White Matter Changes in Elderly People: MR-pathologic Correlations

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(Received April 17, 2006; Accepted May 17, 2006)

Magnetic resonance (MR) imaging features of white matter lesions, often seen in the elderly, are correlated with histologic findings. Dilatation of perivascular spaces is seen, especially in the frontal and/or parietal subcortical white matter; the spaces are less than 3 mm in diameter and have sharp margins with no perifocal abnormality. Old lacunar infarcts are larger than 3 mm in diameter and are irregularly shaped and accompanied by perifocal myelin pallor and gliosis. Periventricular hyperintensity, including cap and rim, histologically shows myelin pallor, dilatation of perivascular spaces, discontinuity of the ependymal lining, and subependymal gliosis. Deep and subcortical white matter hyperintensity reflects myelin pallor and dilatation of perivascular spaces. Diffuse white matter lesion, seen in Binswanger’s disease, shows myelin pallor and tissue rarefaction associated with loss of myelin and axons. U-fibers are usually well preserved. Severe arteriosclerosis and arteriolosclerosis are usually seen in the white matter. Knowledge of the pathologic features of incidental changes in white matter helps in understanding MR imaging findings.

Keywords: white matter, leukoaraiosis, magnetic resonance imaging, pathology, MR-pathologic correlation

Introduction

To further understand the MR imaging features of cerebral white matter lesions in the elderly, we correlated postmortem MR images and pathologic findings of dilatation of perivascular spaces, lacunar infarcts, and leukoaraiosis, which is closely associated with chronic ischemic change. In this review, leukoaraiosis includes periventricular hyperintensities, deep and subcortical white matter hyperintensities, and the diffuse white matter changes seen in Binswanger’s disease.

Postmortem MR images were obtained using a 1.5T system. The 10% formalin-fixed brains were positioned in a standard way in the head coil, and axial and coronal fast spin-echo T2-weighted images (repetition time/echo time [TR/TE], 3500/96; thickness/gap, 4/1) were obtained. Coronal sections of the cerebral hemispheres were cut 5 mm thick. The images were compared to histologic findings.

Dilatation of Perivascular Spaces

Dilatation of perivascular spaces in the cerebral white matter are often seen in the frontal and/or parietal subcortical white matter, especially in the branching zones of medullary arteries. MR findings of dilatation of perivascular spaces shows T2-hyperintense areas of smooth and well-defined round or elliptical shapes up to 3 mm in diameter without halo in the surrounding tissue, being located along the medullary arteries.1

Dilatation of perivascular spaces is clinically associated with aging, hypertension, and other vascular risk factors.2 Several mechanisms for abnormal dilatation of perivascular spaces include mechanical trauma from pulsation of the cerebrospinal fluid (CSF) or vascular ectasia, fluid exudation from abnormalities in vessel wall permeability, and ischemic injury to perivascular tissue.3
Fig. 1. Dilatation of perivascular spaces. (a) Postmortem coronal T2-weighted image shows linear hyperintensities (arrows) in the right parietal white matter. Ill-defined and irregularly margined hyperintensity, showing an old lacunar infarct, is also seen (arrowhead). (b) Myelin-stained section corresponding to (a) shows dilatation of perivascular space of medullary arteries, which is more conspicuous than linear hyperintensities on the MR image. (c) Boxed area in (b) shows tortuous medullary artery in the dilated perivascular space. Note the arterial branches (arrows) ramifying at the arterial branching zone.

Figure 1 shows MR-pathologic correlations of dilatation of perivascular spaces. Linear T2 hyperintensities in the cerebral white matter show dilatation of the perivascular spaces of the medullary arteries. Faint diffuse hyperintensities surrounding linear hyperintensities in the cerebral white matter show not only myelin pallor, but also dilatation of perivascular spaces. The arterial branches ramify at the arterial branching zone.

Lacunar Infarcts

Fisher defined lacunar infarcts according to pathological observations as deep, sharply margined, focal lesions ranging from 3 to 4 mm to 15 to 20 mm in diameter.4,5 On MR imaging, lacunar infarcts and CSF have approximately the same intensity. They are irregular in shape and accompanied by perifocal signal changes.1

Lacunar infarcts show different histologic findings according to their pathologic stages. Necrotic debris and foamy macrophages are seen in recent infarcts and diminish with the age of the lesion. The surrounding tissue of the recent infarcts shows reactive gliosis, which becomes fibrillary with the age of the lesion. Old lacunae show an irregular cavity with dense fibrillary gliosis.4,5

Figure 2 presents MR-pathologic correlations of an old lacunar infarct. The old infarct is ill-defined and irregularly margined central hyperintensity surrounded by halo-like hyperintensity in the deep cerebral white matter. Histologically, the central hyperintensity represents a cystic cavity with ill-defined and irregular margin, and the surrounding halo-like hyperintensity represents mild loss of myelin and axons with mild gliosis. Therefore, T2 hyperintensities seen in lacunar infarct reflect CSF-like fluid within the cavity as well as within the enlarged extracellular spaces in the surrounding tissue caused by loss of myelin and axons.

Dilated perivascular spaces and lacunar infarcts are differentiated as follows. Dilatation of perivascular spaces are less than 3 mm in diameter with sharp margins and without perifocal signal changes. Lacunar infarcts are larger than 3 mm in diameter, irregularly shaped, and accompanied by perifocal signal changes.
Fig. 2. An old lacunar infarct. (a) Magnified postmortem coronal T₂-weighted image shows ill-defined and irregularly margined hyperintensity with halo-like hyperintensity in the deep cerebral white matter. (b-d) Myelin-stained (b), axon-stained (c) and glial fibrillary acidic protein (GFAP) immunostained (d) sections corresponding to (a). (e-h) High-power magnified boxed areas in (a-d). The center of hyperintense area (a, e) shows cystic cavity (b-d, f-h), and peripheral ill-defined and irregularly margined hyperintensity area (arrows in e) shows severe loss of myelin and axons (b, c, arrows in f and g) with moderate gliosis (d, arrows in h), and the surrounding halo-like hyperintense area (a, e) shows mild loss of myelin and axons (b, c, f, g) with mild gliosis (d, h).
Periventricular Hyperintensities

Periventricular T2 hyperintensities are often seen in elderly subjects who have no clinical symptoms. Kertesz’s group separated periventricular hyperintensities into rims and caps. Rims are periventricular hyperintensities surrounding the lateral ventricles, and caps are those surrounding the poles of the lateral ventricles.6

The pathologic findings associated with these hyperintensities include myelin pallor, dilatation of perivascular spaces, and increased extracellular spaces. Discontinuity of the ependymal lining and subependymal gliosis are also seen in the lateral ventricular wall. These subependymal lesions can be found at any age; therefore, mild rims are probably not pathological.7–9

Figure 3 presents MR-pathologic correlations of rim. Rim histologically shows myelin pallor, mild tissue rarefaction, and focal loss of ependymal lining with subependymal gliosis. Dilatation of medullary veins is also seen. These white matter changes, which are also seen in caps, may be associated with increased interstitial fluid caused by ischemic vascular damage or impairment of transportation of interstitial fluid into the ventricle.6,10
Deep and Subcortical White Matter Hyperintensity

Punctuate and/or confluent hyperintense areas are frequently seen in the deep and subcortical white matter on T2-weighted images. They are called hyperintense white matter foci, deep white matter hyperintensity, deep white matter infarction, or unidentified bright objects (UBO). They are observed in elderly people, particularly those with vascular risk factors. Although the pathogenesis of these changes is not completely elucidated, they are generally considered to be produced by chronic ischemia or by brief and repeated ischemic insults of moderate severity occurring in the subcortical white matter.

Histologically, these hyperintensities reflect myelin pallor and dilatation of perivascular spaces. Small lacunar infarcts occasionally coexist with these histologic changes.

Figure 4 shows MR-pathologic correlations of deep and subcortical white matter hyperintensities. Scattered patchy and confluent hyperintense areas in the cerebral white matter show myelin pallor and dilatation of perivascular spaces of the medullary arteries.

Binswanger’s Disease

Binswanger’s disease most often affects hypertensive and elderly subjects. Clinical features include dementia, gait disturbance, and urinary incontinence. Pathological and imaging features of Binswanger’s disease are diffuse cerebral white matter changes. Multiple lacunar infarcts are often seen in the basal ganglia and cerebral white matter.

White matter lesions are not equally distributed over the cerebral white matter. They are most frequent in the frontal lobe, followed by the parietal, occipital, and temporal lobes. The temporal lobe is relatively spared. U-fibers are usually well preserved despite diffuse changes in white matter. Histologically, white matter lesion shows myelin pallor, mild gliosis, and tissue rarefaction associated with loss of myelin and axons. Severe arteriosclerosis and arteriolosclerosis are usually seen in the white matter.

Figure 5 presents MR-pathologic correlations of white matter lesions of Binswanger’s disease. Diffuse hyperintensities in the cerebral white matter show moderate tissue rarefaction associated with loss of myelin, axons, and oligodendrocytes, and mild gliosis. U-fibers are spared. Arteriolosclerosis is also seen. Stenosis or occlusion of arterioles may...
cause lacunar infarct or incomplete infarct of the white matter. In addition, these small vessel alterations could induce loss of autoregulation and blood-brain barrier disruption, causing chronic leakage of plasma into the white matter resulting in brain edema, which might be a further cause of white matter damage.  

Conclusion

White matter changes often seen in elderly people are closely associated with chronic ischemic change, dilatation of perivascular spaces, and lacunar infarcts. It is important to distinguish infarcts from dilatation of perivascular spaces and/or leukoaraiosis. Knowledge of the pathologic features and characteristic location of these changes in white matter helps evaluation of MR imaging findings.

References