Visual T2 Hyperintensity Of Medial Lemniscus Predicts Presence Of Small Vessel Disease

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Purpose

Small Vessel Disease (SVD) is a common finding on routine brain MRI studies. SVD is usually seen in the older population and can be associated with cardiovascular risk factors. White matter and periventricular T2-hyperintensities along with lacunae are typical imaging manifestations of this entity. Despite ubiquitous nature of these findings on neuroradiologic studies, there is no specific imaging pattern of brain involvement in SVD. It may be difficult therefore to differentiate SVD from conditions such as multiple sclerosis (MS), particularly if there is a high prevalence of MS in the population being examined. Similar challenge can be in effect for differentiating SVD from non-specific white matter T2-hyperintensities (WMH), especially in the elderly.

We have been observing symmetrically positioned bilateral hyperintensities on T2 and FLAIR images in the dorsal pons. Location and distribution of these T2-hyperintensities of pontine tegmentum correspond to expected course of medial lemniscus (ML). Even though, there are a large number of patients with multiple sclerosis and non-specific white matter signal changes in our cohort, we have seen T2-hyperintensity of ML (MLH) only in patients with SVD. (Figure 1)

The purpose of our study was to investigate the frequency and association of MLH seen on brain MRI studies in an outpatient setting. We have hypothesized that we can reliably separate SVD from other causes of white matter disease with visual analysis of MLH in the pontine tegmentum.

Images for this section:
Fig. 1: Axial FLAIR image at the level of the pons reveals bilateral Medial Lemniscus Hyperintensity (white arrows).
Methods and Materials

An institutional review board (IRB) approval was obtained prior to this investigation. Informed consent requirement was waived by IRB for this retrospective study. A total of 180 consecutive patients who had MRI of the brain as an outpatient in the data base from 01/01/2008 to 1/14/2008 were included. The patients had presented with nonspecific signs such as headaches. None of the patients were wheelchair-bound. No speech, communication or ambulation difficulty was noted by the technologists for any of the patients. None of our patients reported use of illegal drugs.

The exclusion criteria were (number of patients): acute infarcts(2), old focal or cortical based infarcts(7), known history of malignancy(10), posterior fossa tumor(6), prior cranial surgery(7), prior cranial radiation(6), history of chemotherapy(9), prior trauma requiring emergency room visit(6), and history of HIV (0). Additional exclusions were incomplete imaging protocol(14), artifacts in the images severely hindering the diagnostic interpretation(10). A total of 77(43%)of the 180 patients were excluded prior to imaging review. Final sample size of the study group was 103 (57%).

Patients' medical records were reviewed for prior diagnosis, treatment and duration of MS. The cardiovascular risk factors including hypertension, diabetes, prior history of unstable angina or heart attack, prior diagnosis or treatment of cerebrovascular accident were also recorded.

All patients were imaged by using 1.5 Tesla General Electric Signa, H.Dx twin speed, MRI scanners (G.E. Medical Systems, Waukesha, Wisconsin, USA). MRI protocol for participation in this study required T1-weighted sagittal (TR/TE: 500-600/10-16 msec), T2-weighted (TR/TE: 3000-3400/100-120 msec), FLAIR (TR/TE/ TI: 8000-8100/100-130/2000 msec), diffusion weighted (TR/TE: 8000/65-75 msec), post-contrast T1-weighted (TR/TE: /650-750/8-12 msec), and gradient echo (TR/TE/flip angle: 650-750/10-15/20 msec) axial images of brain. Axial images were acquired parallel to the hard palate.

Two board certified Neuroradiologists reviewed the MRI scans of each patient separately and were blinded to patient information, risk factors and original interpretation. The readers were asked to review T2-weighted, FLAIR, DWI/ADC, post-contrast T1-weighted images of posterior fossa. Each reader specifically evaluated the images of the posterior fossa for hyperintense T2 signal of ML. Hyperintense signal of ML was easier to appreciate on FLAIR than on T2-weighted images. The readers were asked to visually identify abnormal hyperintense signal of ML on FLAIR images noting the presence or absence of increased signal in the region of ML compared to the surrounding brainstem.
ML hyperintensity on FLAIR with excellent contrast to noise ratio provided an easily identifiable finding. In the presence of increased signal, additional note was made if the abnormality was unilateral or bilateral.

Finally, based on T2 and FLAIR images, a third neuroradiologist further subdivided patients with SVD into three subgroups. To make the subdivisions, Periventricular Hyperintensity (PVH) was measured in the thickest part along the lateral edge of the lateral ventricle. Lacunar infarcts of posterior fossa, white matter and basal ganglia were counted. In order to consider an abnormality as a lacunar infarct, it was required to be hypointense on T1 and hyperintense on FLAIR images and less than 1.5 cm in size. The severity levels were (1) Mild SVD: PVH equal or less than 5 mm and no lacuna; (2) Moderate SVD: PVH more than 5 and less than 10 mm and/or 1 or 2 lacunae; (3) Severe SVD: PVH equal or exceeding 10 mm and/or 3 or more lacunae.

Results

Patient's demographic data is shown in Table 1, SVD patients were significantly older than MS and Nonspecific groups (p<0.001). There was no statistical difference in age between the MS and Nonspecific groups. There was female preponderance in our study group. There were no male patients in MS group (Table 2).

The results of visual analysis by two readers revealed excellent correlation (kappa=0.918). Reader J detected 6 patients with bilateral MLH. Reader S detected 2 patients with unilateral MLH and 5 patients with bilateral MLH. All patients with visual MLH noted by both readers belonged exclusively to SVD group. There were no patients with visual MLH in MS or the nonspecific group (Table 3).

The age and cardiovascular risk factors between those with and without visual MLH were compared. Those with MLH were older (85-year vs. 56 years; p<0.001), had higher prevalence of diabetes (38% vs. 7%; p=0.03), hypertension (75% vs. 27%; p=0.009) and hypercholesterolemia (50% vs. 15%; p=0.03).

To further assess the link between MLH and severity of SVD, we divided the SVD patients into three subgroups based on imaging findings. All patients with visual MLH detected by both readers were in moderate or severe groups of SVD.
**Table 1: Demographic Information of Patient Population**

<table>
<thead>
<tr>
<th></th>
<th>SVD (n=37)</th>
<th>MS (n=14)</th>
<th>NS-WMC (n=52)</th>
<th>All Patients (n=103)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-years, mean± sd (range)</td>
<td>76 ± 10a (45-95)</td>
<td>49± 7a,b (36-57)</td>
<td>48 ± 16a,b (17-82)</td>
<td>58 ± 19 (17-95)</td>
</tr>
<tr>
<td>Sex- female, n (%)</td>
<td>20 (55)</td>
<td>14 (100)</td>
<td>29 (56)</td>
<td>63 (61)</td>
</tr>
</tbody>
</table>

*SVD* = Small Vessel Disease  
*MS* = Multiple Sclerosis  
*NS-WMC* = Non-Specific White Matter Change  
*a* = Group different with significance p<0.001  
*b* = Groups statistically not different

**Table 2: Contingency table of sex by subgroups**

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Male (Count, %)</th>
<th>Female (Count, %)</th>
<th>Total (Count, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVD</td>
<td>17 (45)</td>
<td>20 (55)</td>
<td>37 (100)</td>
</tr>
<tr>
<td>MS</td>
<td>0 (0)</td>
<td>14 (100)</td>
<td>14 (100)</td>
</tr>
<tr>
<td>Nonspecific</td>
<td>23 (44)</td>
<td>29 (56)</td>
<td>52 (100)</td>
</tr>
<tr>
<td>Total Count</td>
<td>40 (39)</td>
<td>63 (61)</td>
<td>103 (100)</td>
</tr>
</tbody>
</table>

**Table 1: Contingency table of sex by subgroups**
Table 3: Detailed analysis of FLAIR findings of visually detected T2H in ML

<table>
<thead>
<tr>
<th>FLAIR Findings with ML T2H</th>
<th># Patients Identified by Reader J</th>
<th># Patients Identified by Reader S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral SVD</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Bilateral SVD</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>MS</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Normal</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total Count</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>
Conclusion

WMH are common findings on T2-weighted and FLAIR images of the brain. Differential diagnostic possibilities for WMH are broad and may include SVD related to aging or cardiovascular risk factors, as well as many other possibilities. Although the most common conditions causing white matter changes are SVD, MS and nonspecific changes, differentiating among them can sometimes be problematic even after careful consideration of demographic and clinical findings. Based on our results, we propose that MLH identified on T2-weighted or FLAIR images are a reliable imaging finding to identify a subset of patients with SVD. We did not observe this finding in any patients with MS or those who had normal appearing brain MRI or had subtle nonspecific WMH. Furthermore, within the SVD patients, visually detected MLH were only observed in those who were older and had diabetes, hypertension, or hypercholesterolemia. SVD patients with MLH had also more evidence of chronic ischemic parenchymal changes on imaging studies.

Recognizing SVD accurately and differentiating it from other causes of WMH is imperative in neuroimaging studies since SVD is not a benign entity. It is a progressive disorder with parallel decline in cognitive function. Recurrent stroke risk in patients with lacunar infarcts has been estimated to be similar to other types of recurrent stroke. SVD is present in a majority of vascular dementia cases, which may have a link to compromised cerebral blood flow. There may be an association between SVD and frontal lobe atrophy. Despite a vast amount of interest and research, pathogenesis of SVD remains poorly understood. In addition to well-known associations with cardiovascular risk factors, type I diabetes mellitus has been suggested as a possible cause of stroke in young patients with SVD. Familial forms of SVD as well as a possible genetic connection have been questioned in the pathogenesis. Underlying chemical inflammation facilitating atherosclerotic changes may play a role. Biochemical markers have been implicated. Likely because of this multifactorial background, SVD can be elusive clinically and radiologically early on. Risk factor modification and aggressive therapy remain the main goals of prevention.

It is also essential to correctly diagnose MLH and not to confuse it with possible demyelinating plaques involving median longitudinal fasciculus (MLF). For reliable analysis, we suggest that the readers should familiarize themselves with the anatomic landmarks of pontine tegmentum and tectum. On the floor of the fourth ventricle lies the pontine tectum which is divided by dorsal midline fissure (Figure 2). On each side of this fissure are tiny bumps protruding into the 4th ventricle. These are the facial colliculi at the level of the pontomedullary junction (Figure 3). MLF lies immediately ventral to these and ML is even further more ventrally located. Therefore, a distance of 5 to 8 mm from the 4th ventricular floor can safely separate MLH from abnormalities of MLF. Similar observations and measurements have been made during special staining of anatomic samples of adult brain. Additional typical feature of MLH in SVD is almost always bilateral.
involvement. On the other hand, MLF involvement in MS is usually unilateral involvement with characteristic ocular findings. Corresponding unilateral enhancement can be seen in acute presentations.

There have been previous reports of signal changes in ML. Unilateral ML related pathology has been reported in the setting of isolated ischemic or hemorrhagic insults of the brain stem. Bilateral MLH has also been described in association with acute presentation of vaporized heroin inhalation. However, the findings we described here, according to our knowledge, have not been reported in the setting of SVD. Bilateral MLH in SVD is characterized by intervening normal signal brain parenchyma with the resulting imaging appearance being quite characteristic (Figure 1). Additional features of MLH in our analysis are that they are not associated with diffusion restriction and there is no corresponding enhancement. These imaging characteristics of ML T2H are similar to ischemic gliotic changes seen as part of SVD in the brain. Therefore, they may share common pathophysiology of ischemic demyelination.

Our finding that MLH is seen exclusively in moderate to severe subgroups of SVD may have important clinical implications. MLH may not only confirm SVD in the presence of WMH but, it can also identify a subset of more advanced or aggressive forms of this disease. Previous studies have shown that patients with severe SVD are more likely to have cognitive and gait dysfunction and have difficulties in the activities of daily living.

Visual detection of MLH on FLAIR images is accurate and has high inter-rater reliability in predicting SVD and is a reliable radiologic marker to correctly diagnose a subset of SVD, especially if the finding is bilateral. Higher conspicuity of MLH on FLAIR compared to that of T2-weighted images may be reflective of underlying chronic pathology such as ischemic gliosis or demyelination. This feature of MLH is similar to involvement of other areas of brain with SVD.

Images for this section:
Fig. 1: Axial FLAIR image at the level of the pons reveals bilateral Medial Lemniscus Hyperintensity (white arrows).
**Fig. 2:** Axial T2-weighted image at the level of the pons. Imaginary midline connecting the posterior median sulcus to basilar artery groove.
Fig. 3: Axial T2-weighted image at the level of the pons. Black arrows indicate the bilateral facial colliculi.
Selected References:


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