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MR Imaging of Wallerian Degeneration in the Brainstem: Temporal Relationships

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Degeneration of the myelin sheath and axon distal to the most proximal site of axonal interruption secondary to axonal disease has been called wallerian degeneration. On MR imaging, wallerian degeneration of the pyramidal tract can be observed as an abnormal signal intensity, showing prolonged T1 and T2 relaxation times that correspond to the corticospinal tract, with or without shrinkage of the ipsilateral cerebral peduncle and pons. Review of MR studies in 150 cases of supratentorial cerebrovascular accidents showed abnormal signal alterations in the ipsilateral brainstem in 33 of the cases. Abnormal intensity in the ipsilateral brainstem was seen as early as 5 weeks after the supratentorial ictus and was fully evident after 10 weeks in all 33 cases. Signal alterations were strongest at about 3–6 months when compared with alterations seen at 10 weeks or even 10 months after the ictus. Shrinkage of the ipsilateral brainstem appeared as early as 8 months and was demonstrated in all cases 13 months after the ictus.

MR seems to be the most effective technique for early detection of wallerian degeneration and may provide insight into its pathophysiological and chemical changes.

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Wallerian degeneration is the process of disintegration that affects an axon and its myelin sheath after its connection with the cell body has been interrupted [1]. The degeneration is progressive, occurring over a period of weeks to months, with the end result being atrophy along the neural pathway. Stovring and Fernando [2] demonstrated the end stage of wallerian degeneration by CT as an ipsilateral atrophy of the midbrain in patients with large cortical infarcts. Jolez et al. [3] demonstrated a marked prolongation of both T1 and T2 relaxation times in the degenerated sciatic nerves in rats by MR spectroscopy, and suggested that wallerian degeneration could be detected also by MR imaging.

Prolonged T1 and T2 lesions in the ipsilateral brainstem were described as wallerian degeneration by Cobb et al. [4]. The purposes of this study are to (1) describe these signal alterations of wallerian degeneration in the brainstem, (2) report the earliest time at which wallerian degeneration may be seen on MR images, and (3) describe the evolution of signal alterations and atrophic changes.

Materials and Methods

We selected MR images of patients with known cerebrovascular accidents (CVAs), hematomas, or infarctions. Between August 1985 and July 1986, 150 patients with supratentorial infarctions or intracerebral hematomas were studied by MR and CT. Patients in whom neurologic abnormalities suggested a lesion in the brainstem were excluded. Wallerian degeneration was diagnosed when a small prolonged T1 and T2 lesion was seen in the area corresponding to the corticospinal tract in the ipsilateral brainstem on at least two contiguous slices. In a few patients, coronal images were obtained to confirm our findings.

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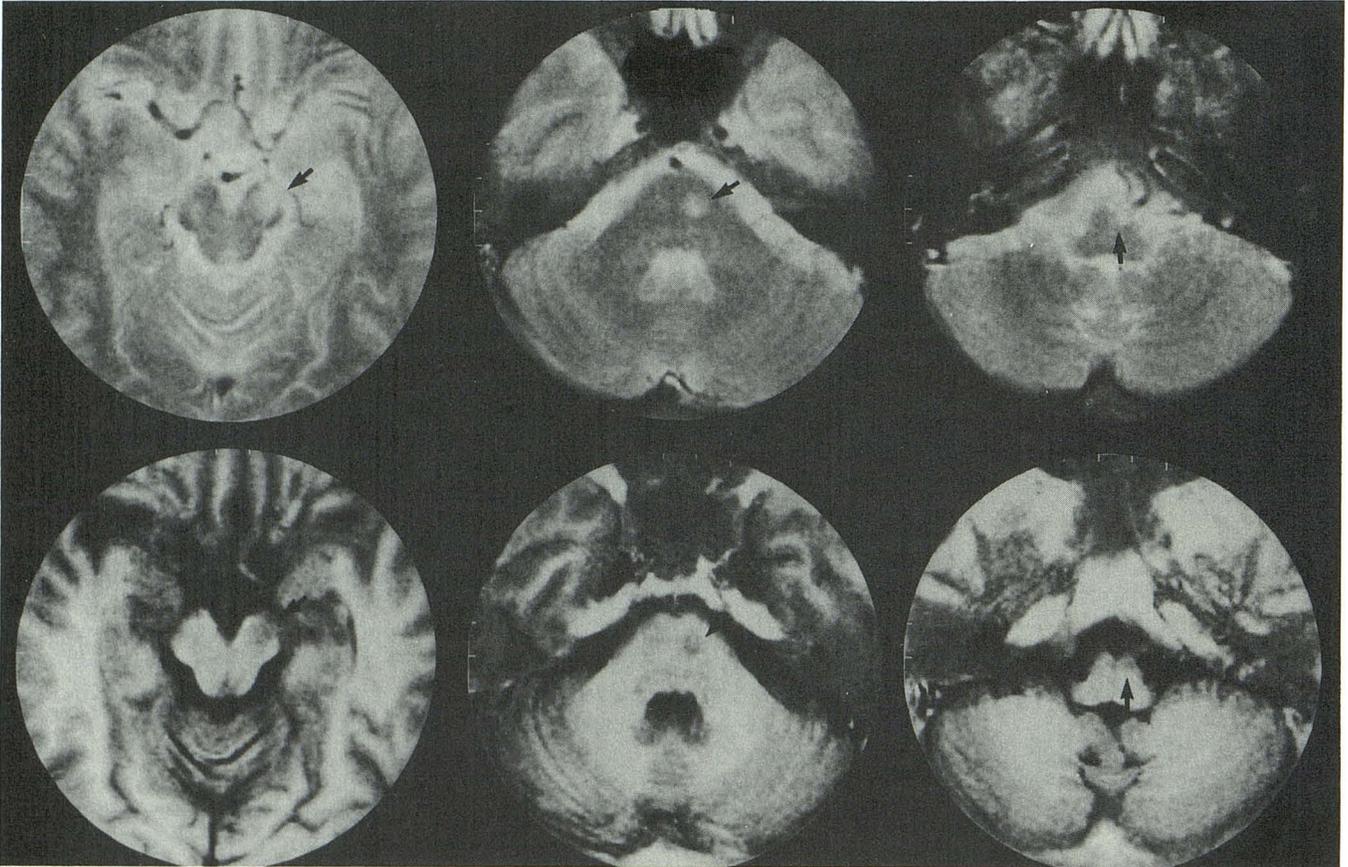
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A

Fig. 1.—Wallerian degeneration in a 49-year-old man with left putaminal hemorrhage. A, CT image on day of ictus shows large left putaminal hematoma extending into posterior limb of internal capsule. B, MR study 19 weeks after ictus. On T2-weighted images, 2000/120 (top), wallerian degeneration is shown as increased intensity (arrows) in left cerebral peduncle, pons, and medulla. On T1-weighted IR images, 2500/500/30 (top), wallerian degeneration is shown as decreased intensity (arrows).



B

Thirty-three patients fulfilled the criteria and are the subject of this report. Twenty patients had intracerebral hematomas and 13 had infarctions. The average age of the patients was 65 years (range, 43–75 years) in the hematoma group and 54 years (range, 45–78 years) in the infarct group. We evaluated the MR studies to determine when prolonged T1 and T2 lesions would appear in the ipsilateral brainstem and when atrophic changes of the ipsilateral brainstem developed after the ictus.

MR studies were obtained with a 0.5-T unit (Picker International, Cleveland, OH). The routine MR study consisted of axial spin-echo (SE) 2000/120 (TR/TE) T2-weighted images with a 10-mm slice thickness and axial inversion-recovery (IR) 2500/500/30 (TR/TI/TE) T1-weighted images with the same slice thickness at the same levels. Twelve contiguous axial images covered the area from the top of the brain to the lower portion of the medulla. Coronal images were obtained occasionally to observe the degenerated nerve tract with

the same pulse sequences. All T2-weighted images were obtained with the motion artifact suppression technique [5].

Results

Whenever wallerian degeneration was demonstrated as signal alterations on MR, there was a lesion in the motor cortex or its subcortical white matter, the corona radiata, the corticospinal tract, or the posterior limb of the internal capsule. In none of the cases without wallerian degeneration was there a primary lesion either in the motor cortex or pyramidal tract. Wallerian degeneration showed high signal on T2-weighted images and low signal on T1-weighted IR images and had a somewhat poorly defined margin in the corticospinal tract of the brainstem (Fig. 1). Coronal imaging, which was not a part of our study protocol, was very helpful in confirming the contiguous nature of the signal abnormalities observed on axial images. Although there were some exceptions, lesions were somewhat larger in the pons compared with those in the cerebral peduncle or in the medulla, probably because of transverse pontine fibers crossing the corticospinal tract.

The relationship of signal alterations in the brainstem to the time after the onset of CVAs is shown in Figure 2. Signal alterations were detected as early as 5 weeks in one patient and were observed in all the patients studied from 10 weeks up to 20 years after a CVA. Atrophy of the ipsilateral cerebral peduncle and the ipsilateral pons was noted as early as 8 months and seen in all patients studied after 13 months. (Fig. 3). In two patients not included in this report, and therefore not plotted in Figure 2, atrophy of the ipsilateral cerebral peduncle and pons was seen but no signal alterations. Both cases were studied by MR approximately 2 years after the ictus. In nine patients, serial MR studies were performed; in five of these, signal alterations were strongest at about 3–6

months when compared with those at 10 weeks or 10 months after the ictus. In two cases in which signal alterations were positive on MR 13 weeks and 10 months after the ictus, earlier MR studies had been performed 3, 6, and 7 weeks after the ictus. Neither signal alterations nor atrophic changes were demonstrated (Fig. 4).

Discussion

According to Rossiter [6], wallerian degeneration can be divided into three stages for the purpose of convenience. The first stage is characterized by the physical disintegration of the axon and the myelin sheath, with little chemical change. Axons show varicosities and a beaded appearance, followed by breakdown into shorter oval and spherical fragments [6, 7]. The myelin sheath swells and breaks at the constrictions and forms a series of ellipsoids enclosing fragments of axons. Breakdown of the myelin into lipids occurs at the same time. The process is slow, much slower than in peripheral nerves, and it is unusual to find positive Marchi material (lipids secondary to degradation of the myelin sheath) by the 20th day [8]. The second stage is characterized by the rapid destruction of the myelin fragments produced during the first stage. In humans, by 3 months, most of the myelin has broken down into simple lipids and neutral fats with some in the process of being removed by phagocytosis [7]. In the third stage, the myelin sheath has almost disappeared, and gliosis and Schwann cells, which form the Schwann bands, occupy the space left by the degenerated axon and myelin sheath [6, 7]. The disappearance of the large corticospinal tract, the end stage of wallerian degeneration, will produce atrophy of the brainstem, which can be detected by CT [2].

No definite time period has been allocated to these stages, since there is a considerable degree of overlap between stages among fibers in the same nerve. In addition, the speed of wallerian degeneration depends on the species, the age of the animals, the fiber diameter, and a number of other factors [6]. It is well known that degenerative change is slower in fine fibers than in large fibers, and that the process of wallerian degeneration is slower in the CNS than in peripheral nerve [7].

Our study demonstrates that wallerian degeneration of the corticospinal tract in the brainstem can be depicted as a prolonged T1 and T2 area in patients with supratentorial CVAs, which must involve either the motor cortex, its subcortical white matter, the corona radiata, or the posterior limb of the internal capsule. Our study also shows that this can be visualized as early as 5 weeks after the ictus and in most cases is seen consistently 10 weeks after the ictus. These signal changes are most likely due to the increase in extracellular water content produced during the process of nerve degeneration. In fact, Jolez et al. [3] measured water content in the degenerated axons and found that the average water content in the degenerated nerves was more than 25% higher than that in the nontransected contralateral sciatic nerve. Persistent signal alterations in wallerian degeneration more than a year to a decade old cannot be explained by the increased extracellular fluid, since the chemical change ends

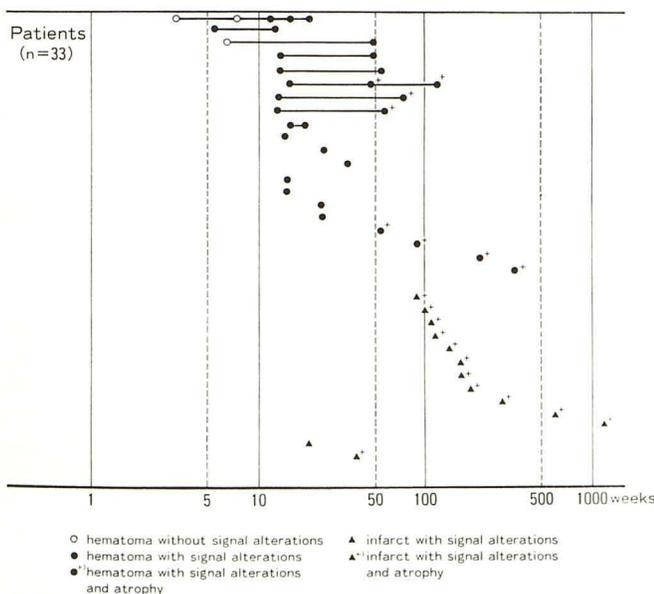


Fig. 2.—Intervals between ictus of cerebrovascular accidents and MR detection of wallerian degeneration in ipsilateral brainstem.

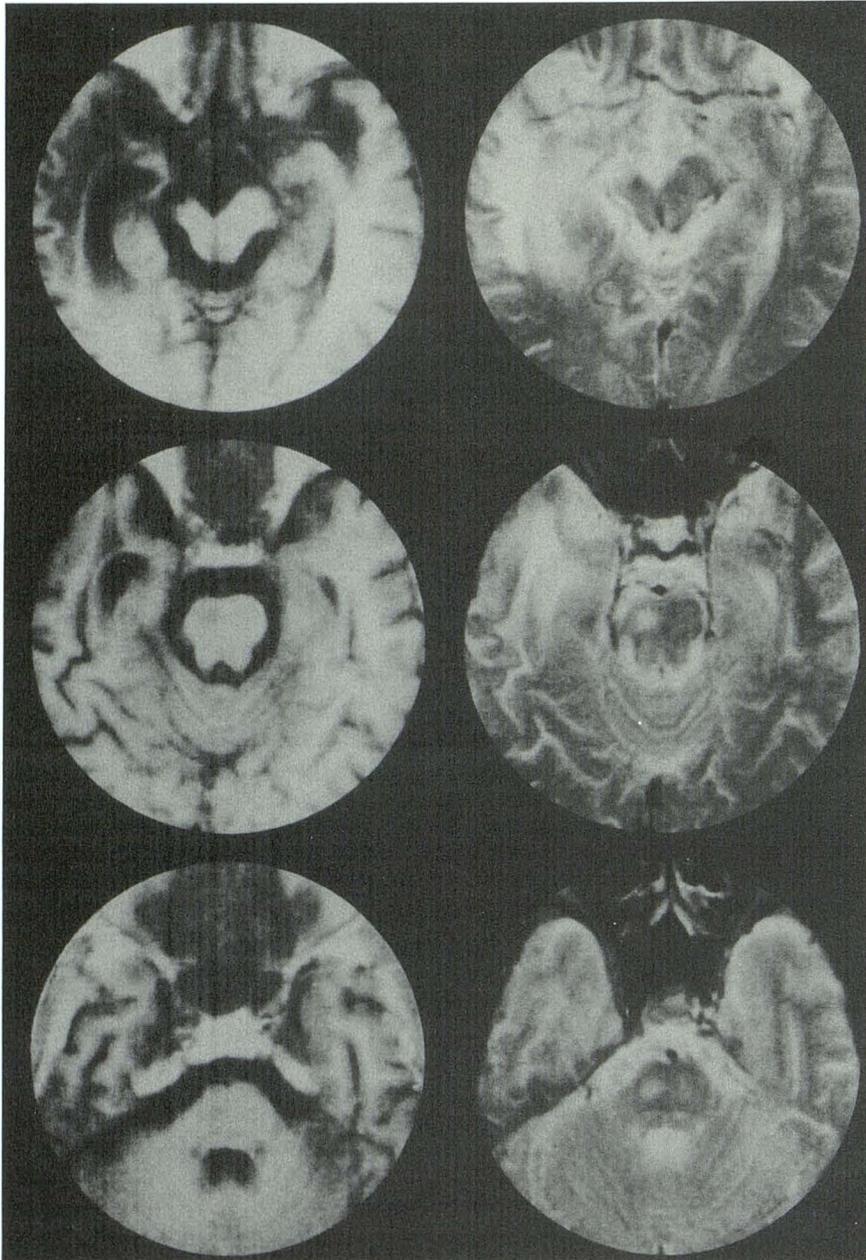


Fig. 3.—Wallerian degeneration (signal alteration with atrophic change) in a 65-year-old man with 2-year-old infarction in territory of right middle cerebral artery. IR 2500/500/30 (left) and SE 2000/120 (right) MR images show signal alteration as well as atrophy in right cerebral peduncle and pons.

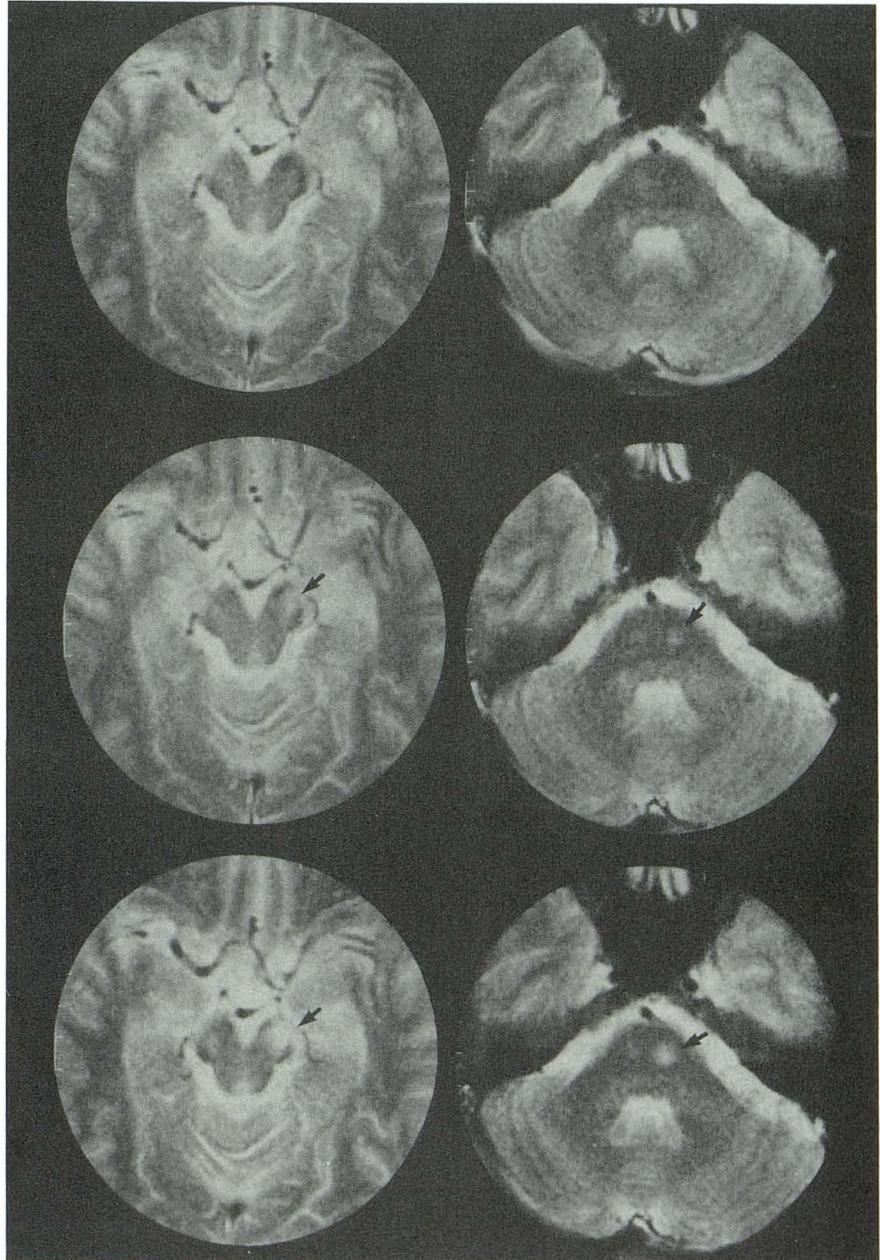
10–12 months after ictus. Therefore, they seem to be due to the gliosis and Schwann bands, the endstage of histologic change of wallerian degeneration.

Our study suggests that MR imaging may be able to define the time periods for each stage of wallerian degeneration in the adult human CNS. The first stage seems to comprise the first 10 weeks, when MR shows no signal alteration. The second stage comprises the period from 10 weeks to 12 months after the ictus. In this period, there is an increase in extracellular water content, which produces T1 and T2 prolongations, and wallerian degeneration is observed as the signal alterations on MR. The third stage may start about a year after the ictus, and is characterized by volume loss and

gliosis. In this period, MR shows ipsilateral brainstem atrophy and signal alterations. We assume that ipsilateral brainstem atrophy alone can be present without signal alteration because this was seen in two of the original 150 patients evaluated for this report. Although we do not know the reason why signal changes were not seen in some cases, there may have been minute signal changes that were not detected by the MR unit used.

Kuhn et al. [9] described MR of wallerian degeneration in 23 patients with varied pathology, including infarcts, hematomas, and neoplasms, and reported that signal change in the brainstem was seen as early as 3 months after the onset of symptoms. Our study agrees with their results. Recently,

Fig. 4.—Serial T2-weighted MR images (2000/120) of wallerian degeneration 7 (top), 11 (middle), and 19 (bottom) weeks after ictus (same patient as in Fig. 1). There is no signal alteration 7 weeks after ictus. A mild increased signal (arrows) is seen in cerebral peduncle and pons 11 weeks after ictus. A stronger signal (arrows) is observed 19 weeks after ictus.



Kuhn et al. [10] reported that wallerian degeneration was detected as early as 4 weeks after cerebral infarction; it was seen as a hypointense band in the corticospinal tract on T2-weighted images using a 1.5-T unit. In our study, this hypointense band was not observed. Such hypointense T2 signal abnormality is to be expected during the first stage of wallerian degeneration, since the myelin lipid structures remain intact while the relative water content is diminished. The reasons that such hypointense signal abnormality was not demonstrated in our study are most likely because of the lower field strength of our magnet (0.5 vs 1.5 T) and a canceling effect caused by the greater T2 weighting of our scans.

Prolonged T1 and T2 lesions in the brainstem are not specific to wallerian degeneration, and can be seen in infarcts, neoplasms, and focal demyelinating diseases such as multiple sclerosis. Wallerian degeneration shows mild to moderate T1 and T2 changes; that is, relatively high signal on T2-weighted images and relatively low signal on T1-weighted IR images. Prolonged T1 and T2 changes in the old brainstem infarct or in multiple sclerosis are usually of profound intensity, there being higher signal than that of wallerian degeneration on the T2-weighted image and lower signal on the T1-weighted IR image. Neoplasms may show a similar degree of prolongation of T1 and T2, and, if they are located in the corticospinal tract, it might be difficult to differentiate them from wallerian

degeneration. However, neoplasms will usually show some degree of mass effect, instead of atrophy.

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