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Research article

Imaging cellularity in benign and malignant peripheral nerve sheath tumors: Utility of the "target sign" by diffusion weighted imaging

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ABSTRACT

Objective: To determine the utility of "target sign" on diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) mapping for peripheral nerve sheath tumor (PNST) characterization.

Materials and methods: This IRB–approved, HIPAA–compliant study retrospectively reviewed the MR imaging (comprised of T2- FS, DWI (b-values 50, 400, 800 s/mm^{2}and ADC mapping), and static contrast-enhanced (CE) T1-W imaging) of 42 patients (mean age: 40 years (range 8–68 years), 48% (20/42) females) with 15 malignant PNSTs (MPNSTs) and 33 benign PNSTs (BPNSTs). MPNSTs were histologically confirmed while BPNSTs were histologically-proven or with stable clinical and imaging appearance for at least 12 months. Two radiologists assessed imaging characteristics (size, signal intensity, heterogeneity, perilesional edema or enhancement) and the presence or absence of "target sign," on each sequence. A "target sign" was defined as a biphasic pattern of peripheral hyperintensity and homogeneous central hypointensity. Descriptive statistics are reported. Cohen's κ statistic or interclass correlation coefficient (ICC) were used to evaluate interobserver agreement between two observers. Univariate and multiple logistic regression analysis were performed to identify MRI features with predictive values.

Results: MPNSTs were larger than BPNSTs (6.3 ± 2.5 cm vs 3.5 ± −2.1 cm, p = 0.0002), had perilesional edema (87%(13/15) vs 18%(6/33), p < 0.0001), heterogeneous enhancement (71%(10/14) vs 13%(4/31), p = 0.0001) and perilesional enhancement (79%(11/14) vs 18%(6/31), p = 0.0001), respectively. The "target sign" was present in: 24%(8/33) BPNSTs vs 0/15 MPNST on T2-FS (p = 0.26); 39%(13/33) BPNSTs vs 20%(3/15) MPNST on DWI using b-value = 50 s/mm^2 (p = 0.5); 55%(18/33) BPNSTs vs 6%(1/15) MPNST on DWI using b-value = 400 s/mm^2 (p = 0.002); 48%(16/33) BPNSTs vs 6%(1/15) MPNST on DWI using b-value = 800 s/mm^2 (p = 0.005) and 64%(21/33) benign vs 0/15 MPNST on ADC mapping(p < 0.0001). By CE-T1 imaging, 32%(10/31) BPNSTs and 7%(1/14) MPNST had a target sign(p = 0.07). The odds of an MPNST in cases with minimum ADC ≤ 1.0 × 10(−3) mm(2)/s are 150 times higher than in cases with ADC > 1.0 × 10(−3).

Conclusion: In this explorative study, a "target sign" suggests a benign PNST and is more often visible on DWI using high b-values and ADC maps compared with anatomic sequences.

1. Introduction

Peripheral nerve sheath tumors (PNSTs) comprise 10–12% of all benign soft tissue neoplasms. Most commonly encountered PNSTs are benign and include neurofibromas (accounting account for 5% of all benign soft tissue tumors) and schwannomas (also accounting for 5% of all benign soft tissue tumors) [1–3]. Solitary neurofibromas are often indistinguishable from schwannomas based on conventional imaging alone. The "tail sign" or continuity with the parent nerve is useful in establishing a neurogenic origin but typically only visible when a large nerve is involved. On T2-weighted (T2W) spin echo or fast spin echo (FSE) images, neurofibromas exhibit a "target sign" characterized by high peripheral and low to intermediate central signal intensity due to the presence of myxoid material peripherally and fibrous tissue

Abbreviations: PNSTs, Peripheral nerve sheath tumors; MR, Magnetic resonance; MPNST, Malignant peripheral nerve sheath tumor; DWI, Diffusion weighted imaging; ADC, Apparent diffusion coefficient

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centrally [3–7]. Although the "target sign" was initially thought to be pathognomonic of neurofibromas, it has also been observed in schwannomas and reported on both fluid-sensitive sequences as well as contrast-enhanced sequences [4]. On histological examination, schwannomas exhibit a "target sign" due to a hypercellular, hypointense center or Antoni A area and a hypocellular periphery rich in macrophages and collagen fibers or Antoni B area [1–6]. Hence, the presence of a "target sign" on magnetic resonance (MR) imaging of an indeterminate soft tissue mass is reassuring and may suggest not only the tissue of origin (nerve sheath) but also typically, benignity [2,4–8]. Of note, this finding has rarely been reported in the setting of a malignant peripheral nerve sheath tumor (MPNST) [5,6].

Diffusion weighted imaging (DWI) imaging using apparent diffusion coefficient (ADC) mapping is a qualitative and quantitative method to assess the brownian motion of water within the intracellular and extracellular spaces [9–17]. On DWI/ADC mapping, restricted diffusion has been observed in soft tissue tumors and attributed to tumoral hypercellularity with its resultant restriction of water motion [9–20]. With respect to PNSTs, quantitative DWI/ADC mapping is a useful technique for the characterization of neoplasms as benign or malignant [23–27]. Furthermore, the qualitative presence and apparent increased conspicuity of the "target sign" has been described on ADC mapping in PNSTs in a small case series of patients with schwannomatosis [19].

The "target sign" is derived from the histological composition or zonal architecture of a PNST, and as such, should be visible on both DWI as well as the ADC map. We hypothesized that DWI with apparent diffusion coefficient mapping could be more sensitive for the detection of cellularity related to the "target sign", and therefore, aide in distinguishing benign from malignant PNSTs. The purpose of our study was to determine the utility of a "target sign" on DWI for PNST characterization.

2. Material and methods

2.1. Overview

This IRB-approved, HIPAA-compliant study retrospective study was performed at a single tertiary referral center and reviewed consecutive MR imaging performed on 42 patients with 48 PNSTs between 8/2010 and 6/2016. Inclusion criteria were PNSTs with a definitive diagnosis (malignant diagnosis based on histology, benign diagnosis based on histology or having 12 months of stability in the setting of a neurocutaneous syndrome of neurofibromatosis type 1, type 2 or schwannomatosis) and MR imaging using DWI/ADC mapping. Exclusion criteria were antecedent systemic or local intervention such as radiation, chemotherapy, percutaneous biopsy or excision that might alter the imaging appearance of the PNST, and absence of DWI sequences, histology or at least 12 month stability.

2.2. Subjects

Between 2010 and 2016, subjects in this study were retrospectively sought from our picture archiving computer system and institutional neurofibromatosis clinic. Clinical data including histology and/or stability were recorded for each PNST.

2.3. MR imaging protocol

MR imaging was performed using a flexible phased array body-matrix coil on a 3.0 T system (Skyra or Verio, Siemens Healthcare, Malvern, PA) (n = 36) or 1.5 T system (Aera, Siemens Healthcare, Malvern, PA) (n = 6). Anatomic sequences were comprised of T1-weighted (T1-W) sequence (TR/TE 960/9, SL 5–6 mm), T2-fat suppressed (FS) sequence (TR/TE 3600–4280/70, SL 5–6 mm) as well as unenhanced and contrast-enhanced 3-dimensional volumetric T1-FS sequence T1-weighted sequence (TR/TE 4.6/1.4, flip angle 9.5, SL 1 mm). Functional sequences of DWI/ADC mapping were performed using spin-echo, single-shot echo-planar imaging (EPI) sequence (TR/TE 7600/80 ms), field of view (FOV) = 180–250 $mm^{2,}$ matrix size = 256 × 256 pixels, section thickness = 5 mm and interslice gap = 1 mm. Three b-values of 50, 400 800 s/mm^2 were utilized [24]. ADC mapping was automatically calculated using a monoexponential fit with inline software from Siemens (Syngo MapIT).

2.4. MR image analysis

Two musculoskeletal radiologists with 6 and 16 years' experience in musculoskeletal imaging and DWI/ADC mapping retrospectively reviewed the MR imaging independently and resolved discrepancies in consensus. First, the imaging quality was reviewed for each sequence on a 4 point semi-quantitative scale, ranging from 0 to 3 (0: non-diagnostic or artifacts involving more than or equal to 75% of the image; 1: artifacts involving 25–75% image; 2: artifact involving less than or equal to 25% of the image; 3: no significant artifact), similar to a previously reported scale [19]. Second, the PNSTs were evaluated on anatomic MR images for location (neck, chest, abdomen, pelvis, thigh, calf, foot, arm, forearm, hand), tissue layer (subcutaneous, intramuscular, intermuscular, intrarticular, mixed, cutaneous), size (anteroposterior (AP), mediolateral (ML), and craniocaudal (CC), mean lesional diameter), and the presence or absence of perilesional edema and a "target sign" [17]. A "target sign" was defined as a biphasic pattern of peripheral hyperintensity and central hypointensity on T2-FS and DWI/ADC mapping as well as homogeneous peripheral enhancement and central hypoenhancement on contrast enhanced sequences (Fig. 1) [6]. Signal characteristics on T2-FS were recorded as hypointense, isointense, or hyperintense (relative to skeletal muscle). Signal heterogeneity on T2-FS imaging was recorded (homogeneous, < 25% heterogeneity, 25–75% heterogeneity, > 75% heterogeneity). In addition, post-contrast images were assessed for the presence or absence of enhancement, a "target sign" pattern, and perilesional enhancement and the degree of enhancement heterogeneity (homogeneous, < 25% heterogeneity, 25–75% heterogeneity, and > 75% heterogeneity). Lastly, on the DWI/ADC mapping, the

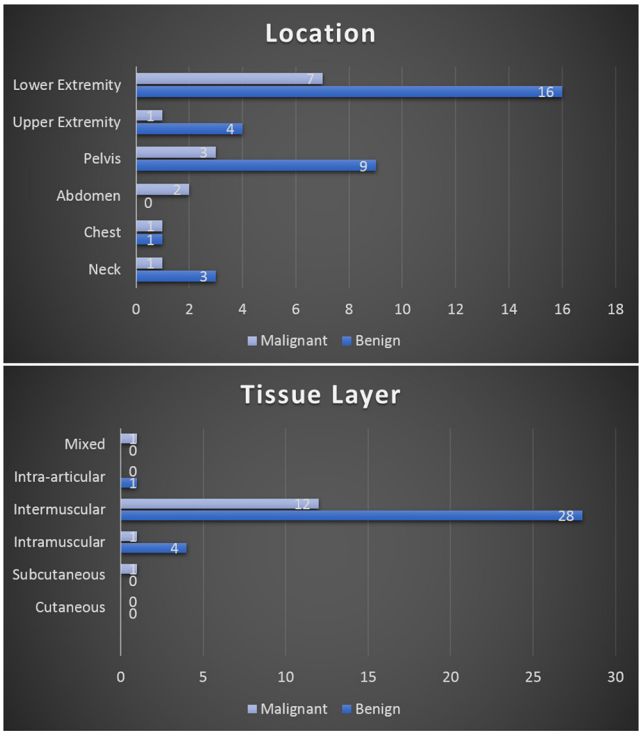

Fig 1. The anatomic location and tissue layer of PNSTs.