Microembolization is a likely contributing factor to leukoaraiosis in patients with symptomatic carotid artery disease

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BACKGROUND

Leukoaraiosis or the presence of white matter hyperintense lesions (WMHL) in fluid attenuated inversion recovery brain scans (FLAIR) is a risk factor for stroke and vascular death. However, controversy currently exists regarding the pathogenesis of WMHL. Theories mainly focus on small vessel disease or loss of autoregulation related to hypertension (1). The evidence for an association with large vessel atherosclerosis is highly controversial. In a small patho-radiological study, we have demonstrated that the unstable plaque defined histologically is associated with a higher number of white matter hyperintense lesions compared with stable plaques (2,3). To allow for a more detailed analysis on a larger study sample, we chose to use an established radiological marker of the unstable plaque as provided by Magnetic Resonance Direct Thrombus Imaging (MRDTI). MRDTI +ve plaques have been shown to accurately predict the unstable plaque (4) which carries a greater thromboembolic risk (5).

The aim of this study was to determine if the extent of WMHL was associated with the unstable carotid plaque as characterized by MRDTI.

METHODS

178 patients with cerebral and ocular ischaemic symptoms underwent successful MRDTI of the carotid artery and FLAIR brain scans between 1999 and 2004. All were assessed clinically and had Duplex ultrasound scans of the carotid arteries.

MR imaging was either performed on a Siemens 1.5 T scanner of Philips 1.5T scanner. The MRDTI sequence used a T1-weighted magnetization-prepared 3Dgradient-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. 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.

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.1)

FLAIR images were processed off-line on UNIX workstations. Analysis was carried out by a single experienced researcher using a semi-automated analysis program (6) and blinded to the MRDTI and symptomatic status. Lesions were separated based on signal intensity on FLAIR and location into WMHL and lacunes.

RESULTS

We tested the effect of recent ischemic symptoms and the MRDTI status on white matter MRI markers of cerebral ischaemia (total WMHL volume, lacunes number and subcortical WMHL as dependent variables), controlling for age, sex, hypertension, previous stroke and the degree of stenosis. Both symptoms and MRDTI status affected MRI markers of WMHL (table) ($F=4.18$, $p=0.006$ and $F=5.14$, p0.002 respectively), but there was no significant interaction between them together. Age exerted the main covariate effect ($F=7.77$, $p<0.001$) with hypertension being significant ($F=3.58$) and the degree of stenosis being marginal but not significant ($F=2.05$) Univariate tests revealed a disparate effect on the individual measures; MRDTI +ve plaques were associated with larger total volume ($F=7.35$, $p=0.007$) and larger number of. Subcortical WMHL ($F=10.18$, $p=0.002$) and there was a trend effect on the number of lacunes ($F=3.11$, p0.08). Symptoms were only associated with more lacunes ($F=10.18$, p=0,002). The age effect was only noted on the total WMHL volume ($F=23.4$,$p<0.001$), whereas hypertension was moderately associated with both total WMHL volume and lacunes no. ($F= 6.56$ and 5.58 respectively). There was a trend associated with the degree of stenosis with lacunes only ($F=2.78$).

CONCLUSION

In conclusion, this study shows that the extent of WMHL in the affected cerebral hemisphere is associated with unstable carotid plaque defined by MRDTI. In contrast, symptoms were only associated with the number of lacunar lesions. This study suggests different pathophysiological mechanisms are involved in the development of lacunar and non-lacunar WMHL. Carotid artery disease was demonstrated to affect both lesion types with plaque morphology being preferentially associated with non-lacunar WMHL as described as leukoaraiosis. This lends strong support to the hypothesis that thromboembolism is indeed an important aetiological factor for the development of WMHL in patients with symptomatic carotid artery disease.

References

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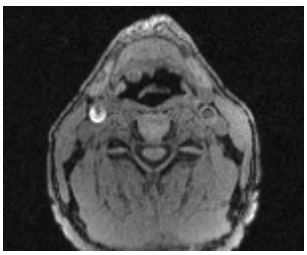

Fig.1 MRDTI R +ve carotid plaque

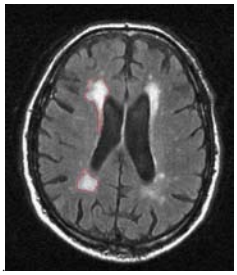

Fig.2 WMHL analysis

	MRDTI +ve	MRDTI -ve
Symptomatic Hemisphere	10.14	**7.19**
Adjusted total WMHL volume means* (ml) and 95% C.I.	(8-65-11.63)	**(5.13-9.25)**
Asymptomatic Hemisphere	**8.38**	**7.08**
Adjusted total WMHL volume means* (ml) and 95% C.I.	**(6.67–10.10)**	**(5.81-8.30)**

Table. The effect of MRDTI status and symptoms on WMHL volume (*adjusted for age, sex, hypertension previous stroke and stenosis.)