Short Communication

Branch Atheromatous Disease (BAD) Versus Lipohyalinosis (LPH)-MRI Brain Imaging Helps to Classify and in Turn Prognosticate Patients with Lacunar Infarcts

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Abstract

Background: Lacunar strokes accounts for up to 25% of all ischemic strokes. 20 to 30% of patients with lacunar strokes show deterioration within hours to days after the acute event. However, factors that predict such deterioration are poorly understood. In this study we aimed at classifying lacunar infarcts as Branch Atheromatous Disease (BAD) and Lipohyalinosis (LPH) using MRI parameters, and then evaluated whether such classification had an impact on prognosticating patients with lacunar syndromes.

Methods: During a 1-year study period, patients with lacunar infarct admitted in a comprehensive stroke center in South India were identified. They were further classified as patients with lipohyalinosis (LPH) or branch atheromatous disease (BAD) based on MRI parameters. The clinical profile of these patients including NIHSS at presentation, comorbidities, modified Rankin scale (mRS) at presentation, at discharge and during follow up, duration of hospital stays and details of any clinical worsening were documented and analyzed. All statistical analysis was carried out using IBM SPSS statistics software.

Results: A total of 63 patients (Males- 42 Females- 21) with lacunar infarct were included in this study. Of these 29 were classified as patients with BAD and 34 had LPH. Worsening of neurological symptoms within 5 days of onset was more often seen in patients with BAD. mRS at presentation was comparable between the two groups, however mRS at discharge and during follow up was significantly better in LPH patients compared to BAD. Major arterial disease, as identified by an MR angiogram, was more often seen in patients with BAD. Hypertension was seen in both the groups; however diabetes was more commonly seen in patients with BAD. Recurrent cerebral ischemic events occurred more frequently in patients with BAD.

Conclusions: Categorizing small infarcts as lipohyalinosis (LPH) and branch atheromatous disease (BAD) could help us portend patients with lacunar strokes.

INTRODUCTION

Lacunar strokes accounts for up to 25% of all ischemic strokes, a proportion similar to cardioembolic stroke and infarcts due to large vessel atherosclerosis [1]. Lacunar infarct is brain infarction < 15 mm in diameter and is accompanied by lacunar syndrome, as defined by National Institute of Neurological Disorders and Stroke [2] and the Trial of Org 10172 in acute treatment of stroke (TOAST) study [3]. Some authors prefer to consider infarcts upto 20 mm as lacunar infarcts [4,5]. Clinically, lacunar strokes are best identified by their syndromes, which were first described by Fisher. The 5 classic lacunar syndromes include pure motor stroke, pure sensory stroke, ataxic hemiparesis, dysarthria/ clumsy hand syndrome and mixed sensorimotor syndrome. These lacunar strokes may occur suddenly or may evolve in a progressive manner [6]. 20 to 30% of patients with lacunar strokes show deterioration within hour’s todays after the acute event [5]. However, it is difficult to predict which patients with lacunar infarcts deteriorate. In this study we aimed at classifying lacunar infarcts as Branch Atheromatous Disease (BAD) and Lipohyalinosis LPH using MRI parameters, and then evaluated whether such classification had an impact on prognosticating patients with lacunar syndromes.

MATERIALS AND METHODS

This study was conducted in a comprehensive stroke center in South India. We analyzed the clinical and imaging findings of patients admitted with acute ischemic stroke, admitted between February 2017 and January 2018 to our comprehensive stroke
centre. A 3.0 tesla MRI (Ingenia Philips) with conventional MRI protocol including a complete set of DW images (motion probing gradients in three directions with a b factor of 1000/mm²), T1 (repetition time/echo time = 2000/9) and T2 (repetition time/echo time = 6000/94) -weighted images and fluid-attenuated inversion recovery images (repetition time/echo time = 8500/94) were obtained from the axial plane with a slice of 5mm. A non-contrast MR angiogram of intracranial and extra cranial arteries was also obtained. Lacunar infarcts were defined as infarcts up to 20 mm in diameter. Imaging findings were interpreted by consensus between an interventional radiologist and two experienced neurologists specializing in stroke.

During the study period, we identified 97 patients with lacunar infarcts (Figure 1). Of these, 16 presented in the window period and were thrombolysed and hence were excluded from the study. The remaining 81 patients with lacunar infarcts were further classified as patients with lipohyalinosis (LPH) or branch atheromatous disease (BAD) based on the MRI parameters as mentioned in Table 1 (Figures 2, 3) [6,7].

Patients were followed up to a period of 3 months. 18 patients were lost to follow up during the 3 months study period. Hence they were excluded from the study. The clinical profile of the remaining 63 patients and information on vascular risk factors were documented. Patients were considered to have a large vessel disease if MR angiogram revealed stenotic lesions in any one of the following arteries- Internal carotid arteries, Middle cerebral arteries, Anterior Cerebral arteries, Posterior cerebral arteries, or basilar artery. Worsening of stroke (defined as an increase in NIHSS by 4 points) within the first 5 days of admission was documented. Modified Rankin Scale (mRS) was used to assess the degree of disability in these patients. mRS was calculated at the time of admission, during discharge and after 3 months. mRS and NIHSS scoring was assessed by a certified neurologist. The collected data were analysed with IBM SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used. To find the significance in categorical data Chi-Square test was used, similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher’s Exact was used. In both the above statistical tools the probability value .05 is considered as significant level.

RESULTS

The patient’s clinical data is summarized in Table 2. The ages of the 63 patients ranged between 36 to 88 with an average of 65.34 and 61.17 in the BAD and LPH groups respectively. Males were more commonly affected than females in both the groups (BAD Males (n) - 19; LPH Males (n) - 23). Worsening of neurological symptoms within 5 days of onset was more often seen in patients with BAD (24.1% in bad versus 2.9% in LPH) (p<0.01) (Figure 4). Major arterial disease, was more often seen in patients with BAD (69%) (p <0.01) (Figure 5). mRS at presentation was comparable between the two groups, however mRS at discharge and after three months was significantly better in LPH patients compared to BAD (p <0.01). Hypertension was seen in both the groups (BAD- 89.7%; LPH- 97.1%); however diabetes was more
Table 1: MRI (Diffusion weighted sequence) based classification of lacunar infarcts [6,7].

<table>
<thead>
<tr>
<th>MRI Parameter</th>
<th>Lipohyalinosis (LPH)</th>
<th>Branch Atheromatous Disease (BAD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size of the lacunar infarct on Diffusion weighted imaging (Axial cuts)</td>
<td>≤ 15 mm in diameter</td>
<td>16 to 20 mm diameter</td>
</tr>
<tr>
<td>Shape of the infarct on Diffusion weighted imaging (Axial cuts)</td>
<td>Round or oval</td>
<td>Elongated or irregular</td>
</tr>
<tr>
<td>Observation of diffusion restriction (Axial cuts)</td>
<td>Diffusion restriction observed in ≤ 2 axial cuts 5 mm apart</td>
<td>Diffusion restriction observed in &gt; 2 axial cuts 5 mm apart</td>
</tr>
</tbody>
</table>

Figure 2 MRI Features of Lipohyalinosis (LPH)- Notice the infarcts are well circumscribed, less than 15 mm in diameter and exist in only two cuts on Diffusion weighted imaging.

Figure 3 MRI Features of Branch Atheromatous Disease (BAD)- Notice the infarcts are irregular, more than 15 mm in diameter and exist in more than two cuts on Diffusion weighted imaging.

commonly seen in patients with BAD (72.4%) (p < 0.01) (Figure 6). Recurrent cerebral ischemic events occurred more often in patients with BAD (41.4%) (p < 0.01) (Figure 7). The average duration of hospital stay was slightly more in patients with BAD (p < 0.05).

DISCUSSION

The phenomenology of lacunar infarction was first introduced by Miller Fisher in 1965 [8]. He observed that the penetrating arteries that supplied the territory of infarcts showed a characteristic vascular pathology. He called these pathological
Table 2: Characteristics of the patients in BAD and LPH groups.

<table>
<thead>
<tr>
<th>Patients Characteristics</th>
<th>BAD (n=29)</th>
<th>LPH (n=34)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male : Female ratio</td>
<td>1.89</td>
<td>2.08</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Age in years (average)</td>
<td>65.34</td>
<td>61.17</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Worsening of Neurological symptoms within 5 days of onset</td>
<td>24.1% (n=7)</td>
<td>2.9% (n=1)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Associated major arterial disease</td>
<td>69% (n=20)</td>
<td>5.9% (n=2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>89.7% (n=26)</td>
<td>97.1% (n=33)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Diabetes</td>
<td>72.4% (n=21)</td>
<td>17.6% (n=6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mRS at presentation (Average)</td>
<td>2.89</td>
<td>2.23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>mRS at Discharge (Average)</td>
<td>2.34</td>
<td>1.91</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>mRS at 3 months follow up (Average)</td>
<td>1.75</td>
<td>1.11</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Recurrent cerebral ischemic events</td>
<td>41.4% (n=12)</td>
<td>14.7% (n=5)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Average duration of hospital stay (number of days)</td>
<td>7.94</td>
<td>4.94</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Figure 4 Worsening of symptoms within the first 5 days of stroke onset.

Figure 5 Lacunar infarcts associated with major arterial disease.
processes segmental arterial disorganization, fibrinoid degeneration and lipohyalinosis. Caplan later classified these infarcts into 4 subgroups- (1) occlusion of penetrating arteries by lipohyalinosis (LPH); (2) occlusion of penetrating arteries by atherothrombosis of main artery (BAD); (3) hemodynamic mechanisms or artery to artery embolism; (4) cardiogenic embolism [9]. The latter two present more as scattered infarcts on imaging and hence easy to differentiate. Lacunar infarcts due to LPH and BAD can be differentiated by assessing imaging parameters. Previous studies have attempted to classify these two infarcts based on the MRI characteristics, which has in turn been incorporated in our study [6,7].

Our study indicates BAD patients are more likely to show early neurological deterioration when compared to patients with LPH. Previous studies have shown similar results [10]. This can be explained by the fact that BAD results in occlusion of the mouth of a branch. Hence, the resulting infarct tends to be larger and progresses over time.

In this study, MR Angiography revealed that BAD was more often associated with large vessel disease and these patients had an increased risk of recurrent cerebral ischemic events. This is reflective of the fact that BAD is not a localized disease of perforator branches, but rather a manifestation of atherostenosis of cerebral blood vessels. This has been shown in other studies as well! There is also literature evidence to suggest that BAD is reflective of widespread atherosclerotic disease and such patients are more likely to have coronary lesions as well [11].

mRS at the time of presentation was similar between the two groups. However, mRS at the time of discharge and on follow up was significantly better in patients with LPH. If the pathology of a widespread atherosclerotic disease is considered and the infarct size progressively increases and is noticeably larger, then it is only natural that BAD patients are likely to have more deficits than LPH and take more time to recover.

Though hypertension was equally present in both the groups, diabetes was more common in patients with BAD. The

Figure 6 Presence of diabetes or hypertension in patients with lacunar infarcts.

Figure 7 Incidence of recurrent cerebral ischemic events in patients with lacunar infarcts.
association of diabetes and atherosclerosis is well documented in literature as atherosclerosis is not only due to hyperglycemia but also from secondary insulin resistance [12-14]. BAD with widespread atherosclerotic disease hence is more likely to be seen in patients with diabetes. Earlier studies have shown that diabetes is selectively associated with BAD [12]. But subsequent studies have failed to show such correlation [7,13]. Previous studies have shown that patients with high LDL levels have BAD and have unfavorable outcomes [10]. Our study, however, did not reveal any difference in LDL levels between the two sub groups.

In acute stroke setting, progressive lacunar strokes remain an unresolved practice problem. Categorizing lacunar infarcts as LPH and BAD using imaging parameters could help us portend patients with lacunar strokes.

REFERENCES

1. Norrving B. Lacunar infarcts: no black holes in the brain are benign. Pract Neurol 2008; 8: 222-228.