Differential MRI pattern in CADASIL and hypertensive leukoencephalopathy

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Introduction

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited microangiopathy characterized by recurrent ischemic episodes and cognitive deficits caused by mutations in the Notch3 gene on chromosome 19.[1] Main pathological alterations are found in leptomeningeal and long perforating arteries showing a non-arteriosclerotic, amyloid-negative angiopathy. One of the leading diagnostic criteria that also served for definition of disease carriers in linkage studies are conspicuous MRI findings with diffuse leukoencephalopathy and lacunar subcortical infarcts.[2,3,4] The purpose of the present study was to evaluate whether CADASIL and hypertensive encephalopathy have different MR patterns.

Material and Methods

Patients 26 patients (mean age: 50.7 years ranging from 32 – 68) with biopsy-proven CADASIL (group 1) and 25 patients with chronic hypertension and leukoencephalopathy compatible with SAE or Binswanger's disease. In order to match severity of white matter lesions due to the later disease onset in group 2, mean age was significantly older (65 yr, range: 40 – 82).

MRI MR examination was performed on a 1.5T clinical scanner (1.5T GE Echospeed) using contiguous axial FastFlair scans (TR=10s, TE=133 ms, TI=2200ms, 2.2×2.2×5 mm nominal pixel size) and sagittal T2w FSE scans (TR=3000, TE=105ms, etl=8, slice thickness: 4mm, gap: 1mm).

Data analysis Semiquantitative regional scores were judged by two investigators blinded for the clinical status of the patients for lobar regions (frontal, temporal, occipital, parietal), subcortical structures (thalamus, basal ganglia), external capsule and corpus callosum. Individual scores ranged from 0 (no lesion) to 4 (maximal confluent lesions). Temporopolar, superior frontal white matter and superior frontal u-fiber involvement was judged separately as well as atrophy, symmetry and cortical infarcts. Multivariate analysis was done to test for significant group effects with and without age as covariate. Finally, a linear discriminant analysis with cross-validation was performed.

Direct automatic pixel-based group comparison was done with SPM96[5]. First all images were normalised to the T1 template structure provided by SPM, followed by a spatial smoothing with a 4mm width gaussian kernel, corresponding to about the size of 2 pixels. Statistical maps were generated for group contrasts after a global normalization of pixel intensities at $p<0.05$.

Results

Different MR lesion patterns were found with significantly higher scores for CADASIL in temporal, temporopolar, frontal, superior frontal, occipital regions, external capsule and symmetry (table 1) compared to SAE. Anterior temporal and superior frontal lesions, mostly involving u-fibers are almost regularly seen in CADASIL and very unusual in SAE (fig.1).

Linear discriminant analysis proved 92.2% correctly classified, cross-validated cases with temporopolar scores having the single best predictive value (80.4% correctly classified).

Score	CADASIL n=26, mean(SD)	SAE n=25, mean(SD)	F-test, p=	age as covariate, p=
Temporopolar	1.9(1.0)	0.3(0.46)	<0.001	<0.001
Frontal u-Fiber	1.7(1.1)	0.5(0.65)	<0.001	<0.001
Caps. externa	1,5(1.1)	0,7(0.8)	0.006	<0.001
Temporal	1.6(0.64)	1.0(0.68)	.005	<0.0001
Occipital	1.5(0.65)	1.1(0.64)	0.039	0.001
Symmetry	1,0(0.66)	0.6(0.65)	.034	.003
Sup frontal.	2.6(0.99)	1.9(0.91)	.017	.001
Frontal	2.4(0.85)	1.9(0.76)	.045	.002
Atrophy	0.2(0.49)	0.7(0.79)	.006	.142
Parietal	2.1(0.74)	1.8(0.52)	.086	0.001

Table 1: Semiquantitative scores showing significant group effect

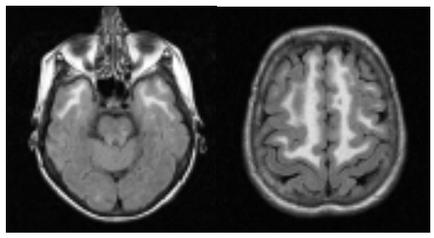

Fig.1: 58 yr old male patient (CADASIL) with advanced leukoencephalopathy affecting anterior temporal and superior frontal white matter including u-fibers

SPM analysis independently revealed significantly brighter pixels bilaterally for temporal, superior frontal and subcortical white matter and external capsule in CADASIL and significantly brighter pixels in the left occipital lobe and cerebellum for SAE (fig.2).

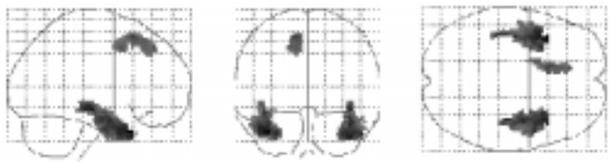

Fig.2: Statistical maps of group comparison showing significantly brighter pixels in CADASIL compared to SAE.

Discussion

This study demonstrates distinctive MR patterns of vascular leukoencephalopathies that allow discrimination between CADASIL and SAE. Awareness of these MR criteria will help to diagnose more undetected cases and provide adequate selection base for further biopsy or genetic tests. Furthermore, we propose that statistical group comparison of normalized FLAIR images is a new and reliable method to analyze typical MR lesion pattern in neurological diseases.

References

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