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High-Intensity Basal Ganglia Lesions on T1-Weighted MR Images in Neurofibromatosis

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Basal ganglia lesions, characterized on MR by increased signal intensity on T1-weighted images, were observed in seven patients with documented neurofibromatosis. These lesions most often involved the globus pallidus and internal capsules in a bilateral and symmetric fashion, and extended across the anterior commissure resulting in a "dumbbell" configuration. Smaller and less prominent foci of increased signal also were present on corresponding T2-weighted images. These lesions did not exhibit mass effect, edema, or enhancement with gadolinium-DTPA. They were not visible on CT (performed in two patients) and demonstrated no progression during a 2-year interval in three patients. Their signal characteristics and morphology suggest that they represent heterotopias containing Schwann cells and/or melanin deposits. Migrational abnormalities of these neural crest derivatives are known to occur in neurofibromatosis, and the presence of such heterotopias has been documented pathologically in patients with this disorder.

While recent reports discuss foci of increased signal intensity on T2-weighted MR images in patients with neurofibromatosis, signal abnormalities on T1-weighted images have not yet been described. When lesions characterized by similar signal as well as morphologic characteristics are encountered on MR, the diagnosis of neurofibromatosis should be considered.

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Neurofibromatosis (NF) is the most common of the phakomatoses, occurring in 1/3000 births [1]. This disorder is transmitted as an autosomal dominant trait, although spontaneous mutations are responsible for half the cases [1]. While the expression of the genetic defect is highly variable among individual patients, intracranial abnormalities account for some of the most frequent and disabling features. CNS neoplasia occurs in the form of optic nerve and chiasm gliomas, other varieties of astrocytomas, meningiomas, and cranial nerve schwannomas [2-4] and is the most frequent cause of death in children with this disease [5]. Patients also are predisposed to CNS dysplasia, which may manifest with a wide spectrum of hamartomatous or heterotopic lesions within the brain and spinal cord [2, 4]. Other anatomic abnormalities that affect the CNS include meningocele, aqueductal stenosis, arachnoid cysts, hydrocephalus, macrocranium, cerebrovascular occlusions, cytoarchitectural anomalies, and syringomyelia [2, 4]. In addition to the neurologic deficits that often result from these anatomic lesions, patients with NF are subject to intellectual handicaps, including mental retardation, as well as headaches, speech impediments, seizures, and other disorders for which a clear origin has not been found [1, 2].

Recent reports have described the effectiveness of MR imaging in the detection of CNS lesions in patients with NF [6-12]. In general, these studies have found MR to be more sensitive than CT in demonstrating the presence of neoplasms and in defining their extent [7, 9]. Several reports describe the frequent identification of foci of hyperintensity on T2-weighted MR images that do not correspond to

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abnormalities on CT or on T1-weighted images [6, 7, 11, 12]. 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 or heterotopias [6, 7, 11, 12].

Although these studies report routine use of T1- and T2-weighted sequences, none has described lesions that demonstrate significantly increased signal intensity on T1-weighted images. We have recently encountered seven children with NF in whom MR has demonstrated unusual lesions involving the basal ganglia characterized by bright signal intensity on T1-weighted images.

Subjects and Methods

A review of cranial MR examinations in 35 patients with documented NF revealed seven patients who demonstrated foci of increased signal intensity on T1-weighted images. These patients included five females and two males ranging in age from 3 to 17 years (mean, 12 years).

MR was performed on two separate superconducting units* operating at 0.5 and 1.5 T. Images were acquired by using spin-echo multisection technique. TRs ranging from 300–750 and TEs ranging from 15–35 resulted in relatively T1-weighted images. A double-echo pulse sequence was used to obtain relatively spin-density- and T2-weighted images. TRs ranged from 1500–3100, with first-echo TE of 35 and second-echo TE of 90–120. A slice thickness of 5–10 mm was used, and images were variably obtained in all orthogonal planes. Patients were not sedated for the examination.

Two of the patients underwent CT scanning,[†] which was performed before and after administration of IV contrast material. Contiguous transaxial images were obtained by using a slice thickness of 8 mm.

Results

Areas of increased signal intensity relative to cerebral white matter were observed in the basal ganglia region on T1-weighted images in all seven patients (Figs. 1–3). This process was bilateral in all cases and usually symmetric. The globus pallidus and portions of the internal capsule were involved in all patients. Apparent extension of signal abnormality across the anterior commissure, resulting in a "dumbbell" configuration, was present in six of the seven patients. The posterolateral aspects of the thalami appeared to be involved in five patients, and in one patient there were foci of increased intensity within the corpus callosum. On T2-weighted images foci of increased signal intensity were demonstrated within at least a portion of the above-described areas in all patients. In five of the seven patients the extent and conspicuity of hyperintensity on T2-weighted images were considerably more limited than the hyperintensity seen on T1-weighted images. In other words, some of the tissue displaying increased intensity on T1-weighted scans was of normal signal intensity on T2-weighted images in these patients. In one patient the distribution of hyperintensity on T1- and T2-weighted images was equivalent, and in the remaining patient

T2-weighted images demonstrated more extensive involvement. On all pulse sequences, the areas involved by abnormal signal intensity were smoothly margined, although somewhat nodular in appearance and without associated mass effect or edema. IV Gd-DTPA was administered in two patients, and no evidence of abnormal enhancement related to these basal ganglia signal abnormalities was noted. Multiple MR examinations were performed in three patients, covering an approximate time span of 2 years in all patients. Although these examinations varied significantly in terms of pulse sequences, imaging planes, and slice thicknesses used, as well as field strength, there was no definite evidence of change in the signal abnormalities. CT scans were performed before and after administration of IV contrast material in two patients, and revealed no abnormalities that correlated with these signal alterations. Numerous abnormalities were observed on MR in these patients in addition to the signal changes described above; these are listed in Table 1.

Discussion

Recent studies concerning MR in patients with NF describe focal areas of increased signal intensity on T2-weighted images as a frequent observation [6–12]. These lesions are characterized by an absence of mass effect or surrounding edema and apparently are not associated with focal neurologic deficits. The frequency of these lesions as cited in recent series has been 23/53 patients [12], four/four patients [11], and nearly half of 15 patients [6]. The most frequent location reported is the basal ganglia [6, 7, 11, 12]. In those reports that further specify location, the globus pallidus is the most frequent site, often with bilateral involvement [11]. Extension of basal ganglia lesions into the internal capsules, as described in our cases, has also been reported [12].

While histopathologic correlation has been lacking, the apparently benign features of these lesions has led the authors of these studies to conclude that the lesions most likely represent hamartomas or heterotopias [6, 7, 11, 12]. This is stated, of course, with the proviso that the limited ability of MR to predict histopathology does not allow for the exclusion of a low-grade tumor without serial studies. The nature of the constituents of these hamartomatous lesions has not been addressed in previous reports. This is presumably because prolongation of T2 relaxation occurs with a wide variety of pathologic lesions and therefore confers almost no specificity regarding tissue composition. The observation of lesions manifesting increased signal intensity on T1-weighted images, however, is unusual, and such signal behavior has been associated with relatively few tissues. These tissues include lipids and paramagnetic species of iron as contained within hemoglobin degradation products such as methemoglobin [13] or melanin (melanoma) [14]. Further consideration of the source of the unusual signal behavior of the lesions we encountered requires a review of some of the basic pathophysiologic aspects of NF.

The diverse forms of pathology that occur in NF are understood through consideration of NF as a neurocristopathy, or complex disorder of the neural crest [1, 15, 16]. From their

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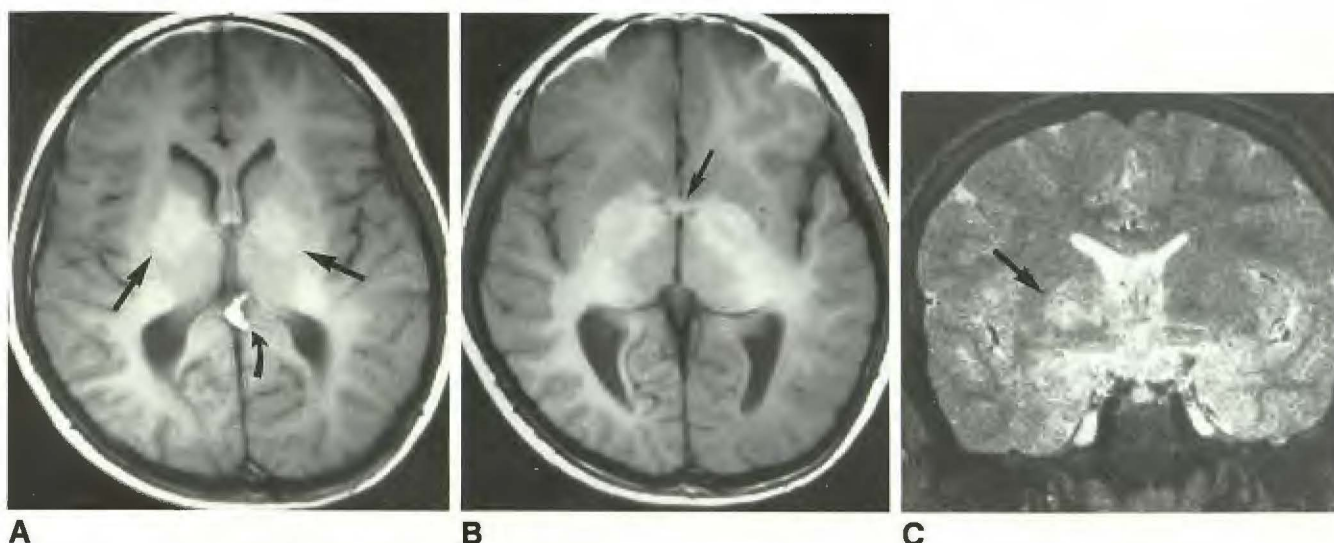


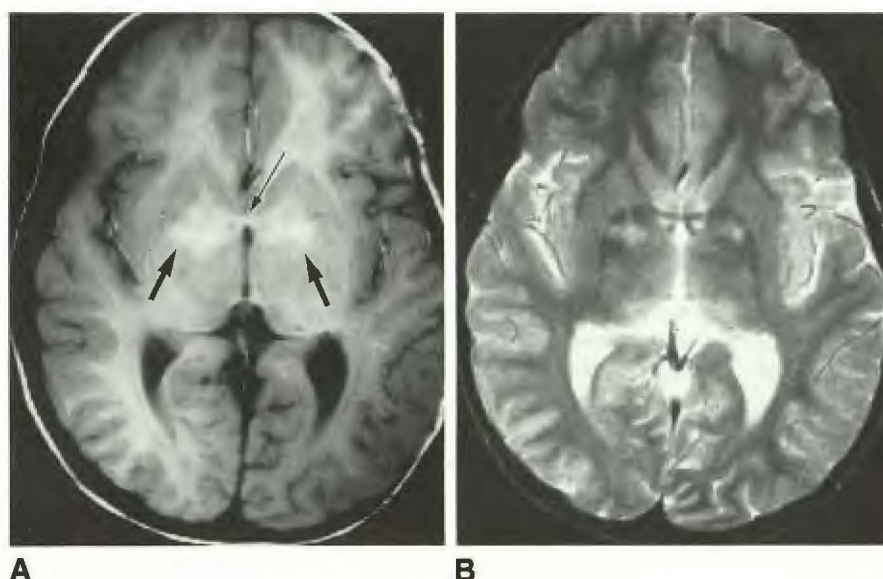
Fig. 1.—A, T1-weighted image (750/21) at 1.5 T shows increased signal intensity involving globus pallidus and internal capsule bilaterally (straight arrows) that was without interval change since a previous examination 2 years earlier. A pericallosal lipoma is also seen (curved arrow). CT revealed no evidence of basal ganglia abnormalities in this patient.

B, T1-weighted image at another level better demonstrates posterior extent of increased signal intensity, as well as involvement of anterior commissure (arrow).

C, Coronal T2-weighted image (3100/90) shows mildly increased signal intensity involving basal ganglia region on the right only (arrow).

Fig. 2.—A, T1-weighted image (750/21) at 1.5 T demonstrates confluent nodular areas of hyperintensity involving globus pallidus and internal capsule bilaterally (wide arrows) with extension across the anterior commissure (thin arrow), resulting in a “dumbbell” configuration.

B, T2-weighted image (3200/90) at a comparable level. There are small nodular foci of increased intensity within globus pallidus and internal capsule bilaterally. The extent and morphology of signal abnormality shown here differ considerably from those seen on corresponding T1-weighted image.



origin along the dorsal surface of the embryonic neural tube, the multipotential cells of the neural crest migrate throughout the embryo [17]. The timing and path of their migration as well as their subsequent differentiation into various specialized cell types is regulated by intrinsic as well as extrinsic or environmental factors [18, 19]. Among the major neural crest derivatives formed as a result of this process are cephalic mesenchyme, leptomeninges, sensory ganglia of cranial nerves, sympathetic and parasympathetic ganglia and plexuses, spinal ganglia, Schwann cells, and pigment cells [18, 20]. Failure in the controls that regulate the formation, migration, and differentiation of neural crest cells results in the

formation of dysplastic and neoplastic aggregations of the neural crest derivatives listed above [15]. We describe two of these derivatives in terms of the possible nature of the MR signal abnormalities encountered.

Schwann cells are involved in many common manifestations of NF. Neoplastic proliferation of these cells results in schwannomas or neuromas of the cranial nerves (particularly cranial nerves eight and five), which are closely associated with NF. Similar tumors may involve the spinal nerves and ganglia. Schwann cells, along with fibroblasts and other tissues, are also major components of the neurofibromas and occasional neurofibrosarcomas, which are the hallmark of this disease.

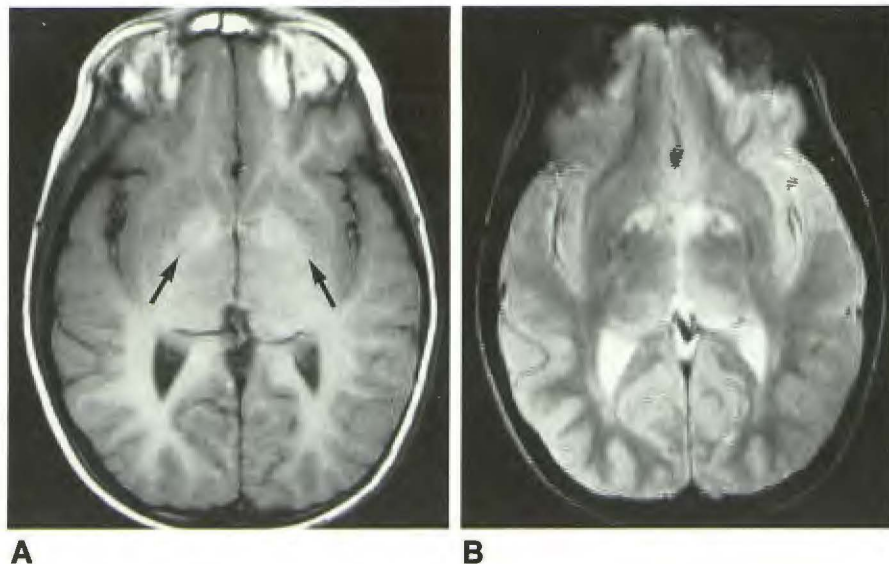


Fig. 3.—A, T1-weighted image (750/20) at 1.5 T shows increased signal intensity (arrows) involving globus pallidus and a portion of the internal capsules bilaterally. Extension of signal abnormality across anterior commissure is again noted.

B, Corresponding T2-weighted image (2200/90) also demonstrates hyperintense foci involving a similar distribution, although a more nodular morphology is demonstrated.

TABLE 1: Additional Abnormalities Demonstrated on MR Images

Case No.	Age	Gender	Additional MR Abnormalities
1	12	F	OC and ON glioma; pericallosal lipoma
2	10	F	Sphenoid dysplasia; buphthalmos
3	14	F	OC and ON glioma extending along OT
4	17	F	OC and ON glioma; infarct
5	17	F	Third ventricular mass; cutaneous NFs
6	3	M	Macrocephaly; ON glioma; plexiform NF
7	9	M	Cerebellar mass

Note.—OC = optic chiasm, ON = optic nerve, OT = optic tract, NF = neurofibroma.

Although neoplasms of Schwann cells are more frequent and widely recognized, hamartomatous collections of Schwann cells also occur in association with NF [4]. Aggregations of ectopic Schwann cells, or schwannosis, within the CNS have been encountered most often in the spinal cord [21, 22]. Hamartomas containing Schwann cells have also been documented in the cerebral cortex and basal ganglia [23]. Additional components of such lesions include meningeal cells, neuroglia, and blood vessels, as well as other neural crest tissues [23].

The signal behavior of the lesions we describe could be explained, at least in part, by the presence of ectopic Schwann cells within the basal ganglia. Myelinated regions in the brain routinely result in relatively increased signal intensity on T1-weighted images as compared with cortex and deep gray matter, CSF, and most other components of the image [24]. That the lesions in our patients were hyperintense relative to surrounding white matter can potentially be explained by a denser clustering of myelinated fibers within the lesions. The observation of smaller foci of increased signal on T2-weighted images could presumably be due to tissues other than Schwann cells (e.g., neuroglia) within the hamartomas, or could result from reactive gliosis leading to increased water content.

The second neural crest derivative to be considered is the melanocytes, or pigment cells. All pigment cells throughout the body, except for those in the retina, originate as stem cells in the neural crest [25]. Among the areas to which they normally migrate are the leptomeninges, particularly pia mater, and the entire CNS [26]. Disruption in this migration also occurs in patients with NF, resulting in many characteristic features such as cafe-au-lait spots, axillary and intertriginous freckling, cutaneous hyperpigmentation, and Lisch nodules (melanocytic hamartomas of the iris) [1, 5, 27]. Hamartomatous collections of melanocytes have also been described within the brain in patients with NF [23, 28]. In such cases, pigment cells that appear to arise from the pia mater migrate along perivascular sheaths [21, 28] resulting in intracerebral masses of melanin in various locations, including the basal ganglia [28].

Several studies have described increased signal intensity on T1-weighted MR of intracranial metastases from malignant melanotic melanoma [29, 30], presumably related to the paramagnetic properties of free radicals in melanin [14, 29]. We are not aware of any reports in which melanin deposits have been identified by MR in the brain in conditions other than melanoma metastases. The documented association between intracranial melanin deposits and NF leads one to consider melanin as a possible contributor to the signal characteristics of these lesions on T1-weighted MR. Since melanoma metastases characterized by shortened T1 also usually show evidence of shortened T2 relaxation [14, 29, 30], the presence of small foci of increased signal on T2-weighted images would have to be accounted for by associated gliosis or additional tissue elements within the hamartomatous lesion.

The neuropathologic studies cited above provide a basis for suggesting the presence of either ectopic Schwann cells or melanocytes within hamartomatous malformations in patients with NF. Experience with MR has shown that either of these tissues is capable of contributing to shortening of T1 relaxation. Pathologic studies indicate that both Schwann

cells and melanocytes may occasionally be found together in NF. This association occurs, for example, in the form of melanocytic schwannomas [15, 21, 31], and some authors state that Schwann cells may actually be capable of producing melanin [21]. The lack of autopsy material in our patients clearly precludes any definitive statements regarding the nature of the lesion observed. These neuropathologic studies, however, support speculation that the basis for the increased signal on T1-weighted MR may relate to inclusion of Schwann cells or melanocytes or both within heterotopic or hamartomatous lesions of the basal ganglia.

The significance of cerebral heterotopias in NF patients is unknown. It has been suggested that such lesions may contribute to the high frequency of mental retardation, learning disabilities, and other related deficits, as well as possibly serving as a focus for seizures [11]. Others believe that such lesions are preneoplastic and the probable origin of the many types of tumors that afflict patients with this condition [22]. MR promises to contribute significantly to the understanding of this disease by providing a means of noninvasively monitoring the progression of such lesions over time. Follow-up imaging in our limited series revealed no evidence of lesion progression. However, longitudinal studies of larger numbers of NF patients will have to be performed to further assess lesion stability.

In summary, basal ganglia lesions characterized on MR by increased signal intensity on T1-weighted images, with smaller foci of hyperintensity of T2-weighted images, were observed in seven patients with NF. The signal characteristics of these lesions as well as neuropathologic information available suggest that such lesions represent heterotopias or hamartomas that contain Schwann cells or melanocytes or both. When lesions characterized by signal and morphologic characteristics similar to those described are encountered on MR, the diagnosis of NF should be considered.

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