Neuroradiology (2000) 42: 492–498

M. Komiyama
H. Nakajima
M. Nishikawa
T. Yasui

Chronological changes in nonhaemorrhagic brain Infarcts with short T1 in the cerebellum and basal ganglia

Received: 1 February 1999
Accepted: 13 September 1999

M. Komiyama (✉) · H. Nakajima · M. Nishikawa · T. Yasui
Department of Neurosurgery,
Osaka City General Hospital, 2–13–22,
Miyakojima-Hondouri, Miyakojima,
Osaka 534–0021, Japan
e-mail: komiyama@japan-mail.com
Tel.: + 81-6-6929 1221
Fax: + 81-6-6929 1091

Abstract Our purpose was to investigate nonhaemorrhagic infarcts with a short T1 in the cerebellum and basal ganglia. We carried out repeat MRI on 12 patients with infarcts in the cerebellum or basal ganglia with a short T1. Cerebellar cortical lesions showed high signal on T1-weighted spin-echo images beginning at 2 weeks, which became prominent from 3 weeks to 2 months, and persisted for as long as 14 months after the ictus. The basal ganglia lesions demonstrated slightly high signal from a week after the ictus, which became more intense thereafter. Signal intensity began to fade gradually after 2 months. High signal could be seen at the periphery until 5 months, and then disappeared, while low or isointense signal, seen in the central portion from day 20, persisted thereafter.

Key words Infarcts, brain · Basal ganglia · Cerebellum · Magnetic resonance imaging, T1 shortening

Introduction

High-signal areas on T1-weighted images of brain infarcts were believed to represent haemorrhagic infarcts [1,2]. However, some are not haemorrhagic, as has been shown by the absence of haemosiderin on T2*-weighted images [3,4,5] or by histological examination [4,6]. Characteristic chronological changes in signal intensity of such lesions in the cerebral cortex on T1-weighted spin-echo and fluid-attenuated inversion recovery (FLAIR) images have been reported [3,5]. We have observed similar nonhaemorrhagic short-T1 lesions in the cerebellar cortex and basal ganglia in patients with infarcts. The purpose of this study was to investigate the chronology of these lesions on MRI and to discuss their possible pathogenesis.

Methods

We studied 12 patients (3 women, 9 men aged 38–75 years, mean 62 years) with a diagnosis of brain infarct and short-T1 lesions in the cerebellum or basal ganglia. There were seven with cerebellar and five with basal ganglia infarcts. The diagnosis of brain infarct was established by clinical presentation, CT and MRI. The probable cause of the infarct was established by clinical presentation and the results of other examinations, including electro- and echocardiogram, catheter cerebral angiography and laboratory data. Patients with haemorrhagic infarcts on CT were excluded. The patients with cerebellar lesions were examined between 2 days and 2 years after the onset of stroke (total examinations, 26; average, 3.7/patient), and those with basal ganglia lesions between 4 days and 15 months (total examinations, 17; average, 3.4/patient). The MRI examination included T1- and T2-weighted spin-echo images at 1.0 or 1.5 T. Selected patients had T1-weighted spin-echo images following gadolinium-DTPA 0.1 mmol/kg body weight, FLAIR images and/or T2*-weighted gradient-echo images. Chronological changes in signal intensity of the lesions relative to the normal counterpart regions were assessed. Two observers (M.K., M.N.) analysed the signal intensity of the lesions independently, without knowledge of temporal information about the lesions, with consensus if there was disagreement. The intensity of the lesions relative to the normal brain was graded as markedly high, high, slightly high, iso- or low, and the degree of contrast enhancement as extensive, moderate, minimal, or none.

Parameters for the T1-weighted images were repetition time (TR) 510–655 ms, echo time (TE) 14–16 ms, two excitations, for T2-weighted images TR 2,015–2,200, TE 80 ms, one excitation, and for fast spin-echo sequences TR 3,830–5,000, TE 90–110 ms, echo

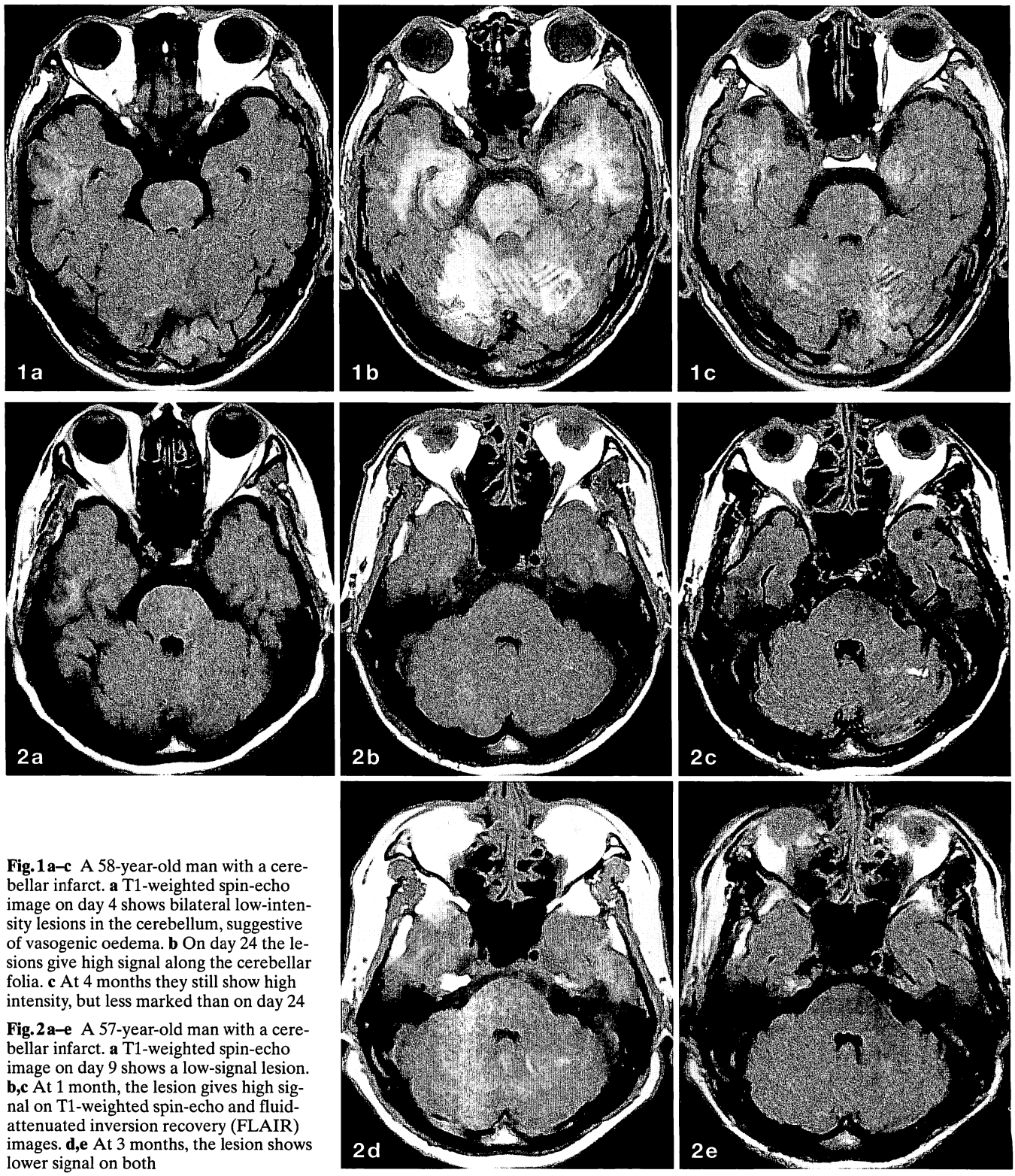

Fig. 1a–c A 58-year-old man with a cerebellar infarct. **a** T1-weighted spin-echo image on day 4 shows bilateral low-intensity lesions in the cerebellum, suggestive of vasogenic oedema. **b** On day 24 the lesions give high signal along the cerebellar folia. **c** At 4 months they still show high intensity, but less marked than on day 24

Fig. 2a–e A 57-year-old man with a cerebellar infarct. **a** T1-weighted spin-echo image on day 9 shows a low-signal lesion. **b,c** At 1 month, the lesion gives high signal on T1-weighted spin-echo and fluid-attenuated inversion recovery (FLAIR) images. **d,e** At 3 months, the lesion shows lower signal on both

Table 1 Changes in signal from cerebellar cortex lesions. *Numbers* patients

	~ 1 week	~ 2 weeks	~ 1 month	~ 3 months	~ 6 months	~ 9 months	~ 1 year	~ 1.5 years	~ 2 years
T1-weighted spin-echo images									
Low/isointensity	3	2	–	–	1	1	–	–	1
Slightly high signal	–	–	2	2	5	2	4	1	–
High signal	–	–	1	–	–	–	–	–	–
Markedly high signal	–	–	1	1	–	–	–	–	–
FLAIR images									
Isointensity	–	–	–	–	–	–	–	–	–
Slightly high signal	2	–	–	1	1	1	1	–	1
High signal	–	1	–	1	2	2	1	1	–
Markedly-high signal	–	–	1	1	1	–	–	–	–
Contrast enhancement									
None	–	–	1	2	3	1	3	1	–
Minimal	–	–	–	1	–	–	–	–	–
Moderate	–	1	1	–	–	–	–	–	–
Extensive	–	–	–	–	–	–	–	–	–
T2*-weighted gradient-echo images									
No haemosiderin	–	–	–	–	1	1	–	–	1

train 7 or 13, 1 excitation. Parameters for FLAIR were a TR 7,500–8,000, TE 105–150 inversion time 1,750–2,000 ms, echo train 7 or 19, 1 or 4 excitations, and for T2*-weighted gradient-echo images TR 500–561, TE 15–18 ms, flip angle 15 deg, 2 or 4 excitations. Axial images with a 192–256 × 256 matrix were obtained, slice thickness 5–7 mm and field of view 200–230 mm.

Results

Cerebellar lesions

In seven patients with cerebellar lesions (Table 1), cortical lesions were evident on T1-weighted spin-echo images, showing low or isointensity within 2 weeks of the onset of stroke. (Figs. 1 a, 2 a). High-signal lesions appeared after 2 weeks and became prominent from 3 weeks to 2 months; and slightly high intensity remained visible until 14 months after the ictus. (Figs. 1 b,c, 2 b,d). The lesions became isointense between 3.5 months and 2 years after the ictus. On FLAIR images, the cortical lesions were of slightly high intensity soon after the onset of the stroke, which then became more prominent from 3 weeks to 3.5 months; high or slightly high signal persisted until 2 years after the ictus (Figs. 2 c,e). Contrast enhancement of the cortical lesions was observed between 2 weeks and 1 month after the ictus, but up to day 52 in one patient. T2*-weighted gradient-echo images did not show low signal suggestive of haemosiderin. Because of the high signal from surrounding cerebrospinal fluid on T2-weighted spin-echo images, it was occasionally difficult to detect increased signal in the cortical lesions. Signal change on T2-weighted spin-echo images was therefore not assessed, except when low-signal foci suggestive of deoxyhaemoglobin or haemosiderin were seen. Low intensity lesions were not evident on T2-weighted spin-echo images at any time in any patient. Embolic mechanisms were strongly suspected in six of seven patients, while the mechanism in the remaining patient was not determined.

Basal ganglia lesions

In five patients with basal ganglia lesions (Table 2), they were evident as low or isointensity on T1-weighted spin-echo images within a week of the onset of the stroke. (Fig. 3 a). In such cases, the entire lesion or its periphery showed slightly high signal from day 8, which increased thereafter. (Figs. 3 c, 4 a), then gradually faded from 2 months after the ictus. High signal remained at the periphery of the lesion until 5 months and then disappeared. The central portion was marked by low or iso-intensity from day 20, which then persisted (Figs. 3 d, 4 b,c). On T2-weighted spin-echo images, the lesions were generally of high intensity; low signal was not seen at any time. On FLAIR images, high intensity was seen throughout the lesion soon after the onset of the stroke. (Fig. 3 b). While the central portion of the lesions was isointense and then showed low signal from day 20 after the ictus, the periphery continued to give slightly high signal even 1 year after the ictus (Fig. 4 d). No contrast enhancement was observed within a week; it was seen between 8 days and 1 month after the ictus, but not thereafter. No low intensity lesions were revealed in the basal ganglia on T2*-weighted gradient-echo images, in any examination, other than in one patient, who had a unilateral brain infarct, and bilateral symmetrical low-signal foci suggestive of physiological iron deposition. (Fig. 3 e).

Table 2 As Table 1: basal ganglia lesions

	~ 1 week	~ 2 weeks	~ 1 month	~ 3 months	~ 6 months	~ 9 months	~ 1.3 years
T1-weighted spin-echo images							
Low/isointensity	2	1	–	–	–	1	1
Slightly high signal	–	1	–	4	2	–	–
High signal	–	–	1	–	2	–	–
Markedly high signal	–	–	1	1	–	–	–
Central isointense or low signal	–	–	1	3	1	–	–
T2-weighted spin-echo images							
Isointensity	–	–	–	–	–	–	–
Slightly high signal	1	1	1	1	1	1	1
High signal	1	–	1	1	2	–	–
Markedly high signal	–	1	–	2	1	–	–
FLAIR images							
Isointensity	–	–	–	–	–	–	–
Slightly high signal	–	–	–	–	–	1	1
High signal	1	–	–	1	1	–	–
Markedly high signal	1	1	2	3	2	–	–
Central isointensity or low signal	–	–	1	3	1	1	1
Contrast enhancement							
None	2	–	–	4	2	1	1
Minimal	–	–	–	–	–	–	–
Moderate	–	–	2	–	–	–	–
Extensive	–	2	–	–	–	–	–
T2*-weighted gradient-echo images							
No haemosiderin	–	1	–	3	2	1	1

Embolic mechanisms were strongly suspected in three of five patients; the mechanism was not determined in the remaining two.

Discussion

Chronological changes in signal intensity on T1-weighted spin-echo and FLAIR images

In the cerebral cortex, high-signal lesions appear on T1-weighted spin-echo images from 2 weeks after the ictus, become prominent at 1–3 months, and then less apparent; but are occasionally seen up to 2 years. High signal on FLAIR images becomes prominent at 1 month, then less prominent after a year, high signal occasionally persisting for 2 years [5]. Short T1 lesions appeared in the cerebellar cortex 2 weeks and in the basal ganglia one week after the stroke. The lesions in the cerebellar cortex and basal ganglia showed high intensity on FLAIR images soon after onset of stroke. High intensity on T2-weighted spin-echo and FLAIR images in the early stage of the stroke (within a week) may be caused by vasogenic oedema and this should be discriminated from the high intensity appearing on FLAIR images more than 2 weeks after the ictus, because oedema usually subsides at this stage. The early high-signal foci on T2-weighted spin-echo and FLAIR images do not correspond to the short T1 lesions which appear 1–2 weeks from the ictus. Despite the difference in timing of the appearance of high signal on T1-weighted spin-echo and FLAIR images in cerebral, cerebellar and basal ganglia lesions, there are similarities: high-signal areas on T1-weighted spin-echo images appeared from 1–2 weeks after the stroke and lasted until 6 months to 1 year, finally disappearing; on FLAIR images they lasted longer than on T1-weighted spin-echo images.

Possible mechanisms for T1 shortening

Chronic brain infarcts typically give low signal on T1- and high signal on T2-weighted spin-echo images due to their prolonged T1 and T2 [7,8]. In some infarcts, high signal is observed on T1-weighted spin-echo images and this was once thought to represent haemorrhagic infarction [1,2]. Haemorrhagic infarcts show characteristic signal changes similar to those of brain haemorrhage, due to deoxyhaemoglobin, methaemoglobin and haemosiderin [9,10]. Petechial haemorrhage may occur in infarcts but cannot explain all brain infarcts with a short T1 [4, 6, 11]. High signal on T1-weighted spin-echo images may represent methaemoglobin, paramagnetic substances, fat, calcification or a high protein concentration [5,6].

Methaemoglobin in haemorrhagic infarcts can be differentiated from nonhaemorrhagic short-T1 lesions

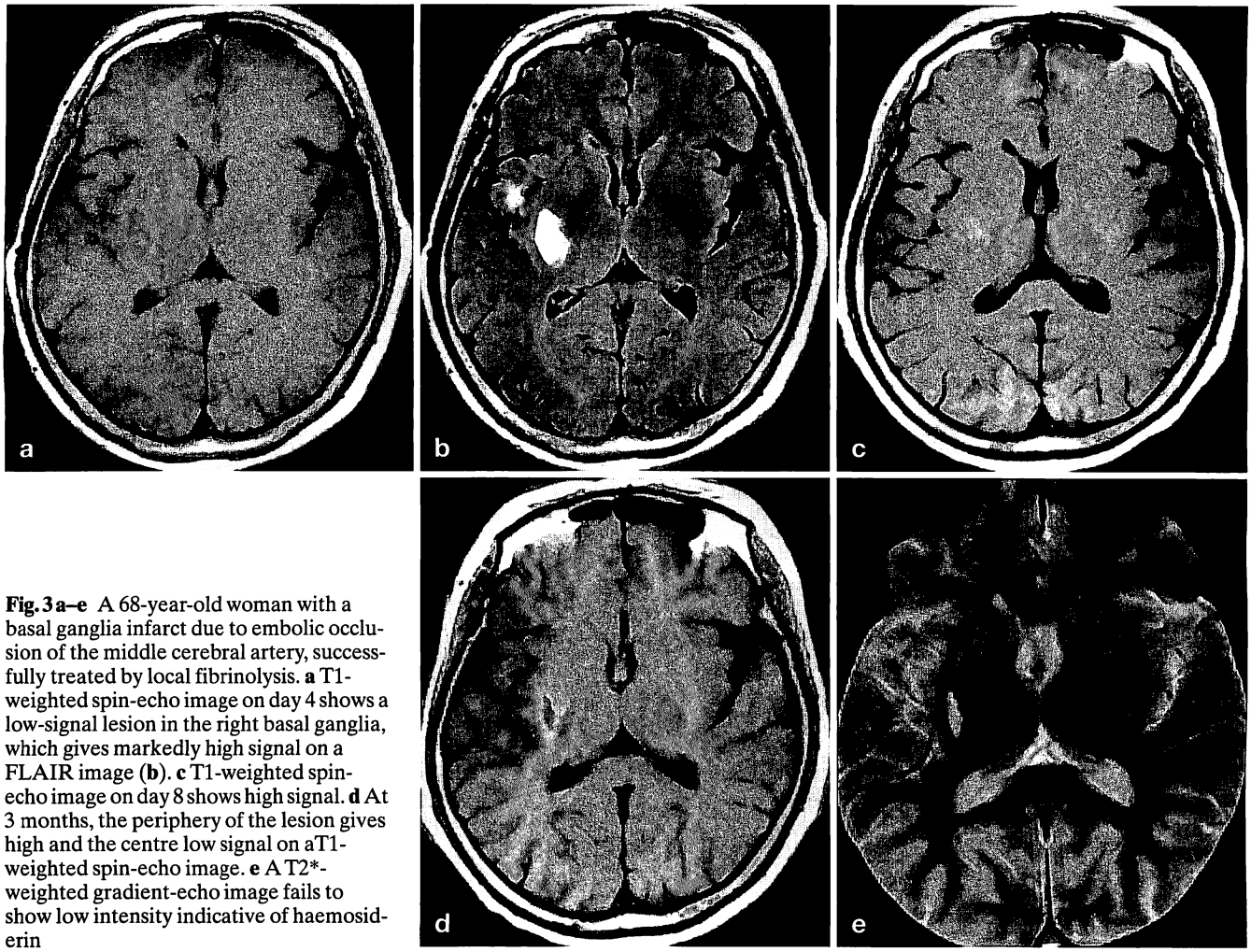

Fig. 3 a–e A 68-year-old woman with a basal ganglia infarct due to embolic occlusion of the middle cerebral artery, successfully treated by local fibrinolysis. **a** T1-weighted spin-echo image on day 4 shows a low-signal lesion in the right basal ganglia, which gives markedly high signal on a FLAIR image (**b**). **c** T1-weighted spin-echo image on day 8 shows high signal. **d** At 3 months, the periphery of the lesion gives high and the centre low signal on aT1-weighted spin-echo image. **e** A T2*-weighted gradient-echo image fails to show low intensity indicative of haemosiderin

by T2*-weighted gradient-echo imaging, which may show haemosiderin as low signal in the chronic stage. Paramagnetic substances potentially shorten both T1 and T2 by preferential relaxation enhancement [12], but probably do not contribute to nonhaemorrhagic short-T1 lesions, since T2*-weighted gradient-echo images do not show a T2* effect. Fat does not contribute to cortical T1 shortening because cortical lesions consistently display high intensity on FLAIR images even after they become iso-intense on T1-weighted spin-echo images. Although calcified lesions occasionally show high signal on T1-weighted spin-echo images [6,13], disappearance of short T1 signals in the chronic stage, absence of high-density lesions on CT [3], lack of T2* effect on T2*-weighted gradient-echo images and absence of any histological evidence of calcification [6] indicate that cortical short-T1 lesions are not caused by calcification. Although the true mechanism of T1 shortening in cortical laminar necrosis is not clear, high signal on T1-weighted spin-echo images is believed to be caused by neuronal damage, reactive change of glia and deposition of fat-laden macrophages [11,14].

Tissue damage in brain ischaemia is generally classified into selective neuronal cell death and pan-necrosis (or infarction). Although histological examination reveals that cortical short T1 lesions represent pan-necrosis [4,6], selective involvement of the central and cortical grey matter strongly suggests that neuronal cell death in these locations is the major cause of T1 shortening. In general, high concentrations of proteins or other macromolecules enhance relaxivity by restricting the motion of water molecules, thus causing T1 shortening (protein hydration-layer effect) [13, 15, 16]. Even a small increase in protein concentration may cause significant T1 shortening. Neuronal cell death and associated pathological changes such as denaturation of proteins and cellular components from the infarcted tissue in the cortical grey matter, are postulated to contribute to T1 shortening [5]. Denatured proteins and cellular components from dead neurones may contrib-

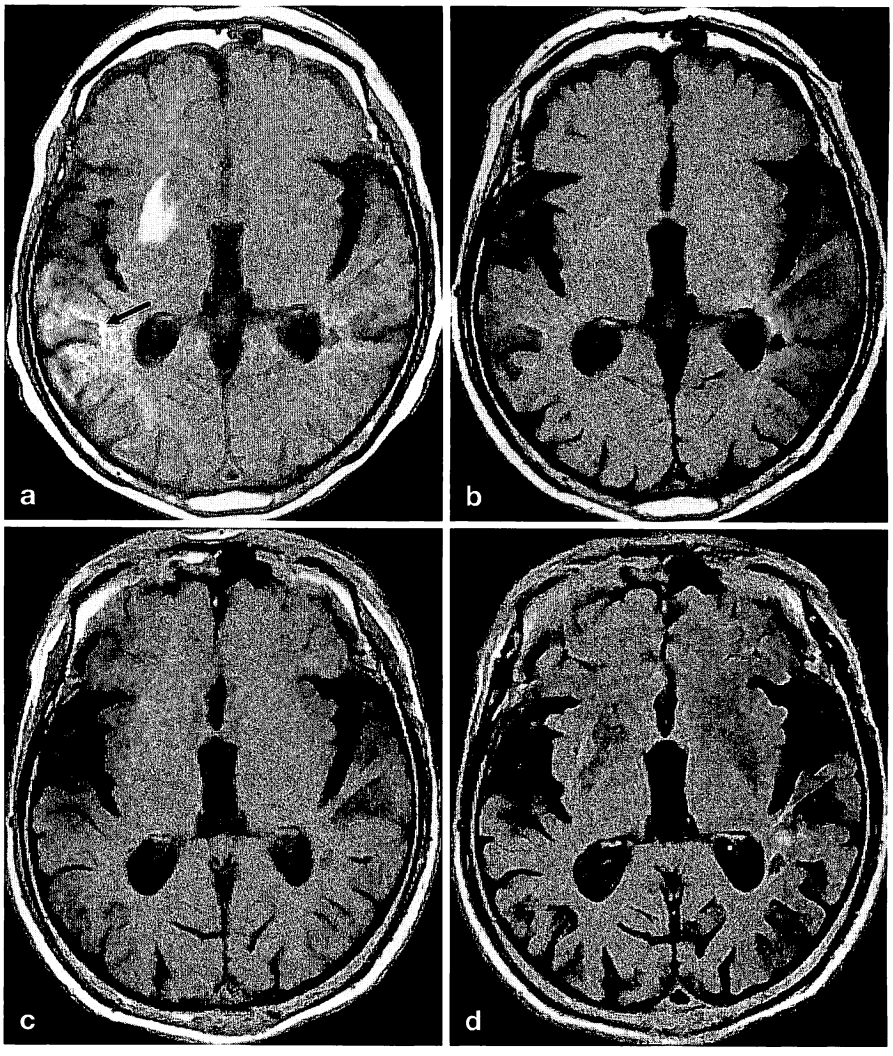

Fig. 4a–d A 74-year-old man with a basal ganglia infarct. **a** A T1-weighted spin-echo image at 1.5 months shows high signal in the right basal ganglia. Cortical high signal is also seen (*arrow*). **b** A T1-weighted image at 5 months shows a smaller high-signal focus. **c** A T1-weighted image at 9 months shows no high signal, but **d** a FLAIR image does

ute to the short T1 of cerebral cortical lesions and could be retained in the macrophages for a long period, which could contribute to persistent high signal on T1-weighted spin-echo images. We postulate that neuronal cell death is also strongly related to short T1 lesions in the cerebellar cortex and basal ganglia.

Types of brain infarct which cause T1 shortening

In brain infarcts, some lesions in the grey matter show evidence of a short T1, but others do not. Although the mechanism of such differences is unknown, we speculate that temporary, profound ischaemia and early reperfusion or collateralisation may play significant roles in the production of short-T1 lesions in the grey matter, because many of our patients with short-T1 lesions had embolic strokes, with high recanalisation rates. Delayed appearance of short-T1 lesions could be caused by delayed neuronal cell death, while persistent ischaemic insults lead to pan-necrosis with a long T1.

We hypothesise that the mechanisms of production of short-T1 lesions in brain infarcts are: transient profound ischaemia and recanalisation, resulting in a disturbance of calcium homoeostasis of the neurones and release of excitotoxic amino-acids at synapses , followed by neuronal cell death. Specific denatured proteins from structural components of the neurones appear to have a short T1 on MRI, due to the protein hydration-layer effect. These denatured proteins remain in isolated forms or in macrophages for several months to 1 or 2 years, then move elsewhere or change their structure. We believe, however, that a study employing histochemical correlation is required to verify this hypothesis.

References

1. Nabatame H, Fujimoto N, Nakamura K, et al (1990) High intensity areas on noncontrast T1-weighted MR images in cerebral infarction. J Comput Assist Tomogr 14: 521–526
2. Fujioka M, Okuchi K, Sakaki T, Hiramatsu K, Miyamoto S, Iwasaki S (1994) Specific changes in human brain following reperfusion after cardiac arrest. Stroke 25: 2091–2095
3. Komiyama M, Nishikawa M, Yasui T (1997) Cortical laminar necrosis in brain infarcts: chronological changes on MRI. Neuroradiology 39: 474–479
4. Kinoshita T, Okudera T, Yoshida Y, et al (1998) Cortical laminar necrosis in cerebral infarcts: MRI. Neuroradiology 40: 609
5. Komiyama M, Nakajima H, Nishikawa M, Yasui T (1998) Serial MR observation of cortical laminar necrosis caused by brain infarction. Neuroradiology 40: 771–777
6. Boyko OB, Burger PC, Shelburne JD, Ingram P (1992) Non-heme mechanisms for T1 shortening: pathologic, CT, and MR elucidation. AJNR 13: 1439–1445
7. Sipponen JT (1984) Visualization of brain infarction with nuclear magnetic resonance imaging. Neuroradiology 26: 387–391
8. Brant-Zawadzki M, Weinstein P, Bartkowski H, Moseley M (1987) MR imaging and spectroscopy in clinical and experimental cerebral ischemia: a review. AJNR 8: 39–48
9. Hecht-Leavitt C, Gomori JM, Grossman RI, et al (1986) High-field MRI of hemorrhagic cortical infarction. AJNR 7: 581–585
10. Hesselink JR, Healy ME, Dunn WM, Rothrock JF, McCreight PHB, Brahme F (1986) Magnetic resonance imaging of hemorrhagic cerebral infarction. Acta Radiol (Suppl) 369: 46–48
11. Takahashi S, Higano S, Ishii K, et al (1993) Hypoxic brain damage: cortical laminar necrosis and delayed changes in white matter at sequential MR imaging. Radiology 189: 449–456
12. Brasch RC (1983) Contrast enhancement in NMR imaging. In: Newton TH, Potts DG (eds) Advanced imaging techniques. Clavadel Press, San Anselmo, CA, pp 63–79
13. Henkelman RM, Watts JF, Kucharczyk W (1991) High signal intensity in MR images of calcified brain tissue. Radiology 179: 199–206
14. Sawada H, Udaka F, Seriu N, Shindou K, Kameyama M, Tsujimura M (1990) MRI demonstration of cortical laminar necrosis and delayed white matter injury in anoxic encephalopathy. Neuroradiology 32: 319–321
15. Daszkiewicz OK, Hennel JW, Lubas B (1963) Proton magnetic relaxation and protein hydration. Nature 200: 1006–1007
16. Abe K, Hasegawa H, Kobayashi Y, Fujimura H, Yorifuji S, Bitoh S (1990) A gemistocytic astrocytoma demonstrated high intensity on MR images. Protein hydration layer. Neuroradiology 32: 166–167