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Evolution of High-Intensity Basal Ganglia Lesions on T1-Weighted MR in Neurofibromatosis Type 1

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PURPOSE: To characterize the temporal evolution of the foci of T1 shortening in basal ganglia lesions in patients with neurofibromatosis type 1 (NF-1). **METHODS:** A retrospective review of MR images of 37 patients with NF-1 revealed 8 patients in whom regions of T1 shortening were noted in the basal ganglia. We reviewed sequential images obtained in these selected patients with special attention to chronological changes in the foci of T1 shortening and their relationship to changes on T2-weighted images. **RESULTS:** Regions of short T1 in the globus pallidus were observed in 8 patients. In 2 of 3 patients in whom foci of T1 shortening were not identified on the initial imaging study, T1 shortening developed and T2 prolongation diminished after an initial increase. In the third patient, T1 shortening and T2 prolongation appeared simultaneously. Sequential scans in the other 5 patients, in whom areas of increased signal intensity in the globus pallidus were present on both T1-weighted and T2-weighted images on the initial MR examination, showed a diminution in the size of the region of T2 prolongation in 2 patients, an increase in the size of the region of T2 prolongation in 1 patient, a mixed pattern of change in the size of the region of T2 prolongation in 1 patient, and no change in the region of T2 prolongation in 1 patient. During the periods of these T2 changes, the areas of T1 shortening showed no significant interval change. **CONCLUSION:** The foci of prolonged T2 relaxation in the basal ganglia appear to evolve in a manner similar to the foci of T2 prolongation in the white matter of the posterior fossa. However, the corresponding foci of short T1 in the basal ganglia may evolve with a different time course. In some patients, the foci of short T1 develop at a later time than the T2 prolongation and progress; these foci of short T1 do not appear to regress over periods as long as 90 months. Possible causes of the T1 shortening are remyelination and calcification.

Index terms: Basal ganglia, magnetic resonance; Neurofibromatosis

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Neurofibromatosis type 1 (NF-1) is the most common phakomatosis, characterized on neuroimaging studies by optic nerve gliomas, parenchymal gliomas, and, on T2-weighted magnetic resonance (MR) images, by foci of increased signal intensity in the cerebellum, pons, midbrain, internal capsules, and basal ganglia. The exact nature of these lesions is unknown. The apparently benign features associated with these lesions and the absence of associated neurologic deficits have led most authors to suggest that the lesions represent hamartomas, heterotopia, or regions of altered myelin (1–5).

The basal ganglia lesions may have accompanying mass effect and may show hyperintensity on T1-weighted images, whereas the lesions confined to white matter are generally isointense with surrounding brain on T1-weighted images and have no mass effect. Because their morphology and signal characteristics are different from those of white matter lesions, the basal ganglia lesions may represent a separate entity. Possible pathologic explanations for the short T1 relaxation time of the basal ganglia lesions include paramagnetic metals released by the disease process, calcification (3,

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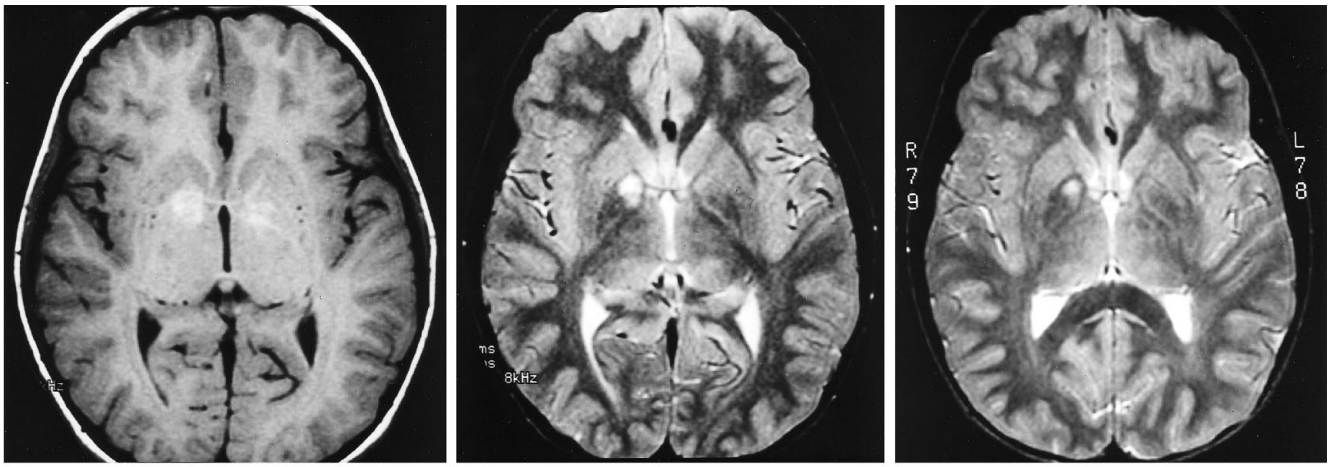

Fig 1. MR findings in an 8-year-old boy with NF-1.
A, Axial T1-weighted image shows hyperintensity in the globi pallidi. The findings did not change over time.
B, Axial T2-weighted image obtained during the same examination as *A* shows hyperintensity in the right globus pallidus.
C, Axial T2-weighted image obtained 33 months after *B* shows the diminution in size of the area of prolonged T2 relaxation.

6), and hamartomas containing Schwann cells and/or melanin deposits (7).

Although a number of studies have described the MR imaging appearance of these basal ganglia and white matter lesions, analysis of the temporal evolution of basal ganglia lesions has been limited (5). In particular, no study has focused on the temporal evolution of the regions of short T1 relaxation time in the globus pallidus. In the hope that such an evaluation might elucidate the underlying cause of these signal abnormalities, we retrospectively reviewed MR images obtained in 37 patients with NF-1 in an attempt to characterize further the temporal evolution of the regions of increased signal intensity in the globus pallidus on T1-weighted images.

Materials and Methods

We retrospectively reviewed the cranial MR images obtained in 37 patients in whom a diagnosis of NF-1 was established by standard criteria (8). The review was performed with special attention to signal changes in the basal ganglia. This review identified 8 patients in whom foci of increased signal intensity in the globus pallidus was seen on T1-weighted MR images. These patients included 5 girls and 3 boys ranging in age from 3 to 17 years (mean age, 9 years) at the time of the initial MR study. Sequential studies of these 8 patients were analyzed with special attention to chronological changes in foci of increased signal intensity on T1-weighted images. All analyses were performed by visual inspection and by a consensus of two neuroradiologists. Follow-up studies were performed between 12 and 90 months (mean, 54 months) after the initial study; the follow-up studies were done to monitor abnormalities in regions other than the basal ganglia. An average of 5 follow-up scans were obtained in the 8 patients. Foci in the globus pallidus that were contiguous with tumors of the optic chiasm or hypothalamus were excluded because of possible alterations of mass effect or signal intensity caused by invasion of the tumor. The MR examinations were performed on a variety of scanners, but all scanners were 1.5-T superconducting units. All MR studies included precontrast T1-weighted spin-echo images and T2-weighted spin-echo images obtained with standard sequences. Postcontrast T1-weighted images were obtained after intravenous administration of gadopentetate dimeglumine (0.1 mmol/kg) in all patients.

Results

By the inclusion criteria, a region of shortened T1 relative to cerebral white matter (Figs 1 and 2) was located in the globus pallidus in all patients on at least one imaging study. This process was bilateral in seven patients and unilateral in one (case 1). On T2-weighted images, the foci of short T1 were noted to have long T2 relaxation times compared with surrounding brain in all patients except one (Fig 1).

A summary of our imaging findings appears in the Table. In three patients, areas of increased signal intensity in the globus pallidus on T1-weighted images were not identified on the initial imaging study but appeared on subsequent scans. In one of the three patients, foci of short T1 and foci of long T2 appeared simul-

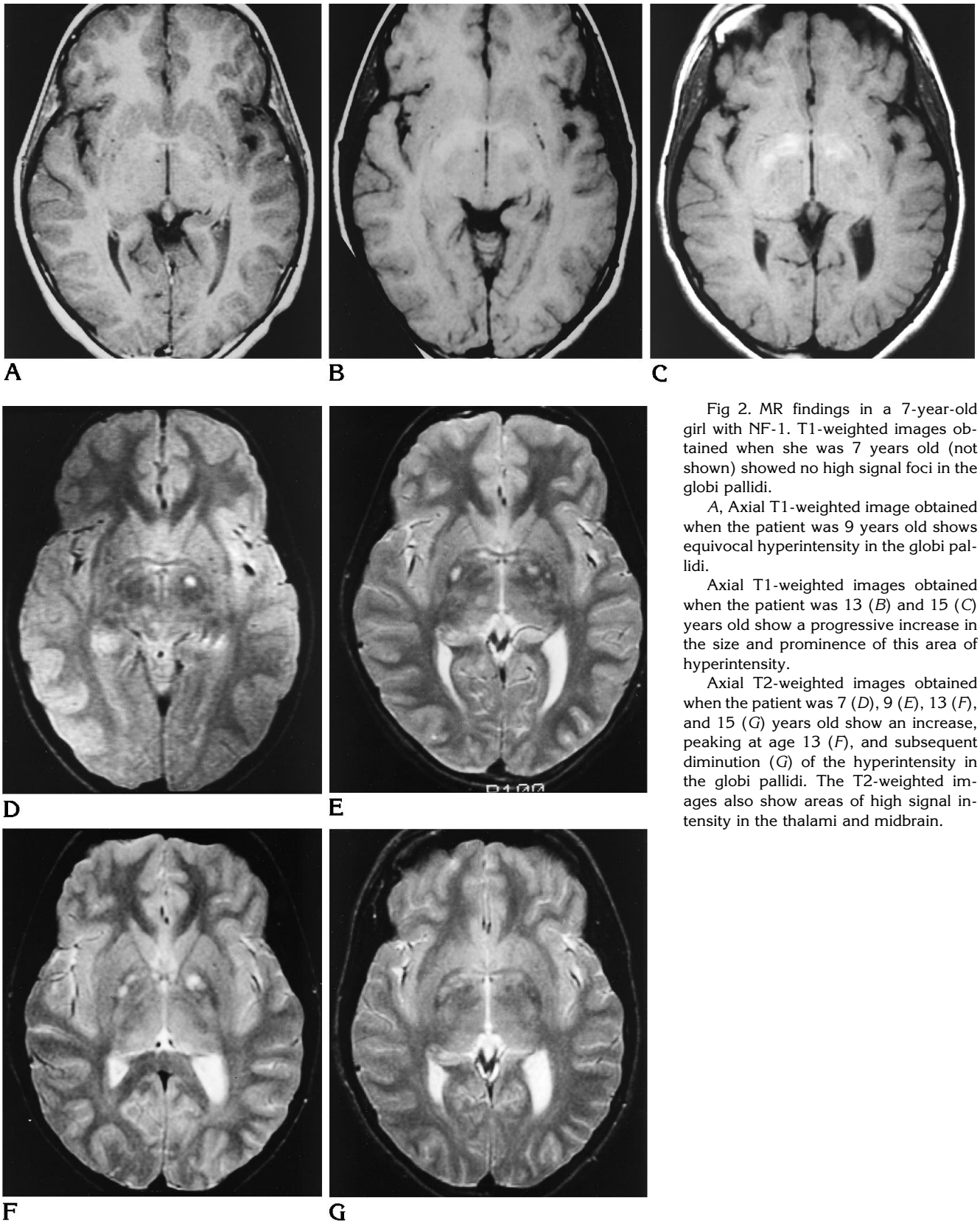

Fig 2. MR findings in a 7-year-old girl with NF-1. T1-weighted images obtained when she was 7 years old (not shown) showed no high signal foci in the globi pallidi.

A, Axial T1-weighted image obtained when the patient was 9 years old shows equivocal hyperintensity in the globi pallidi.

Axial T1-weighted images obtained when the patient was 13 (*B*) and 15 (*C*) years old show a progressive increase in the size and prominence of this area of hyperintensity.

Axial T2-weighted images obtained when the patient was 7 (*D*), 9 (*E*), 13 (*F*), and 15 (*G*) years old show an increase, peaking at age 13 (*F*), and subsequent diminution (*G*) of the hyperintensity in the globi pallidi. The T2-weighted images also show areas of high signal intensity in the thalami and midbrain.

MR findings in eight patients with neurofibromatosis type 1

Patient	High Signal on T1-Weighted Images		High Signal on T2-Weighted Images	
	Initial Study	Follow-up Study	Initial Study	Follow-up Study
1	−	Appeared	−	Appeared
2	−	Appeared	+	Inc and dec
3	−	Appeared and inc	+	Inc and dec
4	+	No change	+	No change
5	+	No change	+	Inc
6	+	No change	+	Inc/dec
7	+	No change	+	Dec
8	+	No change	+	Dec

Note.— − indicates not identified on initial study; +, identified on initial study; inc, increased in size or became more prominent; dec, decreased in size or became less prominent; inc and dec, initially increased and subsequently decreased; and inc/dec, increased on one side and decreased on the other side.

taneously (case 1). In the other two patients, the T2 prolongation appeared earlier than the T1 shortening. In these two patients, many follow-up studies (six and four examinations, respectively) were available over a period of 49 months and 90 months, respectively; in both, the region of T2 prolongation showed an initial increase and subsequent decrease in size (Fig 2D–G). The signal regression in these areas thus followed the earlier regression of the foci of T2 prolongation in the brain stem, cerebellar white matter, and dentate nucleus. In one of these patients, the increased signal intensity appeared and persisted on T1-weighted images while the increased signal intensity on the T2-weighted images increased and then decreased in size (case 2). In the other patient, the regions of increased signal intensity on T1-weighted images appeared and steadily increased in prominence (Fig 2A–C) while the high signal intensity on T2-weighted images peaked and then diminished (case 3).

In five patients, areas of increased signal intensity in the globus pallidus on both the T1-weighted and T2-weighted images were present on the initial MR study. In one of these five patients, the areas of increased signal intensity on T1-weighted and T2-weighted images showed no change during the 39-month interval between the two examinations (case 4). In another patient, the regions of T2 prolongation became more prominent while the T1 shortening in the same regions showed no change (case 5). In yet another patient, the foci of T2 prolongation showed a mixed pattern of change, diminishing on one side and becoming more prominent on other side, while the T1 shortening showed no change (case 6). In two patients, the foci of T2 prolongation regressed while the T1 shortening showed no change (case 7, Fig 1, and case 8). In one of these two patients, the high signal lesions in the bilateral globi palladi showed mild mass effect (case 8). This mass effect did not show significant change over a period of 4 years.

Gadopentetate dimeglumine was administered intravenously to all patients, and no evidence of enhancement related to these basal ganglia signal abnormalities was noted.

Discussion

Recent studies concerning MR findings in patients with NF-1 describe the presence of focal areas of increased signal intensity in the basal ganglia region on T1-weighted images as a relatively less frequent observation compared with the presence of focal areas of increased signal intensity in the basal ganglia region and white matter on T2-weighted images; the latter are often referred to as hamartomas. The frequencies with which focal areas of increased signal intensity are seen in the basal ganglia region on T1-weighted images have been 10 of 53 patients (3), 7 of 35 patients (7), and 10 of 70 patients (9). Aoki et al (3) divided hamartomas into those in the basal ganglia and those in the white matter, and described the transient nature of the white matter hamartomas in patients with optic gliomas. These authors suggested that the lesions in the basal ganglia may be different from lesions in the white matter. Sevick et al (4), in a study that excluded basal ganglia lesions, described the transient nature of the white matter lesions. Itoh et al (5) noted that the lesions in the basal ganglia disappear later than those in the cerebellum. However, none of these studies focused on the regions of increased signal intensity in the globus pallidus on T1-weighted images. Although we are not sure whether all of the lesions in the basal ganglia are different from the white matter lesions, it appears that short T1 relaxation time is a characteristic of only basal ganglia lesions, and not those of the posterior fossa or cerebral white matter. Therefore, we believe that at least some of the basal ganglia lesions are distinct from those in the white matter.

In the two patients in this series in whom many examinations were available over a prolonged time period, the sizes of the foci of prolonged T2 relaxation diminished after an initial size increase. Sequential scans in three other patients also showed diminution of the foci of prolonged T2 relaxation on at least one side of the globus pallidus. This transient nature is the same as was observed in hamartomas in the reports mentioned above. While the T2 changes were taking place, the areas of T1 shortening either increased in size or remained unchanged in all patients.

Mirowitz et al (7) described no clear change in the basal ganglia areas of short T1 in three patients over a period of 2 years. The lack of change in the signal abnormalities in their report differs from our observations of sequential change in T1 shortening in three patients and of corresponding change of T2 prolongation in seven patients. Perhaps the discrepancy results from the limited follow-up period in their series. Shu et al (9) described no evidence of progression of the high signal regions in the basal ganglia on T1-weighted images in seven patients (serial examinations: range, two to six examinations; mean, three). However, they did not mention whether there was any concurrent change in signal abnormalities on T2-weighted images.

Although the precise nature of these basal ganglia signal abnormalities is unknown, their evolving nature would not be consistent with developmental abnormalities such as hamartomas, heterotopia, or other malformative lesions. Itoh et al (5) speculated that the deep gray and white matter MR abnormalities represent areas of disordered myelin maturation caused by abnormal or delayed glial differentiation; they suggested that certain central nervous system cells expressing the abnormal gene later mature and correct the myelin abnormality. The paucity of previous neuropathologic observations of these lesions is consistent with their transient nature, because most pathologic reports of patients with NF-1 have involved adult cases (10). In a report describing histologic findings in NF-1 lesions documented as abnormal by MR imaging (6), tissue from the region of the globus pallidus and cerebral peduncle showed nonspecific protoplasmic astrogliosis, foci of microcalcification associated with perivascular gliosis, and spongiform myelinopathy. Although these findings may explain the evolution of the T2 prolongation if the intramyelinic vacuolization is transient, they do not explain the evolution of the T1 shortening, nor do they explain the apparent temporal relationship between the T1 and T2 changes. A possible explanation may be that the calcifications are in some way related to a reparative process that resolves the intramyelinic edema.

In two patients in our series, the increased signal intensity on T2-weighted images appeared earlier than the increased signal intensity on T1-weighted images. In one of these two patients, T1 shortening appeared and increased in prominence while the increased signal intensity on T2-weighted images peaked and then diminished. These changes also suggest that the high signal on the T1-weighted images may be related to the myelin abnormality or its repair, perhaps representing an early phase of the correction of disordered myelin. Myelinated regions in the brain routinely result in T1 shortening with consequent increased signal intensity on T1-weighted images as compared with gray matter and unmyelinated white matter (11, 12).

That the lesions in our patients were hyperintense relative to surrounding white matter might potentially be explained by a tighter packing of myelinated fibers within the lesions or, perhaps, an overexpression of those components of myelin that cause the T1 shortening (believed to be cholesterol and galactocerebrosides) (13, 14). Such subtle abnormalities of the myelin would not be detected by routine myelin staining. Thus, if the T1 shortening were a result of the remyelination of an area of initially disordered myelination, we would expect just such an appearance of T1 shortening prior to T2 shortening, similar to what is seen in the normally myelinating brain (11). This finding may not be as obvious in white matter lesions because the tissue surrounding it is myelinated white matter and, therefore, isointense. In the globus pallidus, the surrounding tissue is gray matter, which has a lower signal intensity on T1-weighted images. Another possible cause of T1 shortening is foci of microcalcification documented in the above-mentioned pathologic report (6). To support this theory, Dell et al (15) reported a case in which hyperintensity in the basal ganglia on short-repetition-time, short-echo-time images was caused by calcification. More radiologic-pathologic correlations with more sophisticated myelin analyses will be necessary to sort out these hypotheses.

We conclude that, although the foci of prolonged T2 relaxation in the basal ganglia appear to evolve in a manner similar to the foci of T2 prolongation in the white matter, the corresponding T1 shortening in the basal ganglia evolves with a different time course. In some patients, the foci of short T1 develop at a later time than the T2 prolongation, and these foci of short T1 do not appear to regress over periods of up to 90 months.

References

1. Hurst RW, Newman SA, Cail WS. Multifocal intracranial MR abnormalities in neurofibromatosis. *AJNR Am J Neuroradiol* 1988; 9:293–296
2. Bognanno JR, Edwards MK, Lee TA, Dunn DW, Roos KL, Klatte EC. Cranial MR imaging in neurofibromatosis. *AJNR Am J Neuroradiol* 1988;9:461–468
3. Aoki S, Barkovich AJ, Nishimura K, et al. Neurofibromatosis type 1 and 2: cranial MR findings. *Radiology* 1989;172:527–534
4. Sevick RJ, Barkovich AJ, Edwards MSB, Koch T, Berg B, Lempert T. Evolution of white matter lesions in neurofibromatosis type 1: MR findings. *AJR Am J Roentgenol* 1992;159:171–175
5. Itoh T, Magnaldi S, White RM, et al. Neurofibromatosis type 1: the evolution of deep gray and white matter MR abnormalities. *AJNR Am J Neuroradiol* 1994;15:1513–1519
6. DiPaolo DP, Zimmerman RA, Rorke LB, Zackai EH, Bilaniuk LT, Yachnis AT. Neurofibromatosis type 1: pathologic substrate of high-signal-intensity foci in the brain. *Radiology* 1995;195:721–724
7. Mirowitz SA, Sartor K, Gado M. High-intensity basal ganglia lesion on T1-weighted MR images in neurofibromatosis. *AJNR Am J Neuroradiol* 1989;10:1159–1163
8. National Institutes of Health Consensus Development Conference. Neurofibromatosis (conference statement). *Arch Neurol* 1988;45: 575–578
9. Shu HH, Mirowitz SA, Wippold FJ II. Neurofibromatosis: MR imaging findings involving the head and spine. *AJR Am J Roentgenol* 1993;160:159–164
10. Rubinstein LJ. The malformative central nervous system lesions in the central and peripheral forms of neurofibromatosis. *Ann NY Acad Sci* 1986;486:14–29
11. Barkovich AJ, Kjos BO, Jackson DE Jr, Norman D. Normal maturation of the neonatal and infant brain: MR imaging at 1.5 T. *Radiology* 1988;166:173–180
12. Holland BA, Haas DK, Norman D, Brant-Zawadzki M, Newton TH. MRI of normal brain maturation. *AJNR Am J Neuroradiol* 1986; 7:201–208
13. Koenig SH, Brown RD III, Spiller M, Lundbom N. Relaxometry of brain: why white matter appears bright on MRI. *Magn Reson Med* 1990;14:482–495
14. Kucharczyk W, Macdonald PM, Stanisz GJ, Henkelman RM. Relaxivity and magnetization transfer of white matter lipids at MR imaging: importance of cerebrosides and pH. *Radiology* 1994; 192:521–529
15. Dell LA, Brown MS, Orrison WW, Eckel CG, Matwiyoff NA. Physiologic intracranial calcification with hyperintensity on MR imaging: case report and experimental model. *AJNR Am J Neuroradiol* 1988;9:1145–1148