass, presence of peripheral enhanced pattern, presence of perilesional edema-like zone, and presence of intratumoral cystic lesion.<sup>8</sup> They concluded that if a tumor has two or more of these features, the lesion is highly suspicious for malignancy and the lesion should be subjected to biopsy. The epithelioid subtype of malignant peripheral nerve sheath tumor is a rare entity and has not been studied as a separate entity. In our case, one of the features, peripheral enhancement was present (Figure 3). Yu et al. evaluated the radiological features of the malignant nerve sheath tumors and reported peritumoral edema, intratumoral lobulation, and peripheral enhancement are suggestive of malignancy.<sup>9</sup> These findings suggest that malignant peripheral nerve sheath tumors may have a wide range of radiological presentation and considering that peripheral enhancement has been consistently reported by different authors and it may be a more common presentation in the malignant peripheral nerve sheath tumor category. In our case, the only feature of malignancy presented by the authors, is the peripheral enhancement (Figure 3).

Matsumine et al<sup>10</sup> believed that the presence of high signal on T1WI is a diagnostic indicator. The lesion in our

case also demonstrates T1 hyperintensity (Figure 2); however, hemorrhage is also seen in Schwannoma and T1 hyperintensity and is likely nonspecific.

## CONCLUSION

In summary, EMPNST is a rare tumor that is considered a differential diagnosis for malignant melanoma. Features that favor EMPNST are diffuse S-100 protein expression and INI 1 expression loss. MR features that may suggest malignancy include: increased largest dimension of the mass, presence of peripheral enhanced pattern, presence of perilesional edema-like zone, and presence of intratumoral cystic lesion, intratumoral lobulation. The findings in our case and the prior studies suggest that ultrasound cannot be reliably used to differentiate benign from malignant lesion. Moreover, although MR features of malignancy when present can aid in diagnosing malignant peripheral nerve sheath tumors, these features are not consistent and presence of any of the aforementioned features should be considered as possibility of malignancy and with appropriate work up to be followed.

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