Neurofibroma revealed as malignant peripheral nerve sheath tumor: a case report

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European Journal of Medical Case Reports
Volume 2(2):75-79

https://doi.org/10.24911/ejmcr/2/17
Discover Publishing Group

ABSTRACT

Background: Peripheral nerve sheath tumors (PNST) can be categorized into benign or malignant on the basis of imaging findings on ultrasonography (USG) and magnetic resonance imaging (MRI).

Case Presentation: We report a case of a 28-year-old male presented with a huge swelling in his right forearm. While the features of MRI suggested neurofibroma, some of the features of USG were in favor of malignant PNST (MPNST). Finally, the histopathology and immunohistochemistry features were found to be consistent with that of MPNST.

Conclusion: This case is an example of the additive value of USG over MRI in identification of MPNSTs that can be helpful for appropriate management.

Keywords: USG, MRI, malignant peripheral nerve sheath tumor.

Received: 11 March 2018 **Accepted:** 27 April 2018

Type of Article: CASE REPORT

Funding: None

Declaration of conflicting interests: None

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Background

Among the peripheral nerve sheath tumors (PNST), neurofibromas (NFs) are benign, usually single and commonly occur anywhere in the body, there is a low incidence of involvement of hands (0.8%) as a site of occurrence [1]. Malignant PNST (MPNST) affects 0.001% of the population [2] with a pre-dilection for extremities [3]. Magnetic resonance imaging (MRI) can sometimes differentiate between benign NF and MPNST. The current standard of management relies on MRI for surgical planning. Fluorodeoxyglucose positron-emission tomography (FDG-PET) is being increasingly deployed to help differentiate between benign NF and MPNST. Histopathology (HP) can also be non-specific unless complemented by immunohistochemistry (IHC) [4]. A number of ultrasonography (USG) features have been described that can potentially complement MRI in differentiating benign NF from MPNST [5,6]. We report a case having USG features of MPNST, which was pre-operatively identified as NF both by MRI and fine needle aspiration cytology (FNAC), and then, finally, proven to be MPNST with the help of HP and IHC.

Case Presentation

A 28-year-old male had an asymptomatic swelling in the right forearm for 12 years; this had progressively grown bigger to encroach the entire forearm. On examination, there was a 10-cm, hard, fixed, and non-tender lump with its major portion on the proximal radial aspect of the right forearm (Figure 1). MRI showed multiple well outlined, oval and solid masses of varying size in the intermuscular location, stretching the adjacent muscles without invasion. All lesions showed post-Gadolinium enhancement (Figure 2). Sonographically, there were multiple well outlined, oval and solid masses of varying size (78 × 36 mm, 51 × 40 mm, and 36 × 25 mm) and echotexture; situated in the anterior, posterior, and medial compartments of the right forearm adjacent to the flexor digitorumprofundus, lying in between the supinator and the brachioradialis muscles with the median nerve in its immediate

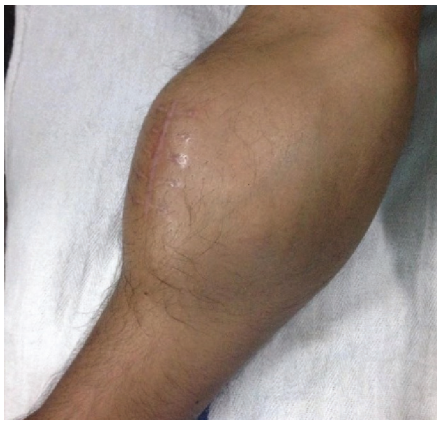

Figure 1. *Preoperative appearance of the right forearm swelling.*

vicinity (Figure 3). The duplex study of the lesion as well as radial and ulnar arteries revealed minimum intra-lesional vascular signal with no evidence of compression of distal arterial flow by the mass. Considering the size of the lesion and presence of the intra-lesional vascularity, the sonography team recommended FNAC correlation. FNAC from that mass revealed the feature of spindle cell mesenchymal lesion, consistent with neurofibroma. The MRI and FNAC features directed the provisional diagnosis to neurofibroma. Excision and biopsy were done.

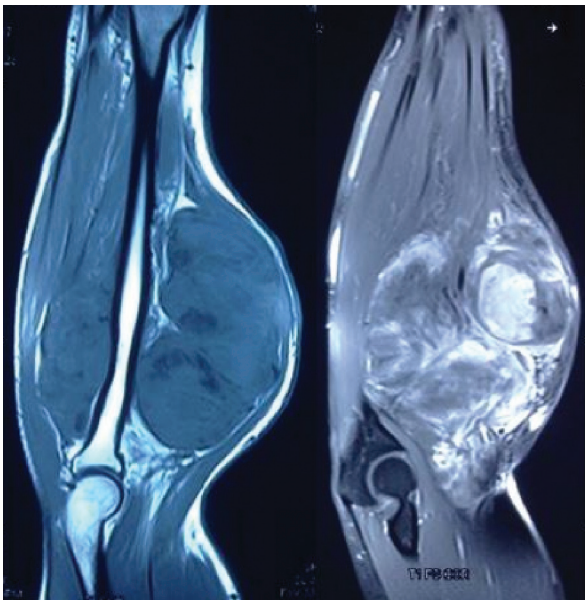

Figure 2. *MRI: Multiple soft tissue masses showing post-contrast enhancement.*

Histopathologic features were compatible with that of Grade 1 MPNST with mitotic rate of 3/10 high power field belonging to pT2a (tumor size 7 × 5 cm), pNx, and pMx.On IHC, cells were negative for S100 which suggested likelihood for MPNST (Figure 4). In addition, cells were also negative for Desmin, smooth muscle actin, and HMB45.

Follow-up on 18th post-operative day (Figure 5) showed no clinical sign of functional impairment, neurological deficit, or local recurrence. A regional ultrasound scan revealed no definite lesion, and the intermuscular spaces were hypoechoic due to post-excision residual inflammatory collection (Figure 6).

Discussion

The ultrasound features of the lesion, which were suggestive of MPNST, were the size of lesion being greater than 50 mm, irregular margin, hypoechogenicity with heterogeneous echotexture, and intra-lesional vascular signal. The vascular signal, which was probably from vasa

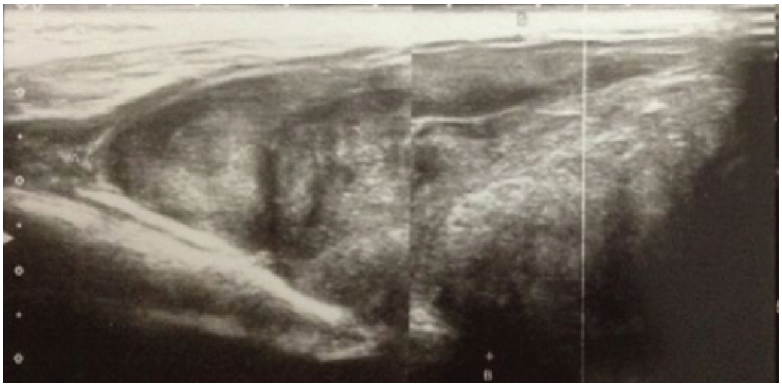

Figure 3. *USG: Multiple soft tissue masses.*

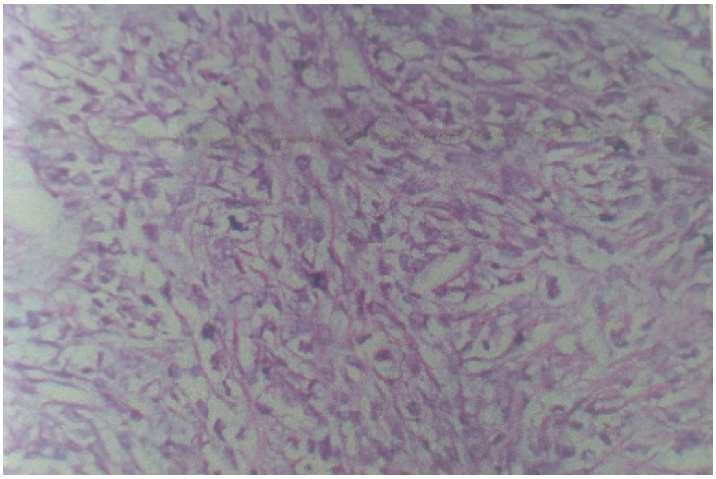

Figure 4. *Immunocyto-histochemistry revealed malignant nerve sheath tumor.*

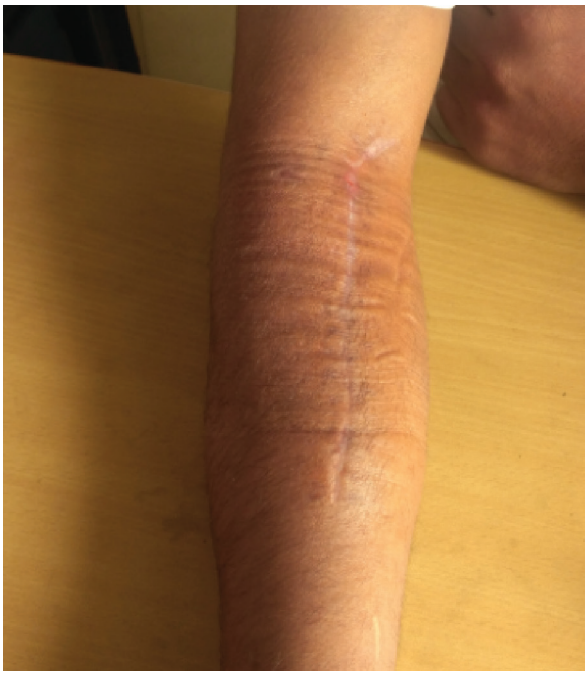

Figure 5. *After operation.*

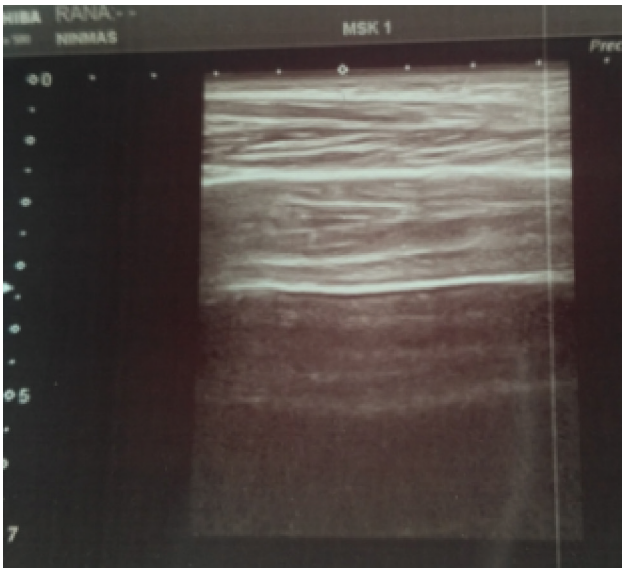

Figure 6. *USG findings after operation.*

nervorum is a feature in favor of malignancy, was considered of high clinical significant only retrospectively. Retrospective analysis of the ultrasound scan revealed additional features such as absence of intra-lesional cystic areas and presence of peri-lesional edema, which is considered significant [7]. Besides, the pre-operative MRI that stated about contrast enhancement was lacking detail in term of the enhancement pattern being peripheral or heterogeneous which in turn could have suggested the likelihood of the lesion being an MPNST. The reported imaging features are summarized in Table 1.

Extremities are among the sites reported for the commonest involvement by MPNST [8]. MPNST has been observed to arise either from proximal extremity involving a major nerve trunk [9] or from subcutaneous tissue of distal extremity without involving a major nerve trunk [10]. Most of the MPNSTs are more than 5 cm at the time of diagnosis [11].

MPNST on MRI may appear as isointense to muscle or heterogeneous in T1 [6], but low signal in T2 due to its high collagen content [7]. Yu et al. [10] in their series did not find difference in T1 and T2 signals as a significant discriminator among benign PNSTs and MPNSTs. Large diameter (over 5 cm), ill-defined margin, intratumoral lobulation, peri-tumoral edema, and adjacent bone destruction are described as significantly discriminative imaging features of MPNST from benign [10,12]. Wasa et al. [7] in addition to dimension and peri-lesional edema described the presence of peripheral enhancing pattern and intra-tumoral cystic lesions as pathognomonic. The heterogeneous enhancement owing to hemorrhage or necrosis may also suggest likelihood of MPNSTs [13]. MPNST is often devoid of target sign, fascicular sign, split fat sign, and cystic changes [7,14]. Yu et al. [10] did not find the absence of target sign, split fat sign, and cystic change as a significant discriminator of MPNST from benign ones.

Reported features of MPNST on high-resolution USG includes connection with a peripheral nerve, fusiform shape, inhomogeneity, and hypoehoicity with hyperchoic and irregularly thickened outer nerve sheath [9]. Findings that are described as suspicion raiser for MPNST include diameter larger than 5 cm, poorly defined outer margin [6], central necrosis or hemorrhage, edema, and calcification. Color and power and spectral Doppler surrogates of vascular changes evincing malignancy such as occlusion, stenosis, shunts, trifurcation, and loops [5] are recommended to be sought for. In addition, demonstration of hypertrophied vasa nervorum as "cork-screw type vessels," increased vascularity [15], high velocity in newly formed vessels, variability of velocity and spectral waveform in different parts of the same tumor, and low resistance index in the presence of arterio-venous communication [6] are also suggestive of malignancy.Histological appearance of MPNST is considered non-specific which is monotonous spindle cells arranged in intersecting fascicles. Though there is no pathognomonic molecular or immunohistochemical study for MPNST, S100 protein is positive in 50%–70% of cases and low in high-grade MPNSTs, while a strong and diffuse staining excludes the diagnosis of MPNST in most instances. Identification of ultrastructural features of Schwann cells by electron microscopy has also been suggested as the most reliable method of diagnosis [4].

Table 1. Comparative features of benign and MPNST on multi-modality imaging.

IMAGING FEATURES	MODALITY	MPNST	NEUROFIBROMA	SCHWANNOMA
Shape	Plain X-ray, ultrasound, MRI, CT	Fusiform	Variable	Variable
Size	Plain X-ray, ultrasound, MRI, CT	Diameter > 5 cm	Smaller	Small
Margin definition	Ultrasound, MRI, CT	Ill defined	Well defined	Well defined
Calcification	Ultrasound, MRI, CT	Present	Present in long standing cases	
Central necrosis/hemorrhage	Ultrasound, MRI, CT	Present	Present in long standing cases	
CT appearance	CT	Heterogeneous ± high attenuation values in unenhanced CT	Hypodense + minimal or no enhancement	Low-to-intermediate attenuation + intense enhancement
Ultrasound appearance	Ultrasound	Hypoechoic, heterogeneous	hypoechoic+ homogeneous with posterior acoustic enhancement	
Neural distribution	Ultrasound, MRI	Along major nerve trunk		Located along cutaneous or deep nerves
Position of parent nerve	Ultrasound, MRI	Often lies central to lesion	Central	Usually eccentric
Intra-tumor cysts	Ultrasound, MRI	Occasional	Rare	Common
Bony destruction	Ultrasound, MRI	Present	Absent	Absent
Peri-lesional edema	Ultrasound, MRI	Present	Absent	Absent
Corkscrew-vessels, loops, shunt, trifurcation	Doppler ultrasound, angiography	Often	Sometimes	Sometimes
High PSV ± low RI	Spectral Doppler	Present	Absent	Absent
Target sign	MRI	Absent	Present, often	Present
Fascicular sign	MRI	Occasional	Present	Present
Split fat sign	MRI	Absent	Present	Present
T1 enhancement	MRI	Often heterogeneous	Often homogeneous	
Thin T2 hyperintense rim	MRI	Absent	Rare	Present
Post contrast enhancement	MRI	Solid, peripheral, and heterogeneous	Central	Peripheral and heterogeneous
18-FDG avidity	PET/CT	High SUVs	Low SUVs	Low-to-intermediate SUVs
MDP uptake	Bone scintigraphy	Mild uptake	Variable	Variable
Ga-67 uptake	Ga-67 scintigraphy	High uptake	Low uptake	Low uptake

CT = computed tomography; MDP = methylene diphosphonate; PSV = peak systolic velocity; RI = resistive index; SUV = standardized uptake value.

Our limitations were that we could not perform nuclear imaging and we could not determine the association of this case with neurofibromatosis type 1.

Conclusions

Careful identification of USG and MRI features can complement each other in the categorization of PNST in terms of benign or malignant and thus the two imaging modalities in combination can guide institution of appropriate management.

Acknowledgement

The authors would like to thank the medical staff taking care of the patient.

List of abbreviations

CT	Computed tomography
FNAC	Fine needle aspiration cytology
HP	Histopathology
IHC	Immunohistochemistry
MPNST	Malignant Peripheral Nerve Sheath Tumor
MRI	Magnetic Resonance Imaging
NF	Neurofibroma
PET	Positron emission tomography
PNST	Peripheral nerve sheath tumor
USG	Ultrasonography

Consent for publication

Informed consent was obtained from the patient.

Ethical approval

IEC approval was obtained.

Author details

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Summary of the case

Patient (gender, age)	1	Male, 28 years old
Final diagnosis	2	Malignant peripheral nerve sheath tumor of right forearm
Symptoms	3	Asymptomatic swelling
Medications	4	N/A
Clinical procedure	5	MRI, Ultrasound & Duplex, FNAC, Excision & Biopsy, HP and IHC
Specialty	6	Radiology and imaging