



# Hybrid Schwannoma/Perineurioma: Case Report of a Diagnostically Challenging Uncommon Tumor and a Brief Review of the Literature

Nicole DiTommaso<sup>1\*</sup>, Christopher Taylor<sup>1</sup>, Ibrahim El-Mais<sup>1</sup>, Abdel Aziz Elsayed<sup>2</sup>, Ali Aziz<sup>3</sup>, Alexander Garcia<sup>1</sup>, and Mohamed Aziz<sup>1</sup>

<sup>1</sup>Department of Pathology, American University of the Caribbean, USA

<sup>2</sup>Ain Shams University, Cairo, Egypt

<sup>3</sup>Drexel-Hahnemann University, PA, USA

## Abstract

We report a case of a 26-year-old woman presented with a 2.6 cm solitary slowly growing subcutaneous nodule covered by normally appearing skin on her left groin. The Original pathological examination of the mass was described as storiform-appearing cellular with slight subcutaneous fat infiltration positive CD34 immunostain. On second opinion the mass was described as well-circumscribed surrounded by a thin, membranous layer. Histomorphologic examination of the lesion described a storiform architectural pattern composed of spindle cells with plump nuclei, characteristic of Schwann cells. Further evidence of a schwannoma was supported by a positive S-100 stain along with the positive CD34 stain. However, an additional stain of epithelial membrane antigen (EMA) was positive, more consistent with a perineurioma. The clinicopathologic and immunohistochemical features of the lesion supported the diagnosis of a hybrid perineurioma/schwannoma, a unique form of peripheral nerve sheath tumors.

**Keywords:** Perineurioma; Schwannoma; Hybrid; Immunohistochemistry; Tumor; Benign; Malignant

## Abbreviations

PNST: Peripheral Nerve Sheath Tumor; BPNST: Benign Peripheral Nerve Sheath Tumor; MPNST: Malignant Peripheral Nerve Sheath Tumor; HSP: Hybrid Schwannoma Perineurioma; IHC: Immunohistochemistry; DFSP: Dermato Fibro sarcoma Protuberance

## Introduction

Benign peripheral nerve sheath tumors (PNST) are common neoplasms. Although there are many classic features for identification of these tumors, they can often be diagnostically challenging. Subtypes of peripheral nerve sheath tumors have been described early in the history of surgical pathology, yet there remain controversies regarding the classification of these tumors [1]. Diagnostic criteria and differential diagnosis for the major categories of nerve sheath tumors are well established, including neurofibroma, schwannoma and perineurioma [1]. In

the peripheral nervous system, the myelin sheath of each axon in a nerve is wrapped in a delicate protective sheath known as the endoneurium. Within the nerve, axons targeting the same anatomical location are bundled together into groups known as fascicles, each surrounded by another protective sheath known as the perineurium. A benign neoplasm of the perineurium is known as perineurioma. Other than these defined types of PNST, there apparently exist tumors in which features that are characteristic of perineurioma and schwannoma or neurofibroma can be observed within a single lesion to create a hybrid PNST. These hybrid tumors of peripheral nerve sheath origin seem to be uncommon, but do exist [2].

Schwannomas are benign neoplasms of Schwann cell origin. The gross appearance is characteristic, in the form of well circumscribed masses with degenerative changes and variable admixture of compact spindled areas as well as areas rich in macrophages and collagen fibers. Furthermore, a formed collagenous capsule is a consistent finding. By immunohistochemistry, schwannomas typically show diffuse, strong expression of S100 protein [1].

In contrast, a perineurioma contains cells with elongated, tapering nuclei with long and thin cytoplasmic processes, usually arranged in fascicular, whorled, and storiform pattern. The tumor cells are usually positive for epithelial membrane antigen and collagen type IV and negative for S-100 protein [3].

Benign nerve sheath tumors showing predominantly schwannian cytomorphology and perineurioma-like architecture are composed of an admixture of both cell types. These tumors usually arise in the dermis and subcutis and occur over a wide age range and anatomic distribution. Degenerative nuclear atypia (akin to that seen in ancient schwannoma and atypical neurofibroma) is relatively common. Hybrid

**Submitted:** 04 February 2020 | **Accepted:** 17 February 2020 | **Published:** 19 February 2020

**\*Corresponding author:** Nicole DiTommaso, Department of Pathology, American University of the Caribbean, 17 Judson Lane, Farmington, USA, Tel: 860-951-2412; Email: nicole.a.ditommaso@gmail.com

**Copyright:** © 2020 DiTommaso N, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

**Citation:** DiTommaso N, Taylor C, El-Mais I, Elsayed AA, Aziz A, et al. (2020) Hybrid Schwannoma/Perineurioma: Case Report of a Diagnostically Challenging Uncommon Tumor and a Brief Review of the Literature. JSM Clin Cytol Pathol 5: 3.



schwannoma/perineuriomas have no evident association with neurofibromatosis and rarely recur [4].

The main differential diagnosis for hybrid PNST includes other BPNST and low-grade MPNST. The composite nature of these lesions could be easily overlooked if only limited immunohistochemistry is performed (for example only S100 protein or EMA). As nuclear atypia could be seen in the hybrid tumors, a low-grade MPNST might be considered, but represent only approximately 10 percent of tumors encountered by a peripheral nerve surgeon and are known not to arise from Schwannoma [5].

MPNSTs encompass a wide extent of biological behavior ranging from low to high grade malignancy and a variety of clinical manifestations; hence, it is not surprising to find that the genetic and molecular findings in these tumors reflect a heterogeneous mixture of various aspects of MPNSTs [4]. However, MPNST show variation in cellularity and mitotic activity that is generally either very low or absent in hybrid BPNST [6]. MPNSTs make up 5-10% of non-rhabdomyosarcoma soft tissue sarcomas in children and originate from peripheral nerves' sheath such as Schwann cells, perineural cells, or fibroblasts [7]. In addition, MPNST are known to be associated with high tumor proliferation markers such as Ki-67.

### Case Presentation

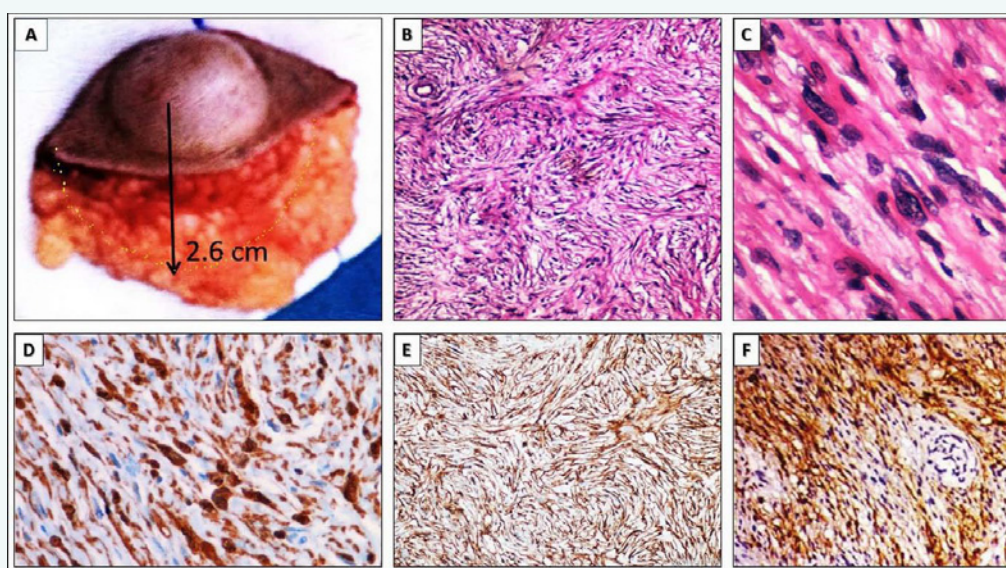
A 29-year-old female presented with a 2.6 cm superficial soft tissue mass located in the inner left thigh that had been present for the past 10 years but recently had begun to enlarge. There was no other significant medical history. The mass was clinically compatible with a benign mesenchymal neoplasm. Upon excision, the mass appeared to be well-circumscribed but was reported to demonstrate slight subcutaneous fat infiltration. A CD34 immunostain was positive and diagnosis of

a dermatofibrosarcoma protuberance (DFSP) was made with recommendation for a second surgery to remove a wide safe surgical margin.

The patient sought a second opinion from a different institution in hesitation of an additional surgery. As a consultation case in our department, analysis of additional samples demonstrated a well-circumscribed, un-encapsulated 2.6 cm mass arising from the subcutis (Figure 1A) and composed of spindle cells with plump tapering nuclei, pale eosinophilic cytoplasm and indistinct cell borders. The cells were arranged in a storiform, whorled, and lamellar architecture with occasional scattered Schwann cells with large hyperchromatic nuclei without mitosis or necrosis (Figure 1B&C). Cytomorphologic malignant features were not present. There was no evidence of subcutaneous infiltration and the areas that can be identified as true margins show the tumor well circumscribed and surrounded by a thin membranous layer. Immunohistochemical studies were positive for S100 (strong nuclear and cytoplasmic) (Figure 1D), CD34 (Figure 1E), EMA (positive in about 25% of cells mostly in the periphery) (Figure 1F), and CD99<sup>+</sup>. Other studies included negative Desmin, SMA, and CD163. The tumor cells displayed low proliferation with only 2% nuclear staining with proliferation marker Ki67 leading to a diagnosis of a benign hybrid schwannoma and perineurioma. Submitting original institution accepted and appreciated the revised diagnosis. The patient was advised that no second surgery was required, the schwannoma was completely shelled out during the first surgery and treatment was complete. Five years post-operation there was no evidence of tumor recurrence or metastasis.

### Discussion

Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous tumor that is often misdiagnosed. DFSP has a high



**Figure 1** Hybrid Schwannoma/Perineuroma (HSP), histomorphology and Immunohistochemistry studies. **A:** Surgically excised gross specimen; **B:** Storiform, whorled, lamellar architecture (H&E stain X20); **C:** Spindle cells with plump tapering nuclei, pale eosinophilic cytoplasm and indistinct cell borders (H&E stain X40); **D:** S-100 positive (nuclear and cytoplasmic); **E:** CD34 Positive; **F:** EMA positive.



rate of recurrence but a low rate of metastasis. DFSP usually occurs in young to middle-aged patients but can present in all age groups. Over 90 percent of dermatofibrosarcoma protuberans (DFSPs) are characterized by a unique translocation  $t(17;22)$ . DFSPs should be suspected in any patient with a history of a firm, slow-growing cutaneous nodule [8]. It is commonly found on the trunk, however, it can also develop in the extremities, head or neck demonstrating infiltrative growth. DFSP is divided histopathologically into classical and non-classical types. Classical-type DFSP typically forms a radial or storiform pattern, with the malignant tissue extending into the subcutaneous fat and forming a honeycomb-like structure [9]. Clinically, DFSP often masquerades as a benign, indolent tumor. Microscopically, it extends into the dermis and subcutaneous tissue. DFSP has a distinctive histologic appearance but can mimic other diseases, thus, histological immunostaining is the gold-standard for diagnosing DFSP and surgical removal remains the optimal treatment [9].

The patient's initial diagnosis was based on the positive CD34 stain and the storiform histomorphologic pattern with no additional IHC studies performed. The original studies of the mass were said to demonstrate subcutaneous fat infiltration. However, after the additional sections and IHC studies, it was found that the lesion did not extend into the subcutaneous tissue, in support of the benign nature of the HSP. The cytomorphology of the lesion expressed spindle cells with plump nuclei, characteristic of Schwann cells. Further evidence of a schwannoma was supported by a positive S-100 stain along with the positive CD34 stain. However, an additional stain of epithelial membrane antigen (EMA) was positive, more consistent with a perineurioma, which was also supported by the storiform appearance. Therefore, the stain profile was S100+, CD34+, EMA- in the schwannomatous mix and S100-CD34-, EMA+ in the perineuromatous mix.

Although uncommon, the HPS is not rare. Such tumors have a predilection for superficial (dermal or subcutaneous) locations, usually are unencapsulated and are composed of biphasic, non-overlapping S100 and EMA positive cell components [1]. Michal and colleagues reported six tumors with hybrid schwannoma and perineurioma components [10]. Hornick and colleagues reported a subsequent series of 42 such cases. Storiform growth and a collagenous stroma were dominant architectural features, typical of perineurioma, but schwannian cytology predominated. Degenerative nuclear atypia was present in a subset of cases [4].

We report this case to raise awareness of clinicians and pathologists for this uncommon tumor, which can be diagnosed erroneously as sarcoma. When the diagnosis of HSP is suspected, an adequate panel of IHC studies should be performed to avoid making the diagnosis of a more advanced tumors such as a DFSP as clinically, DFSP often masquerades as a benign, indolent tumor [9]. There have only been rare single case reports of malignant

transformation of HSP [11]. We hope that continued investigation drives further development of efficacious knowledge, diagnosis, and safe treatments for improving patient outcomes.

## Acknowledgements

Special thanks to Hannah Pulido and Makenzie Gairrett, MD candidates, at the American University of the Caribbean and David Adelstein, MD, the American University of the Caribbean for their assistance in critical review of this manuscript.

## References

1. Rodriguez FJ, Folpe AL, Giannini C, Perry A. Pathology of peripheral nerve sheath tumors: diagnostic overview and update on selected diagnostic problems. *Acta Neuropathol.* 2012; 123: 295-319.
2. Kazakov DV, Pitha J, Sima R, Vanecek T, Shelekhova K, Mukensnabl P, et al. Hybrid peripheral nerve sheath tumors: schwannoma-perineurioma and neurofibroma-perineurioma. A report of three cases in extradigital locations. *Ann Diagn Pathol.* 2005; 9: 16-23.
3. Kim JM, Choi JH. Soft Tissue Perineurioma - A Case Report . *Korean J Pathol.* 2009; 43: 266.
4. Hornick JL, Bundock EA, Fletcher CDM. Hybrid schwannoma/perineurioma: clinicopathologic analysis of 42 distinctive benign nerve sheath tumors. *Am J Surg Pathol.* 2009; 33: 1554-1561.
5. Kim DH, Murovic JA, Tiel RL, Moes G, Kline DG. A series of 397 peripheral neural sheath tumors: 30-year experience at Louisiana State University Health Sciences Center. *J Neurosurg.* 2005; 102: 246-255.
6. Shanouda S, Kaya G. Benign Cutaneous Peripheral Nerve Sheath Tumor with Hybrid Features: Report of Two Cases with Schwannoma/Perineurioma and Schwannoma/Neurofibroma Components. *Dermatopathology.* 2017; 4: 1-6.
7. DS Geller, M Gebhardt. Malignant peripheral nerves heath tumors (MPNSTs), *Electronic Sarcoma Update Newsletter.* Newsletter. 2006.
8. Nishio J, Iwasaki H, Ishiguro M, Ohjimi Y, Yo S, Isayama T, et al. Supernumerary ring chromosome in a Bednar tumor (pigmented dermatofibrosarcoma protuberans) is composed of interspersed sequences from chromosomes 17 and 22: a fluorescence in situ hybridization and comparative genomic hybridization analysis. *Genes Chromosomes Cancer.* 2001; 30: 305-309.
9. Lyu A, Wang Q. Dermatofibrosarcoma protuberans: A clinical analysis. *Oncol lett.* 2018; 16: 1855-1862.
10. Michal M, Kazakov DV, Belousova I, Bisceglia M, Zamecnik M, Mukensnabl P. A benign neoplasm with histopathological features of both schwannoma and retiform perineurioma (benign schwannoma-perineurioma): a report of six cases of a distinctive soft tissue tumour with a predilection for the fingers. *Virchows Arch.* 2004; 445: 347-353.
11. Rekhi B, Jambhekar NA. Malignant transformation in a hybrid schwannoma/perineurioma: Addition to the spectrum of a malignant peripheral nerve sheath tumor. *Indian J Pathol Microbiol.* 2011; 54: 825-828.