Is Leukoaraiosis due to microembolization from the unstable carotid plaque?

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BACKGROUND

Leukoaraiosis or the presence of cerebral white matter hyperintense lesions (WMHL) in fluid attenuated inversion recovery brain scans (FLAIR) is a risk factor for stroke and vascular death. They are believed to reflect primarily ischaemic cerebral small vessel disease (1). However, controversy currently exists regarding the pathogenesis of WMHL. Theories include small vessel atheroma, microembolization and loss of autoregulation (2). There is very limited evidence to suggest a link between LA and carotid artery disease. Magnetic Resonance Direct Thrombus Imaging (MRDTI) is a non-invasive technique that has been shown to demonstrate the advanced carotid plaque (3). The aim of this study was to determine if the degree of leukoaraiosis was associated with the advanced carotid plaque which has a greater thromboembolic potential.

METHODS

57 consecutive symptomatic patients (with >65% carotid artery stenosis) underwent successful MRDTI of the carotid artery, FLAIR brain scans and a successful carotid endarterectomy (CEA).

MR imaging was performed on a 1.5 T scanner (Siemens). The MRDTI sequence used a T1-weighted magnetization-prepared 3D gradient-echo sequence, acquired in the coronal plane. The sequence included a selective water-excitation radio frequency pulse to abolish fat signal, and the effective inversion time was chosen to null the blood signal. The pixel size and effective slice thickness were 1.2 mm. In addition, a standard FLAIR sequence (TR 9000 ms, TE 110 ms, TI 2500 ms, FOV 180x240 mm, 176x256 , 4 mm slice thickness, 2 mm gap, 2 averages) was acquired.

The CEA specimens were collected, fixed in 10% formal saline and transversely sliced before embedding into paraffin wax blocks. After staining with Gill's haematoxylin and eosin and atheromatous lesions were assessed according to the American Heart Association (AHA) classification. Specimens were defined as either complicated (type VI) or non-complicated (type V) (fig.1)

A plaque was defined MRDTI positive and complicated when bright material of high contrast was noted within the lumen or wall of the carotid artery (1 cm in either side of the stenosis) when compared visually to the adjacent skeletal muscle (fig.2) FLAIR images were processed off-line on UNIX workstations. Analysis was carried out by trained researchers using a semi-automated analysis program (4) and blinded to the CAD status. Lesions were separated based on signal intensity on FLAIR and location into white matter hyperintense lesions and lacunes. Both areas of periventricular and punctate subcortical hyperintense lesions (greater than 2 mm in diameter) were classed together as WMHL (fig.3). Lacunes, areas of completed infarction, were defined as areas of hypointensity in these images. The lesions were manually outlined in each of the 15 FLAIR axial slices, separately for each hemisphere, and summed to give a total number of lesions. Additionally the total intracranial volume (TICV) was calculated for each patient.

RESULTS

There were no differences in age and other vascular risk factors between the MRDTI positive and negative groups; and between complicated (AHA VI) non-complicated (AHA V) plaques based on histology.

73.7% and 66.7% of the plaques were defined as complicated by pathology and MRDTI respectively. There was substantial correlation between pathology and MRDTI (Pearson Corr.0.68, $p<0.05$).

Complicated plaques on MRDTI were found to have more WMHL than uncomplicated plaques (7.9 +/- 5.6 vs. 3.7 +/- 3.4; $p<0.005$) with similar results based on histological strata. A direct inter-hemispheric comparison controlling for individual variations revealed significant more WMHL on the symptomatic hemisphere ($p<0.001$) and the MRDTI status to significantly interact with this effect for both the number ($p<0.001$) and volume of WMHL ($p=0.005$).

The number and volume of WMHL lesions did not correlate with the grade of ipsilateral carotid stenosis (Pearson Corr. 0.08 and 0.10 respectively, $p>0.47$).

CONCLUSIONS

In conclusion, this study shows that the extent of WMHL in the affected cerebral hemisphere is associated with complicated carotid plaque defined both histologically and by MRDTI. We propose that thromboembolism from the carotid plaque is a factor in the development of WMHL and leukoaraiosis. The lack of association between the degree of carotid stenosis and WMHL reinforces the importance of carotid artery morphology to be more important than the grade of stenosis. There is therefore a theoretical basis for examining the diagnostic utility of MRDTI in patients with prominent WMHL in future studies.

Fig.1

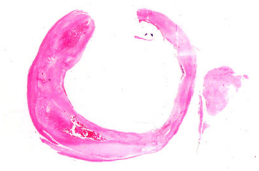


Fig.2

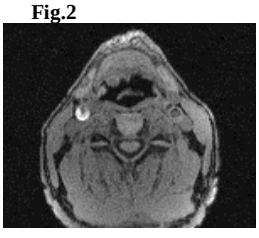
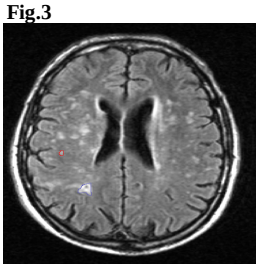


Fig.3



Figures. 1. Histological complicated carotid plaque demonstrating intraplaque haemorrhage. **2.** Hyperintense signal in the right carotid artery using MRDTI. **3.** WMHL analysis in the FLAIR axial slices.

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