CLINICAL IMAGE

**Diffusion-weighted Imaging of Retroperitoneal Malignant Peripheral Nerve Sheath Tumor in a Patient with Neurofibromatosis Type 1**

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We present the diffusion-weighted imaging (DWI) findings for a malignant peripheral nerve sheath tumor arising in a retroperitoneal plexiform neurofibroma in a patient with neurofibromatosis type 1. Signal intensity of the malignant area was high on DWI and low on the apparent diffusion coefficient map and differed from findings for the benign area. DWI enabled clear differentiation between malignant and benign areas of the tumor.

Keywords: diffusion-weighted imaging, malignant peripheral nerve sheath tumor, neurofibromatosis type 1

**Introduction**

Neurofibromatosis type 1 (NF 1) is an autosomal dominant disease whose characteristic clinical features include café au lait spots, neurofibromas, Lisch nodules of the iris, and skinfold freckling. About 5% of patients with NF 1 develop malignant peripheral nerve sheath tumor (MPNST), which arises from plexiform neurofibromas and often has a poor prognosis.1 Optimal management depends on early and accurate histological grading and staging of the disease. MPNST cannot be reliably differentiated from benign tumors using conventional imaging techniques, including computed tomography (CT) and magnetic resonance (MR) imaging.2 Recently, DWI has been used to detect or characterize tumors.3,4 To our knowledge, no studies have correlated the differentiation of malignant from benign tumors using DWI with that using histopathological findings in patients with NF 1. We present DWI findings of MPNST arising in retroperitoneal plexiform neurofibromas with histopathologic correlation in a patient with NF 1.

**Clinical History and Imaging**

A 24-year-old woman with NF 1 with plexiform neurofibromas in the left retroperitoneal, peripelvic, and perisacral regions was being followed. At age 13, she underwent resection for a growing retroperitoneal tumor that had extended into the spinal canal and caused gait disturbance. On pathology, a neurofibroma was diagnosed. At age 17, she underwent another resection because of tumor regrowth. On pathology, MPNST was diagnosed, and intra- and postoperative radiotherapy was administered. At age 24, the patient’s follow-up MR images showed a growing retroperitoneal tumor in the previously identified retroperitoneal plexiform neurofibroma. The MR imaging was done using a 1.5T MR unit (Avanto S, Siemens, Erlangen, Germany) and sequences: T1-weighted spin-echo images (repetition time [TR] = 462 ms, echo time [TE] = 9.7 ms) in the axial and coronal planes; fat-suppressed T2-weighted fast spin-echo images (TR = 4440 ms, TE = 103 ms, echo train length = 15) in the axial, coronal, and sagittal planes; and DWI (fat-suppressed single shot spin-echo echo-planar imaging, TR = 5200 ms, TE = 67 ms, average n = 10, b = 0 and 800 s/mm2 with 3 orthogonal directional motion-probing gradients, the generalized autocalibrating partially parallel acquisition [GRAPPA] algorithm with an acceleration factor of 2) in the axial plane. Subsequently, using the MR unit’s software, isotropic DWI and the apparent diffusion coefficient (ADC) map were generated. The retroperitoneal tumor was isointense to the muscle on T1-weighted images and had inhomogeneous high signal intensity on fat-suppressed T2-
Magnetic resonance imaging of the retroperitoneal tumors (Figs. 1a–c). The growing portion in the retroperitoneal tumor had a high signal on isotropic DWI and a low signal on the ADC map (Figs. 1d, e). The center of the growing portion showed a low signal on isotropic DWI and a high signal on the ADC map. The previously identified retroperitoneal tumors had a slightly high signal on both isotropic DWI and the ADC map; those findings were different from the findings of the area that was enlarging. The average ADC value of the area of relatively low signal in the growing portion of the tumor on the ADC map was $1.25 \times 10^{-3}$ mm$^2$/s (range, $1.02$ to $1.32 \times 10^{-3}$ mm$^2$/s) using 7 regions of interests (ROIs) (size, 1.2 to 3.8 cm$^3$),

Fig. 1. Magnetic resonance imaging of the retroperitoneal tumors

a: An axial T$_1$-weighted spin-echo image (repetition time/echo time [TR/TE], 462/9.7 ms) shows round and irregularly shaped tumors in the left retroperitoneal, peripelvic, and perisacral regions (arrows). The tumor’s signal was nearly isointense to muscle. b,c: Fat-suppressed T$_2$-weighted spin-echo images (TR/TE, 4400/103 ms) in the axial (b) and sagittal (c) planes show the irregular high signal of the retroperitoneal tumor. A growing portion (arrows) was found in a previously identified plexiform retroperitoneal neurofibroma (arrowheads). d,e: A high signal area on a diffusion-weighted image (TR/TE, 5200/67) (d, arrows) and a low signal area on the apparent diffusion coefficient map (e, arrows) were found in the previously identified retroperitoneal tumor with a relatively slightly higher signal (arrowheads).
Fig. 2. Contrast-enhanced computed tomographic image shows an irregularly shaped tumor located in the left retroperitoneal, peripelvic, and perisacral regions (arrows). The tumor shows inhomogeneous enhancement.

Fig. 3. Pathologic findings
a: Microscopic examinations show a highly cellular, interlacing fascicle of tightly packed spindle cells with wavy elongated nuclei. The tumor cells show marked nuclei atypia, large bizarre, multinucleated cells, and mitosis (hematoxylin and eosin × 100). b: Peripheral area displaying spindle-shaped cell proliferation and collagen. The tumor cells are loosely arranged, and no mitotic activity is noted (hematoxylin and eosin × 100).

Discussion

MPNSTs are often difficult to detect and may metastasize to many sites before being diagnosed. Although progressive enlargement and pain related to the mass suggest malignancy, retroperitoneal MPNST is often clinically silent. Conventional imaging modalities, such as CT and MR imaging, are the standard methods for defining the anatomic extent of the tumor. CT and MR imaging findings that suggest malignant degeneration include size asymmetry, irregular infiltrative borders, bone erosion, and internal inhomogeneity. However, it has been shown that these criteria are not reliable indicators of malignancy and can be present in benign neurofibromas.

Recently, DWI has been used to detect and characterize tumors. DWI is a technique in which phase-defocusing and -refocusing gradients are used to evaluate the rate of microscopic water diffusion within tissue. Several investigators have noted an inverse correlation with ADC and tumor cellularity in brain tumors. In the present case, ADC was lower in the malignant area of the tumor and...
higher in the benign areas, perhaps because when compared to a benign area, a malignant area has high cellularity, enlarged nuclei, hyperchromatism, and angulation of the nuclear contour, which reduce water proton diffusion and result in a lower ADC. Benign neurofibromas are composed of Schwann cells and fibroblasts located in a myxoid or mucinous matrix that is surrounded by collagen; the higher ADC noted in the present case may reflect these characteristics. DWI and the ADC map may be sensitive to these histologic differences. In the present case, the ADC of the malignant portion was approximately $1.2 \times 10^{-3}$ mm$^2$/s, whereas that of the benign portion was approximately $2.0 \times 10^{-3}$ mm$^2$/s. Though this is simply one case, cut-off value to distinguish malignant from benign tumor in patients with NF 1 may be approximately 1.6 to 1.7 $\times 10^{-3}$ mm$^2$/s.

In general, the utility of DWI to differentiate malignant sarcomas from benign soft tissue tumors is controversial, and criteria for identifying sarcomas with DWI have not been established. Einarsdóttir’s group demonstrated the utility of analyzing true diffusion on DWI to differentiate malignant from benign soft tissue tumors. However, there are reports that the ADCs of benign and malignant soft tissue tumors overlap and thus cannot be used to differentiate malignant from benign soft tissue tumors. Soft tissue sarcomas are often inhomogeneous when hemorrhage or cystic formation is present in the tumor. Although ADC values are generally lower in malignant sarcomas than in benign soft tissue tumors, the ADC may increase when there are necrotic or cystic areas in the sarcoma. Furthermore, local vessel perfusion may affect the ADC value. Possible solutions for analyzing the ADC to help distinguish malignant from benign tumors may include measuring the ADC of the solid component or identifying the minimum ADC of the tumor. In the present case, the signal changes on DWI and ADC map helped distinguish the malignant from benign portions in the tumor. However, the utility of DWI to detect MPNST in patients with NF 1 should be studied in larger series.

Gallium 67 citrate scintigraphy was reported useful in differentiating benign from malignant nerve sheath tumors. However, the sensitivity for detecting malignancy is unknown. The utility of positron emission tomography (PET) of fluoro-deoxyglucose (FDG) was noted to differentiate MPNST from benign neurogenic tumors in patients with NF 1 because FDG uptake is higher in MPNST than in benign neurofibroma. However, the reported standard uptake value (SUV) of MPNST varied, and a higher SUV was found in a benign neurofibroma. Scintigraphy and PET scanners are much less available than MR scanners in hospitals, and their scanning times are usually longer than those of MR scanners. Among the various noninvasive techniques, DWI is available in many hospitals. When obtaining DWI, scanning of the abdominal region usually takes several additional minutes. The post-processing of the data is simple. We believe DWI can serve additional information in tumor characterization.

In conclusion, we report a case of MPNST arising from a retroperitoneal plexiform neurofibroma in a patient with NF 1 and the usefulness of DWI and ADC in distinguishing malignant sarcomas from benign tumors in this patient.

References

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