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Transsynaptic Degeneration of Lateral Geniculate Bodies in Blind Children: In Vivo MR Demonstration

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PURPOSE: To investigate signal alterations in the thalamic lateral geniculate bodies of blind patients compatible with transsynaptic degeneration of these nuclei caused by pregeniculate or postgeniculate interruption of the visual pathway. METHODS: Six patients were selected from a group of blind children in our care. Four had cerebral palsy caused by periventricular leukomalacia, one had infantile neuroaxonal dystrophy, and one had Chiari I malformation and hydrocephalus, which was worsened by bilateral ischemic lesions of the occipital lobes. MR examinations (obtained at 0.5 T) were reviewed retrospectively by two neuroradiologists, with particular attention to the visual pathway. RESULTS: Symmetric, focal areas of T2 prolongation were found at the precise site of the lateral geniculate bodies. CONCLUSION: Anterograde (pregeniculate) and retrograde (postgeniculate) transsynaptic degeneration of the second neurons of the visual pathway produce alterations in MR signal.

Index terms: Neurons; Thalamus; Vision


Transsynaptic degeneration is the term used to describe the alteration of neurons caused by the loss of synaptic input when fibers afferent to them are damaged: atrophy slowly subsides, followed by neuronal cell loss and reactive gliosis (1). This process has been well documented in the visual pathway, wherein cells of the lateral geniculate bodies are known to degenerate after loss of an eye, and in lesions of the retina, optic nerve, and optic tract. It is also known that transsynaptic degeneration may occur in a retrograde fashion, in which lesions of the optic radiation or calcarine cortex cause degeneration of retinal ganglion cells across the lateral geniculate body (1–4).

Until the advent of magnetic resonance (MR) imaging, the lateral geniculate body was difficult to see radiologically, owing to its size and position (5). Recently, however, an MR study of the optic pathways in two blind children with periventricular leukomalacia has suggested that the finding of a symmetric signal hyperintensity in the lateral geniculate body may represent a secondary degeneration of the neural cell bodies (6).

In this study, we investigated the MR signal alterations in the lateral geniculate bodies of blind children with different diseases and with lesions at different locations in the visual pathway (ie, pregeniculate and postgeniculate).

Materials and Methods

We retrospectively reviewed the MR images of 20 blind children who had undergone neuroradiologic examination for associated clinical problems to search for possible involvement of lateral geniculate bodies. Six MR studies were selected in which two neuroradiologists independently verified the appearance of signal alteration at this site. The patients were four boys and two girls, ranging in age from 15 months to 6 years (mean age, 4 years). Underlying diseases included periventricular leukomalacia (four patients), Chiari I malformation (one patient), and neuroaxonal dystrophy (one patient).
MR imaging was done with a 0.5 T magnet. Sagittal 5-mm-thick spin-echo images were obtained with parameters of 520/20/2 (repetition time/echo time/excitations), axial and coronal 6-mm-thick spin-echo images were obtained at 2500/40–100/1, and coronal 5-mm-thick T1-dependent inversion-recovery images were obtained at 1500/30/2. None of the examinations required anesthesia; four patients were sedated.

According to the World Health Organization’s categories of sight, the diagnosis of blindness was made in cases of visual acuity of less than 0.05 (7). Visual acuity was determined by means of Teller’s Acuity Cards, a behavioral test based on a preferential looking technique, which is applicable even for young and uncooperative children (8–10).

All the patients received a complete ocular examination, after which they were divided into two groups, pregeniculate and postgeniculate, according to the location of the lesion. Criteria for inclusion in the pregeniculate (anterior visual pathway) group were ocular findings that explained the severe visual loss, such as marked optic nerve atrophy or an absent or sluggish light reflex. Inclusion criteria for the postgeniculate (posterior visual pathway) group were ophthalmologic findings that were normal or too mild to explain the visual loss; in these cases, the visual deficit was called cerebral visual impairment (10).

**Results**

In all the MR examinations considered, a focal, symmetric T2 prolongation in the precise location of the lateral geniculate bodies was detectable. No corresponding signal alteration was found on T1-dependent images. The focus of altered signal was always best seen on axial images, and it was sometimes not recognizable on coronal images.

**Periventricular Leukomalacia**

Four patients were born preterm, between 30 and 34 weeks’ gestation (mean, 32 weeks), with no clinical evidence of major complications, such as severe asphyxia, hypotension, cardiorespiratory arrest, or sepsis, and all had neuroradiologic signs consistent with the diagnosis of extensive periventricular leukomalacia according to criteria established by Flodmark (11). On MR studies, signal hyperintensity and reduction in the amount of peritrigonal white matter where optic radiations run were particularly evident. Cortical atrophy of the calcarine cortex was observed on all the examinations (Figs 1 and 2).

One patient (case 1) had bilateral optic nerve atrophy at the ocular examination. In another patient (case 3), blindness was due to a severe retinopathy of prematurity. The other two children had no ocular alteration sufficient to ex-
plain their blindness, and were considered to have cerebral visual impairment.

Hydrocephalus Associated with Chiari I Malformation

In one child, the MR examination showed a Chiari I malformation with an inferior displacement of the cerebellar tonsils to about 1.5 cm below the bottom of the foramen magnum. A bilateral infarction of the occipital lobes was found in the distribution territory of the posterior cerebral arteries (Fig 3). At the time of the examination, the patient had a ventriculoperitoneal shunt, but from birth until the age of 3 months his severe hydrocephalus was not shunted. MR findings in the optic nerves and optic chiasm were normal. Clinical examination revealed no significant ocular lesions.

Neuroaxonal Dystrophy

In one patient, MR imaging showed a severe cerebellar atrophy, particularly marked in the vermis, a prominent hyperintensity of the cerebellar cortex on T2-weighted MR images, and diminished cerebral matter with enlarged lateral ventricles. No occipital atrophy was found (Fig 4). Ocular examination revealed important alterations bilaterally, including very pale optic disks and loss of normal pigmentation of the retina.

Discussion

The lateral geniculate body is a caplike structure located in the posterior aspect of the thalamus above the lateral recess of the ambient cistern. It is the main thalamic visual center, linking the retina and the striate cortex. However, the function of lateral geniculate body cells is not only to relay their visual input but also to serve as a variable gate, determining what, when, and how much retinal information gets passed into the visual cortex. Owing to the size and vascularization of the lateral geniculate body, its lesions are rarely isolated. Their clinical correlate seems to be sectoranopia; that is, a homonymous, horizontally oriented, wedge-shaped visual defect (12). Lateral geniculate bodies are considered the classic site of transsynaptic degeneration. Pathologic examinations have shown retrograde degeneration of retinal ganglion cells after unilateral removal of the striate cortex and anterograde degeneration after enucleation of one eye, with marked neuronal loss in lateral geniculate body cells in both cases (4).

Neuroradiologic demonstration of the lateral geniculate body was difficult before the advent of MR imaging. In 1990, by a correlative anatomic approach with brain specimens obtained at autopsy, Horton et al (5) mapped the lateral geniculate bodies, defining the optimal imaging technique by which to observe their precise location (at the edge of the lateral recess of the ambient cistern) and MR signal intensity characteristics (they resemble gray matter most closely, although they contain both neurons and myelinated fibers). MR imaging evidence of an isolated lesion of the lateral geniculate body...
was an alteration in signal intensity seen after head trauma (13). Another MR study showed that lesions involving the lateral geniculate body can cause a wallerian degeneration of ipsilateral optic radiation, visible as an abnormal signal along its course (14).

It seemed interesting to us to determine whether the alterations induced by transsynaptic degeneration could be made visible by neuroimaging. It is well known that the severity of this phenomenon is inversely proportional to the age of the subject at the time of injury (4), so we thought it would be appropriate to search for this alteration in blind children with objectively demonstrated deficits in whom the level of the lesion was known with certainty.

In all six patients studied, a small, symmetric area of T2 prolongation was evident at the exact site of the lateral geniculate bodies. Since normal signal intensity of these structures is the same as gray matter, this finding was judged to be indicative of gliosis, as determined by pathologic studies.

Four of our six patients had spastic tetraplegia resulting from periventricular leukomalacia. Barkovich et al (15) effectively described thalamic alterations in children who had perinatal asphyxia. Nevertheless, we are inclined to think that in our patients the MR signal alterations found in the lateral geniculate bodies were attributable to a degeneration of their cells rather than to a direct thalamic involvement by asphyxia, since the clinical history of these children did not reflect serious complications, such as a profound hypotensive event of cardiocirculatory arrest. Furthermore, asphyxia generates lesions in the lateral portions of the thalami, not just in the location of the lateral geniculate bodies, and these lesions are also found in the medial and posterior portions of the lentiform nuclei, presumably because these regions at the moment of injury are in the same active stage of the process of myelination, with the same higher metabolic requirements, as other portions of the brain.

In two of the four children with periventricular leukomalacia, severe abnormalities of the retina, including pale optic disks and optic nerve atrophy, were revealed by ocular examination. The signal alteration in these cases was judged to be attributable to anterograde degeneration. In the other two children, no significant ocular lesions were found. It is well known that central visual impairment is common among patients with cerebral palsy associated with periventricular leukomalacia (10, 16). This disease characteristically affects the peritrigonal white matter, where the optic radiations run; in more severe cases, the amount of white matter is reduced sufficiently to cause atrophy of the calcarine region (17–19). A strong correlation between such MR alterations and visual impair-

Fig 4. Case 6: Blind patient with neuroaxonal dystrophy, pallor, and atrophy of both optic disks. 
A, Sagittal spin-echo T1-weighted (520/30) MR image shows marked cerebellar atrophy. 
B, Coronal spin-echo T2-weighted (2500/100) MR image shows abnormal hyperintensity (arrows) of the cerebellar cortex. 
C, Axial spin-echo T2-weighted (2500/100) MR image shows signal alteration of the lateral geniculate bodies (arrows).
ment in children with periventricular leukomalacia has been demonstrated (6). The MR signal alterations seen in the lateral geniculate bodies in our two children with no ocular lesions can be attributed, therefore, to retrograde transsynaptic degeneration.

In the patient with Chiari I malformation, the occipital lesions were the result of downward tentorial herniation of the parahippocampal gyri, with compression of the posterior cerebral arteries against the tentorial incisura during an episode of increased intracranial pressure caused by hydrocephalus (20, 21). The ischemic lesion of the occipital cortex provoked a retrograde degeneration of the second neurons of the visual pathways.

The MR findings in the child with the infantile form of neuroaxonal dystrophy were congruent with those previously described (22, 23); specifically, a hyperintensity of the cerebellar cortex associated with extensive astrogliosis and neuronal loss. A common finding in the late stage of neuroaxonal dystrophy is blindness resulting from optic atrophy, as was the case of the patient we observed. We therefore think that, in this patient, the alterations found at the level of the lateral geniculate bodies can be attributed to anterograde degeneration. Another explanation could be primary degeneration, such as was found in one study, in which pathologic specimens showed multiple necrotic foci and foam cells in the thalami (22). This hypothesis, however, appears less likely, because it is difficult to imagine how this type of degeneration could selectively affect only a portion of the thalamus, such as the lateral geniculate body.

In our study, the altered lateral geniculate bodies were best seen on axial scans; however, Horton et al (5) found that both axial and coronal sections provided good views. We think that these investigators achieved good coronal views because they scanned 20° from the standard coronal plane along the orbitomeatal line (orbitomeatal + 70°) with 3-mm-thick sections, which provide the clearest coronal images, while our retrospective study depended on examinations obtained with standard scan planes and 5-mm-thick sections, which are rather inadequate parameters for demonstrating anatomic structures of such small dimensions. We therefore believe that signal alterations of the lateral geniculate bodies could be shown in a greater percentage of blind children with the use of appropriate imaging parameters.

By means of MR imaging, it is possible to see not only the location and morphology of the lateral geniculate bodies but also to ascertain the presence of pathologic changes within them; in particular, the anterograde and retrograde degeneration of their cells. The accuracy and precision of MR imaging is beginning to reach the sensitivity level of anatomicopathologic examinations.

References