Proton MR Spectroscopy in a Possible Enhancing Hamartoma in a Patient with Neurofibromatosis Type 1

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Summary: A patient with neurofibromatosis type 1 was found to have an enhancing lesion in the cerebellum. Proton MR spectroscopy was performed and showed findings similar to those seen in healthy volunteers. A 3-year follow-up MR study showed the lesion was unchanged. Proton MR spectroscopy might prove useful in the diagnosis of hamartomas.

Index Terms: Neurofibromatosis; Hamartoma; Magnetic resonance, spectroscopy

Brain lesions in patients with neurofibromatosis type 1 include optic gliomas, cerebral astrocytomas, aqueductal stenosis, and “hamartomas.” The presence of hamartomas was unknown before magnetic resonance (MR) imaging. Hamartomas are probably of no clinical significance, and their importance lies in differentiating them from astrocytomas. When shown on computed tomography and MR, enhancing brain lesions in patients with neurofibromatosis type 1 should be considered actively growing tumor (1–3). We describe a patient with an enhancing lesion in the cerebellum in whom the findings on MR spectroscopy were similar to those in normal cerebellum. A biopsy was avoided, and a 3-year follow-up showed the lesion to be unchanged.

Case Report

As an asymptomatic 12-year-old boy with an unequivocal clinical diagnosis of neurofibromatosis type 1 underwent baseline MR imaging of the brain. A 1.5 × 1.4 × 2-cm rounded, deeply enhancing lesion was present in the superior cerebellar vermis (Fig 1A). This lesion was of high signal intensity on T2-weighted images (Fig 1B). Two small focal areas of high signal intensity in the globus pallidus bilaterally were also noted on T2-weighted sequences. The remaining brain and optic pathways were normal. Single-volume (3 × 3 × 3 cm) proton MR spectroscopy of the cerebellar lesion was done (Fig 1B and C). MR spectroscopy was done with PRESS (point-resolved spectroscopy) spin-echo localization, and water was suppressed by using the water elimination Fourier transform inversion-recovery sequence. Spectra were obtained at 2000/272/256 and compared with those of four healthy volunteers. An outside MR follow-up study 3 years after the initial study showed the lesion to be unchanged on both T2- and postcontrast T1-weighted sequences (Fig 1D). The patient remains asymptomatic.

Discussion

Abnormal areas of increased signal intensity on proton-density and T2-weighted MR sequences are seen in up to 43% of patients with neurofibromatosis type 1 (1). These abnormalities are usually located in the cerebellum, pons, midbrain, internal capsules, basal ganglia, and cerebral white matter (2). Their pathologic nature is indeterminate, and possible explanations include low-grade tumors, heterotopias, areas of delayed or disordered myelination, gliosis, and hamartomas (3). In one case, stereotaxic biopsy of one lesion showed normal brain (Schorry EK, presented at the Annual Clinical Care Conference of the National Neurofibromatosis Foundations, October 1988). On MR images, these lesions have no significant mass effect, no contrast enhancement, and generally grow very slowly, if at all. Therefore, the term hamartoma is generally used and accepted to describe them. Growth of these hamartomas occurs in approximately 10% of patients with neurofibromatosis type 1 (2). Growth is extremely unlikely after 10 years of age, and if it occurs it warrants careful follow-up to exclude tumor (2). Hamartomas of the basal ganglia can be larger than those elsewhere in the brain and occasionally are hyperintense on unenhanced T1-weighted images (3). The presence

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of Schwann cells and melanocytes is believed to be responsible for this high signal on images obtained with short echo and repetition times (3). Despite these observations, in our experience these hamartomas have a fairly typical MR appearance. Difficulty in differentiating them from tumor is encountered when the hamartomas occur near the intracerebral optic tracts, especially in patients who have concomitant optic gliomas. In one series, brain hamartomas were present in 17 of 19 patients with optic gliomas (3). It has been suggested that when patients with neurofibromatosis have brain lesions that enhance after administration of gadopentetate dimeglumine, the lesions should be considered neoplastic until proved otherwise (3, 4). Cerebral astrocytomas might be present in 6% to 15% of patients with neurofibromatosis type 1 (3, 4). On the basis of our clinical experience, the presumed diagnosis of hamartoma can be made if these criteria are met: lack of significant growth over a 3-year period, no surrounding edema, no mass effect (unless it occurs in the basal ganglia, particularly the globus pallidus), and no contrast enhancement. Also, in our experience and that of others, these lesions are not associated with any clinical symptoms (4).

Fig 1. A, Coronal T1-weighted spin-echo MR image (500/25/2 [repetition time/echo time/excitations]) after contrast administration shows a rounded, well-demarcated enhancing lesion in the left superiormost aspect of the cerebellum.
B, Axial localizing T2-weighted image (2400/80/1) through the upper cerebellum shows the volume (3 × 3 × 3 cm) sampled.
C, Proton MR spectra (2000/272/256) corresponding to the cerebellar lesion: 1 indicates choline; 2, creatine; and 3, NAA. Note that these spectra are remarkably similar to those of the normal cerebellum, shown in Figure 2.
D, Axial postcontrast T1-weighted image (500/25/2) 3 years after the initial study shows the lesion to be unchanged. (Coronal images were not obtained.)
Our case is remarkable because most of the criteria for the diagnosis of hamartoma were met, yet the lesion showed marked contrast enhancement (Fig 1A). Proton MR spectroscopy showed a pattern similar to that seen in normal cerebellum and remarkably unlike that seen in astrocytomas (Figs 1C, 2, and 3). In most astrocytomas, the choline peak is markedly elevated and N-acetylaspartate (NAA) and creatine peaks are low (5) (Fig 3). In our patient, the lesion was unchanged on a 3-year follow-up, thus supporting its benign nature (Fig 1D). It has been suggested that hamartomas, which comprise normal cells in an abnormal location, will show proton MR spectra similar to that seen in normal brain (6). Our experience with the present case supports that observation. Comparison of the peak areas of NAA, creatine, and choline found in our four healthy volunteers (voxel size = 3 x 3 x 3 cm) in whom approximately the same coil loading factor and voxel location were used suggests that the levels of NAA and choline in the volunteers (NAA, 1.19±0.03; choline, 7.58±1.36 [metabolite peak area ± SD]) were similar. The major difference was a 30% increase in the peak area of creatine in the hamartoma (9.75±) when compared with that in the volunteers (7.61±1.21). Visual inspection of the peak intensities also confirms the increase in creatine levels. The significance of the elevated creatine is uncertain; the spectra were obtained in a partially relaxed condition, and therefore the increase might reflect possible changes in relaxation times and not true changes in metabolite concentration. Caveats in our case report include the possibility that a small amount of tumor was present within the lesion but was not observed because of partial volume averaging effects; the lack of pathologic proof (hard to justify in the absence of any indication of malignancy); and the relatively small size of the hamartoma when compared with the overall size of the voxel. Three-dimensional chemical shift imaging might have been useful to sample smaller volumes but was not available at our institution when this study was performed. Although the percentage of the voxel that is occupied by tumor increases the sensitivity for the detection of abnormal levels of metabolites, the size of the lesion is not the sole determinant. Tumors can have up to a 200% difference in the rate of transport and
metabolism of nutrients when compared with normal brain (7). Thus, some small lesions within a large voxel might show strikingly abnormal metabolite concentrations, whereas large lesions occupying a voxel entirely that are metabolically slow might show only very subtle changes in metabolites when evaluated with hydrogen MR spectroscopy. Also, if a glioma is present, tumor cells might be present up to 2 cm beyond the border of the lesion, as shown by contrast-enhanced MR imaging (8). For these reasons, we believe that the spectra obtained in our patient truly reflect the benign nature of the hamartoma (further collaborated by lack of change in a 3-year period).

In summary, we propose that hamartomas in patients with neurofibromatosis type 1 rarely show enhancement. The presence of enhancement still justifies careful follow-up. MR spectroscopy offers an alternative to biopsy, because it may help to differentiate hamartoma from the more ominous astrocytoma.

References