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Serial MR observation of cortical laminar necrosis caused by brain infarction

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Abstract To examine the chronological changes characteristic of cortical laminar necrosis caused by brain infarction, 16 patients were repeatedly examined using T1-, T2-weighted spin-echo, T2*-weighted gradient echo, fluid attenuated inversion recovery (FLAIR) images, and contrast enhanced T1-weighted images at 1.0 or 1.5 T.

High intensity cortical lesions were visible on the T1-weighted images from 2 weeks after ictus and became prominent at 1 to 3 months, then became less apparent, but occasionally remained at high intensity for 2 years. High intensity cortical lesions on FLAIR images became prominent from 1 month, and then became less prominent from 1 year, but occasionally remained at high intensity for 2 years. Subcortical lesions did not display high intensity on T1-weighted images at any stage. On FLAIR images, subcortical lesions initially showed slightly high intensity and then low intensity from 6 months due to encephalomalacia. Cortical lesions showed prominent contrast enhancement from 2 weeks to 3 months, but subcortical lesions were prominent from 2 weeks only up to 1 month. T2*-weighted images disclosed haemosiderin in 3 of 7 patients, but there was no correlation with cortical short T1 lesions.

Cortical laminar necrosis showed characteristic chronological signal changes on T1-weighted images and FLAIR images. Cortical short T1 lesions were found not to be caused by haemorrhagic infarction.

Key words Brain infarction · Contrast enhancement · Cortical laminar necrosis · FLAIR images · Magnetic resonance imaging

Introduction

High intensity cortical lesions are clinically observed on T1-weighted MR imaging in cases of brain infarction, although there have been relatively few reports [1–3]. Initially thought to be caused by haemorrhagic infarction [1], histopathological examination has demonstrated these cortical short T1 lesions to be "cortical laminar necrosis" without haemorrhage or calcification [2]. No long-term follow-up studies over 1 year have been performed on such lesions, and there have been no studies employing fluid attenuated inversion recovery (FLAIR) images or magnetic susceptibility-sensitive gradient echo (T2*-weighted) images. This report presents the results of such a long-term study using a variety of MR imaging techniques to analyse the nature and chronological MR changes characteristic of such lesions.

Patients and methods

A total of 16 brain infarction patients (11 men and 5 women aged 24 to 84 years, mean 63.8 years) underwent MR examination using a 1.0 or 1.5 T MR system from 4 hours to 2.5 years after ictus. The follow-up period ranged from 3 months to 2.5 years (mean, 18.1 months). Inclusion criteria for this study were the presence of

Table 1 Chronological change in MR signal intensity and contrast enhancement of cortical and subcortical lesions associated with cortical laminar necrosis. Number indicates total number of patients in which MR shows specific signal intensity during the given period

	~ 2 Weeks	~ 1 Month	~ 2 Months	~ 3 Months	~ 6 Months	~ 9 Months	~ 1 Year	~ 1.5 Years	~ 2 Years	> 2 Years
T1-weighted image/cortex										
Iso-	4	2		1	1	5	1	6	9	6
Slightly high		4		3	8	5	7	5	3	1
High		4	6	4	2		1		1	
Markedly high		1								
T1-weighted image/subcortex										
Iso-	4	4	2	1						
Slightly low		7	2	4		1	1			
Low			2	3	11	9	8	11	13	7
T2-weighted image/subcortex										
Iso-	1									
Slightly high	2	4	2	1						
High	1	7	4	7	11	10	9	11	13	7
FLAIR image/cortex										
Iso-		2								4
Slightly high						1	1	3	9	2
High			1	1	1	3	3	2	1	1
Markedly high				1	3		1			
FLAIR image/subcortex										
Low				1	1	3	3	4	10	7
Iso-				1	3	1	2	1		
Slightly high		2	1							
High										
Contrast enhancement/cortex										
Negative	1		1	1	2	6	6	7	7	7
Slightly positive	1			2	4	2	1	3		
Positive				1						
Markedly positive		4	1	1						
Contrast enhancement/subcortex										
Negative	2		2	4	4	8	7	10	7	7
Slightly positive		1		1	2					
Positive		1								
Markedly positive		2								
T2*-weighted image/cortex										
Negative						2	2	4	3	2

high intensity "cortical laminar" lesions on T1-weighted images at any time during the clinical course. Patients with haemorrhagic infarction were thus not excluded if they fulfilled the aforementioned criterion. Each patient underwent multiple MR examinations (5.1 on average).

The basic examination protocol included T1-weighted and T2-weighted axial spin-echo images, and contrast enhancement with gadolinium diethylenetriamine-pentaacetic acid (Gd-DTPA) at a dose of 0.1 mmol/kg. In addition, FLAIR and T2*-weighted gradient echo images were also frequently added to the basic examination protocol. FLAIR images were obtained on 40 occasions for 15 patients. T2*-weighted images were obtained on 21 occasions for 7 patients. T1-weighted spin-echo images using fat suppression techniques were also obtained in two patients.

The MR scanning parameters for the T1-weighted images were a repetition time (TR) of 510–655 ms, an echo time (TE) of 14–16 ms, and 2 excitations for spin-echo sequences. For T2-weighted images, a TR of 2015–2200 ms and a TE of 80 ms with 1 excitation for the conventional spin-echo sequence, and a TR of 3830–5000 ms, TE of 90–110 ms, and echo train of 7 or 13 with just 1 excitation for fast spin-echo sequences. The FLAIR image parameters were a TR of 7500–8000 ms, a TE of 105–150 ms, an inversion time of 1750–2000 ms, an echo train of 7 or 19, and 1 or 4 excitations for fast spin-echo sequences. For T2*-weighted gradient echo images, a TR of 500–561 ms, a TE of 15–18 ms, a flip angle of 15°, and 2 or 4 excitations. Axial images with a 192–256 × 256 matrix were obtained with a slice thickness of 5–7 mm and a field of view of 200–230 mm.

Results

The signal intensities of both cortical and subcortical lesions were evaluated relative to the intensity of normal structures on the T1- and T2-weighted spin-echo images and FLAIR images. Contrast enhancement of the lesions was also evaluated on the T1-weighted images. The presence of haemosiderin was determined using T2*-weighted gradient echo images. The results were then tabulated in Table 1.

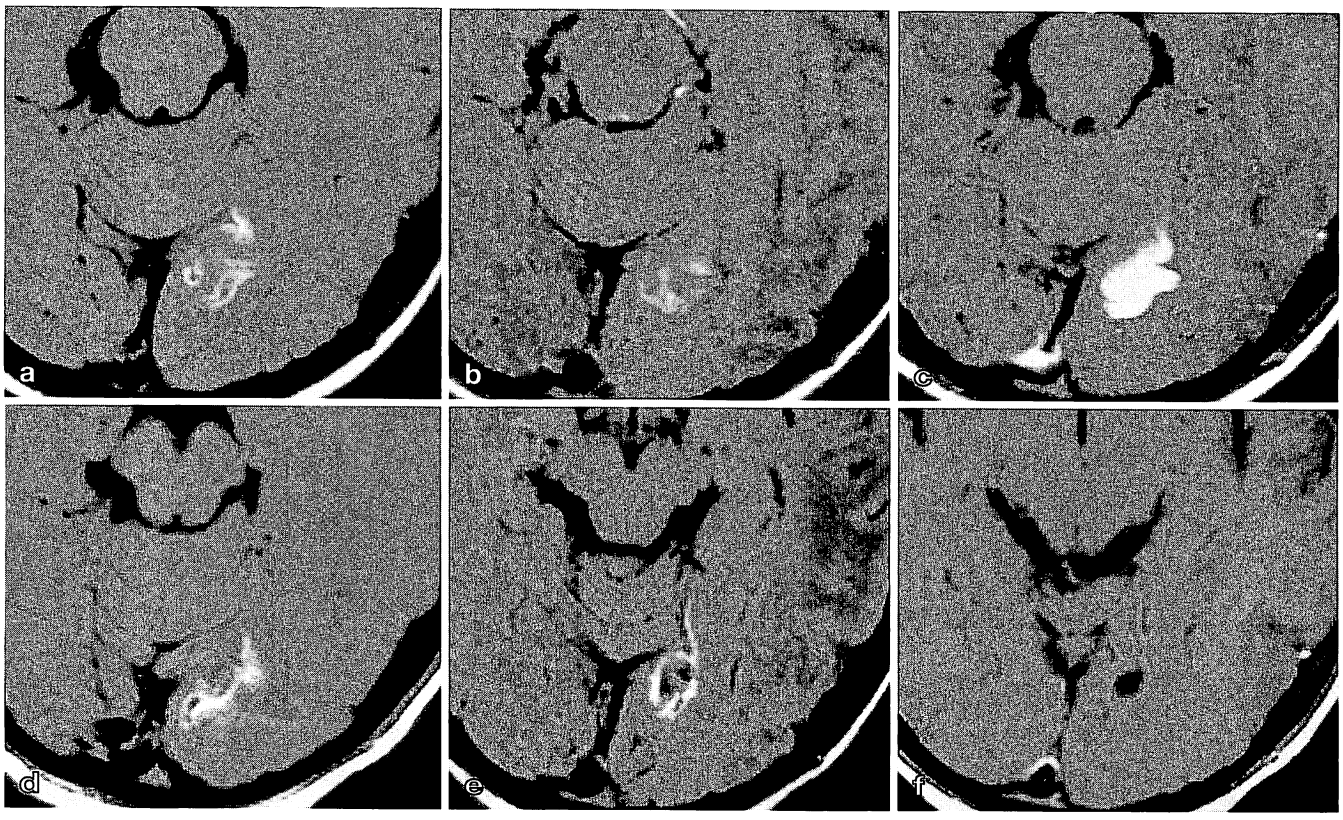

Fig. 1 A 23-year-old woman with right occipital infarction. **a–c** were obtained at 2 weeks after ictus, and **d–f** at 2.5 months. **a** T1-weighted spin-echo image shows a high intensity cortical laminar lesion while a subcortical lesion displays iso-intensity. **b** On the FLAIR image the cortical lesion is iso-intense and the subcortical lesion is slightly high intensity. **c** Both the cortical and subcortical lesions are markedly enhanced by the contrast material. **d** The cortical lesion is high intensity while the subcortical lesion is partially low intensity. **e** The FLAIR image shows the cortical lesion as high intensity and the subcortical lesion as low intensity. **f** There is no apparent contrast enhancement of the lesions

Cortical lesions showed iso-intensity on T1-weighted images up to about 2 weeks after ictus and high intensity from 2 weeks (Fig. 1 A). They became particularly prominent at 1–3 months and then gradually faded, but some parts of the lesions occasionally remained at high intensity for 2 years (Figs. 1 D, 2 A, 2 C, 2 F, 3 A, 3 B, 4 A). On FLAIR images, cortical lesions initially displayed iso-intensity for up to about 1 month after ictus, then became high intensity and prominent from 1 month to 1 year (Figs. 1 B, 1 E, 2 B, 2 D, 3 D, 4 B). After 1 year they became less prominent, but occasionally remained high intensity even after 2 years (Figs. 2 G, 3 C). Cortical lesions never displayed low intensity at any stage on either T1-weighted images or FLAIR images.

Subcortical lesions initially displayed iso-intensity on T1-weighted images, then iso-/low intensity for up to about 1 month, after which they became low intensity (Figs. 1 A, 1 D, 2 A, 2 C, 2 F, 4 A). On T2-weighted spin-echo images, subcortical lesions initially showed iso-intensity in the acute stage, but high intensity thereafter. On FLAIR images, subcortical lesions showed slightly high intensity initially within 2 months, but they showed iso-intensity from 2 to 6 months and low intensity after 6 months, remaining low intensity thereafter (Figs. 1 B, 1 E, 2 B, 2 D, 3 C, 4 B).

There was no Gd-DTPA contrast enhancement of either cortical or subcortical lesions until 2 weeks after ictus. Cortical lesions were prominently enhanced from 2 weeks to 3 months, and subcortical lesions from 2 weeks to 1 month only (Fig. 1 C). There was no subcortical enhancement after 1 month, but slight cortical enhancement could be observed as long as 1 year after ictus (Fig. 1 F). In most cases, however, cortical enhancement had disappeared by 6 months after ictus.

No low intensity lesions suggesting the presence of haemosiderin could be observed on the T2*-weighted gradient echo images of 4 out of 7 patients so examined, either upon initial examination or during the follow-up period (Figs. 2 E, 3 E, 3 F). In the remaining three patients, however, low intensity lesions without a cortical laminar pattern were observed from 3 months to 2 years after ictus (Fig. 4 C). These low intensity lesions, however, which were consistent with haemorrhagic infarction, were not identical in location to the high in-

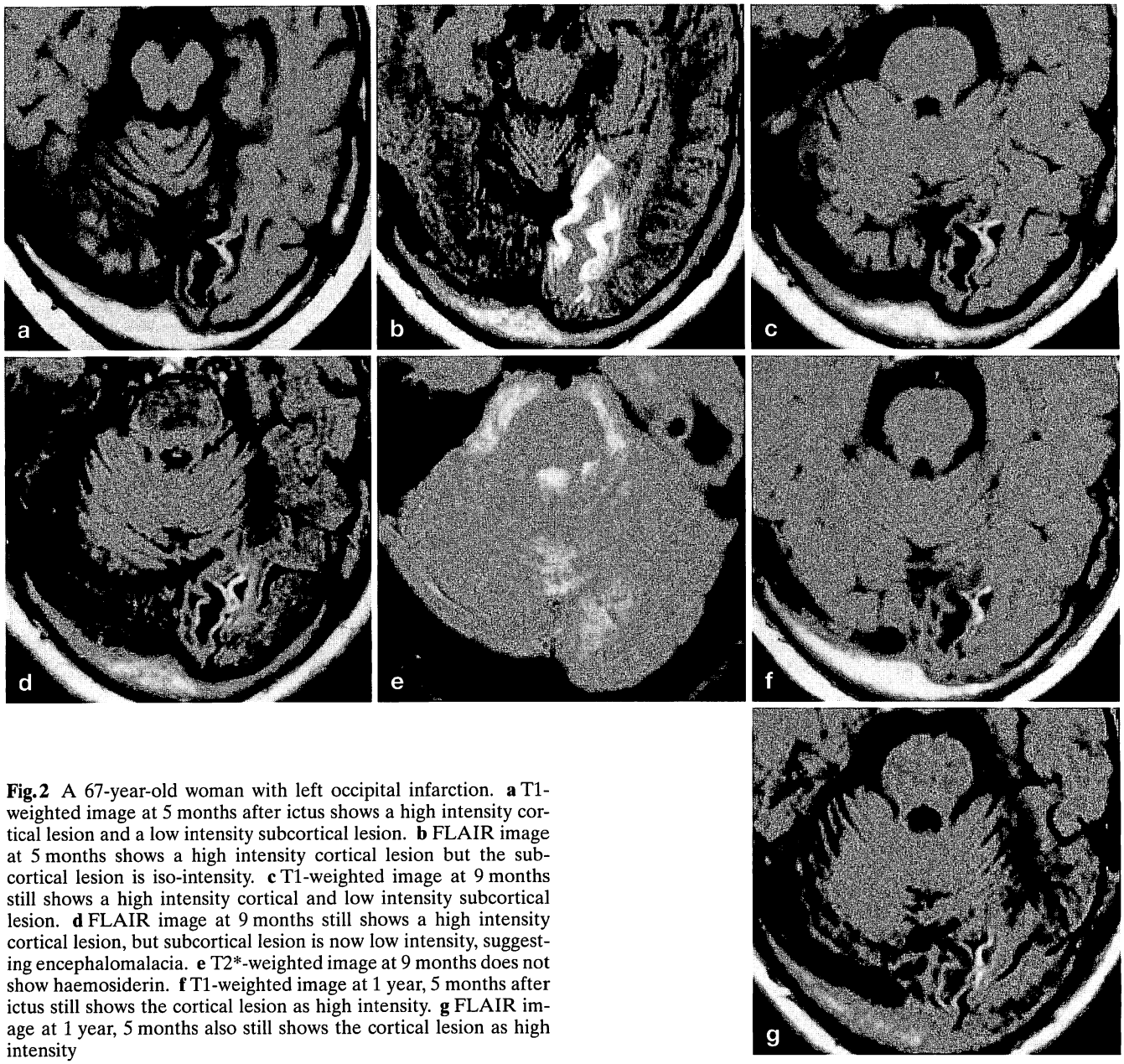

Fig. 2 A 67-year-old woman with left occipital infarction. **a** T1-weighted image at 5 months after ictus shows a high intensity cortical lesion and a low intensity subcortical lesion. **b** FLAIR image at 5 months shows a high intensity cortical lesion but the subcortical lesion is iso-intensity. **c** T1-weighted image at 9 months still shows a high intensity cortical and low intensity subcortical lesion. **d** FLAIR image at 9 months still shows a high intensity cortical lesion, but subcortical lesion is now low intensity, suggesting encephalomalacia. **e** T2*-weighted image at 9 months does not show haemosiderin. **f** T1-weighted image at 1 year, 5 months after ictus still shows the cortical lesion as high intensity. **g** FLAIR image at 1 year, 5 months also still shows the cortical lesion as high intensity

tensity lesions with laminar pattern which were observed on the T1-weighted images. Even in these three patients with haemorrhagic infarction, it should be noted that high intensity cortical lesions with a laminar pattern could be observed on the T1-weighted images (Fig. 4 A).

In the two patients for whom T1-weighted spin-echo images were obtained using fat suppression techniques, there was no reduction in signal intensity of the cortical short T1 lesions (Fig. 3 G). The signal changes characteristic of cortical and subcortical lesions are schematised in Fig. 5.

Discussion

Boyko et al. [2] reported that cortical short T1 lesions in cases of brain infarction histopathologically presented as "cortical laminar necrosis" without haemorrhage or calcification. Komiyama et al. [3] subsequently reported that cortical laminar necrosis displayed characteristic chronological changes in signal intensity on T1-weighted and T2-weighted spin-echo images up to 1 year after ictus. In this report, we extended their study with the following: (1) observation of cortical laminar necrosis for as long as 2 years, (2) study with FLAIR images, and

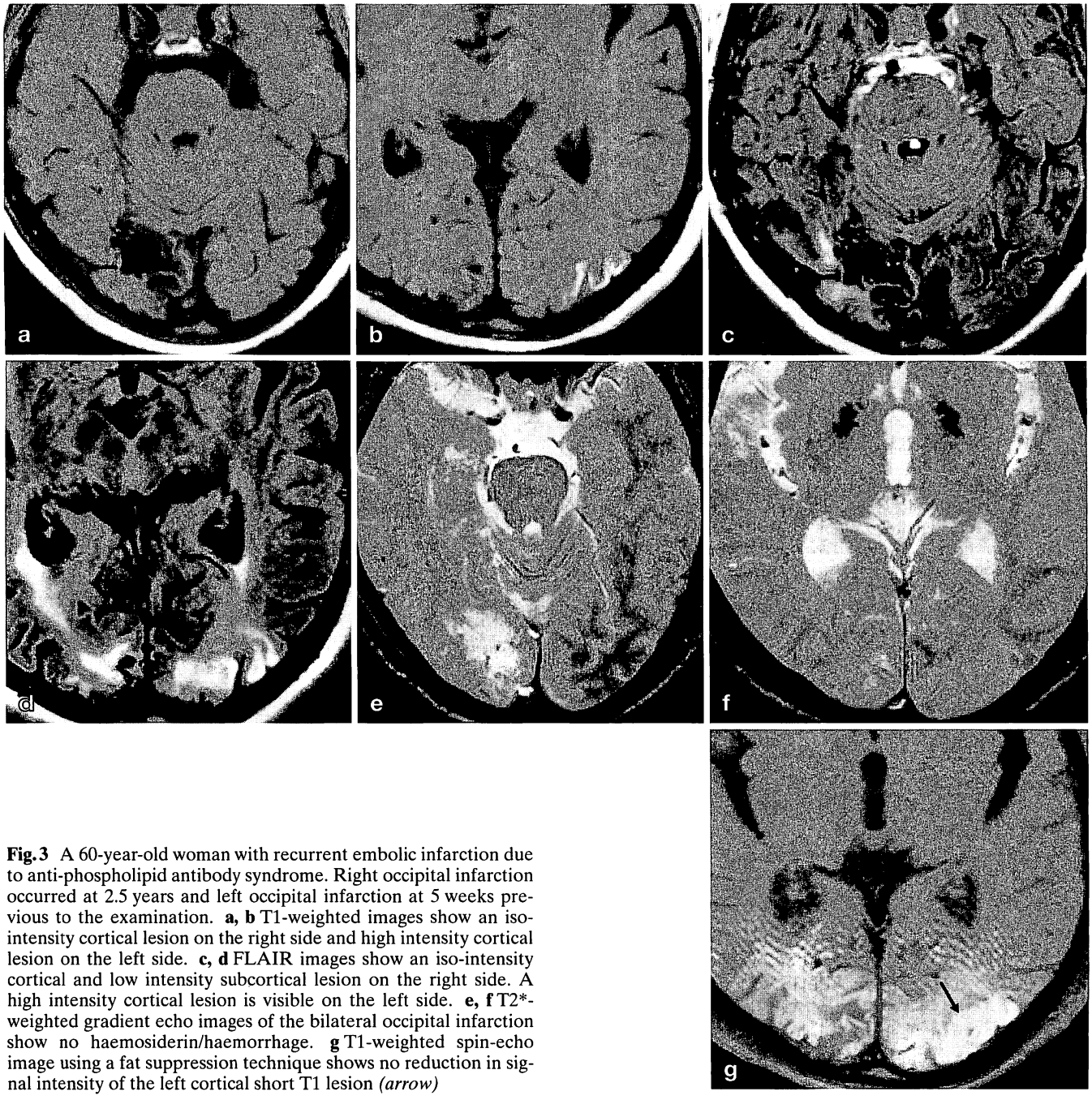

Fig. 3 A 60-year-old woman with recurrent embolic infarction due to anti-phospholipid antibody syndrome. Right occipital infarction occurred at 2.5 years and left occipital infarction at 5 weeks previous to the examination. **a, b** T1-weighted images show an iso-intensity cortical lesion on the right side and high intensity cortical lesion on the left side. **c, d** FLAIR images show an iso-intensity cortical and low intensity subcortical lesion on the right side. A high intensity cortical lesion is visible on the left side. **e, f** T2*-weighted gradient echo images of the bilateral occipital infarction show no haemosiderin/haemorrhage. **g** T1-weighted spin-echo image using a fat suppression technique shows no reduction in signal intensity of the left cortical short T1 lesion *(arrow)*

(3) study with T2*-weighted gradient echo images to detect haemosiderin. On T2-weighted spin-echo images, cortical laminar necrosis displayed iso-intensity or high intensity, but due to the high signal intensity from the surrounding cerebrospinal fluid (CSF), it was difficult to determine the exact signal intensity using T2-weighted spin-echo images. FLAIR images were found to be superior for detecting brain infarction, especially of cortical lesions because signals from the surrounding CSF are essentially nulled [4]. Chronological changes in the subcortical white matter from high or iso-intensity to low intensity on FLAIR images suggest that subcortical lesions become cystic and filled with CSF due to encephalomalacia.

Cortical laminar necrosis displayed high intensity both on T1-weighted spin-echo images and FLAIR images, indicating short T1 and long T2 lesions. Interestingly, cortical high intensity appears 2 weeks after ic-

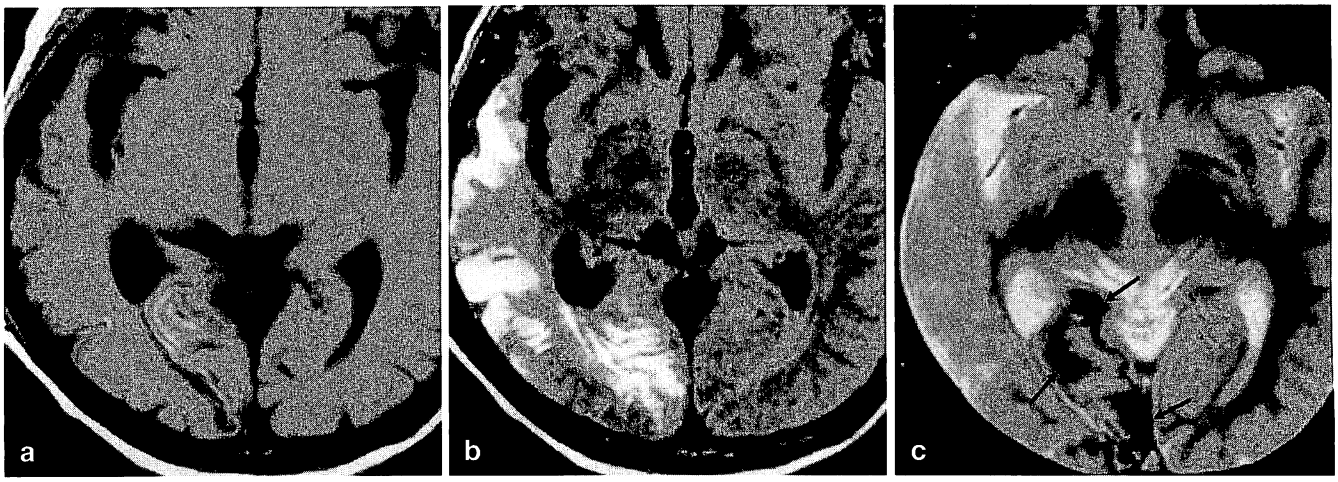

Fig. 4 A 53-year-old woman with a right temporo-occipital cardioembolic infarction. These images were obtained at 3 months after ictus. **a** T1-weighted image shows a high intensity cortical lesion and low intensity subcortical lesion. **b** FLAIR image shows the high intensity cortical lesion but the subcortical lesion remains isointensity. **c** T2*-weighted gradient echo image shows low intensity haemosiderin *(arrows)*, which does not correlate with the cortical lesions with short T1 values

tus, but on FLAIR images becames prominent from 1 month. Even after the cortical shot T1 signal fades, the cortical high signal on FLAIR images remains prominent up to about 1 year. Although cortical laminar necrosis may show characteristic signal changes on MR, the exact mechanism causing such changes still has not been elucidated.

High intensity lesions associated with brain infarction on T1-weighted images may represent methaemoglobin/haemorrhage, paramagnetic substances, fat tissue, calcification, high protein concentration, and cortical laminar necrosis [2]. It can be inferred that the short T1 lesions in our series were not caused by methaemoglobin/haemorrhage because in the chronic stage there was no haemosiderin with a cortical laminar pattern on the T2*-weighted images. From our observations, cortical short T1 lesions can be present in cases of haemorrhagic infarction, but the T1 shortening is independent from the haemorrhage itself. Paramagnetic substances, such as Fe^{++}, Fe^{+++} and Cu^{++}, potentially shorten both T1 and T2 values by preferential relaxation enhancement [5]. However, such paramagnetic substances may not contribute to cortical short T1 lesions because of the prolonged T2 values of such lesions.

It was found that fat tissue does not contribute to cortical T1 shortening because: (1) cortical lesions displayed constantly high intensity on FLAIR images even after they become iso-intense on T1-weighted images, (2) fat suppression techniques on T1-weighted images did not reduce the signal intensity of cortical short T1 lesions, and (3) there was no chemical shift artifact by fat tissue.

Calcified lesions commonly display low MR signals due to reduced mobile protons, but occasionally are high intensity on T1-weighted images [2, 6]. Such high intensity is frequently found with heavily calcified lesions. The disappearance of T1 short signals in the chronic stage, absence of high density lesions on x-ray computed tomography [3], lack of T2* effect on T2*-weighted gradient echo images, and absence of any histological evidence of calcification [2] indicate that cortical short T1 lesions in brain infarction are not caused by calcification.

"Cortical laminar necrosis" as described in this report can be histopathologically defined as pan-necrosis, i.e. the death of neurons, glia and blood vessels in the affected area [2]. One possible result of pan-necrosis is protein degradation. As T1 shortening occurred exclusively in the cortex, this suggests that neuronal necrosis and its resultant denatured protein were closely related to the MR signal changes. Although protons in proteins do not usually contribute to MR signals, the protein concentration and amount of free water may influence the T1 and T2 relaxation characteristics [7]. In general, higher concentrations of proteins or other macromolecules enhance relaxivity by restricting the motion of water molecules, thus causing T1 shortening [6, 8, 9]. Even a small elevation of the protein concentration may cause significant T1 shortening. This close interrelation between the protein concentration and free water content makes MR signal changes more complex. We believe that these factors, which exclusively occur in the cortex, may play a major role in the production of MR signals characteristic of cortical laminar necrosis.

In conclusion, it was found that cortical laminar necrosis displays characteristic chronological MR signal changes on T1-weighted and FLAIR images. The exact

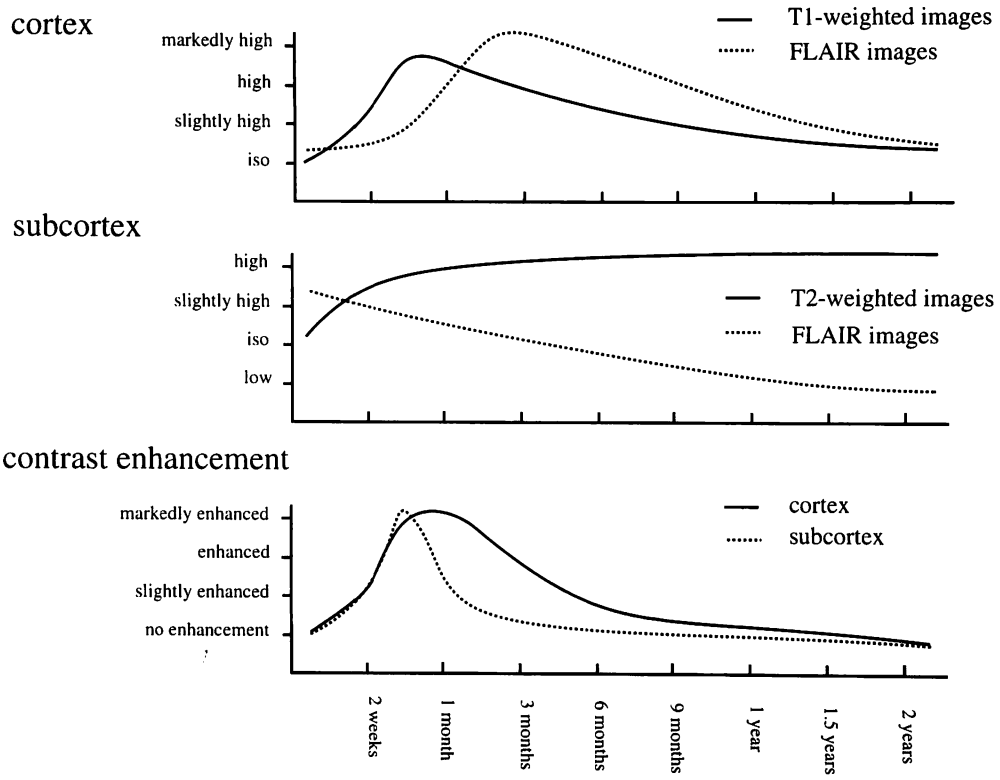

Fig. 5 Chronological change in signal intensity and contrast enhancement of cortical and subcortical lesions in association with cortical laminar necrosis caused by brain infarction

mechanism behind the high intensity on T1-weighted and FLAIR images still remains to be elucidated, but we believe that neuronal necrosis and associated pathological changes in the cortex, such as denatured proteins and cellular components from the infarcted tissue, may contribute to such signal changes. Haemorrhagic infarction does not contribute to these chronological changes in MR signal intensity.

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