

Case report

## Laminar cortical necrosis in adrenal crisis: Sequential changes on MRI

Yoshiaki Saito <sup>a,\*</sup>, Toshihide Ogawa <sup>b</sup>, Jun-ichi Nagaishi <sup>c</sup>, Takehiko Inoue <sup>a</sup>,  
Yoshihiro Maegaki <sup>a</sup>, Kousaku Ohno <sup>a</sup>

<sup>a</sup> Division of Child Neurology, Institute of Neurological Sciences, Faculty of Medicine, Tottori University, 36-1 Nishi-cho, Yonago 683-8504, Japan

<sup>b</sup> Division of Radiology, Faculty of Medicine, Tottori University, Japan

<sup>c</sup> Division of Pediatrics and Perinatology, Faculty of Medicine, Tottori University, Japan

Received 22 January 2007; received in revised form 27 April 2007; accepted 11 May 2007

### Abstract

We describe the serial magnetic resonance imaging (MRI) findings in a six-year-old girl with congenital adrenal hyperplasia, who presented with seizures and unconsciousness during a hypoadrenal crisis. Initial neuroimaging revealed the presence of brain edema with high signal changes in the fronto-parietal cortex on diffusion-weighted MRI. The brain edema worsened four days into admission, and by day 14 low-density areas were seen over the frontal lobes bilaterally using computed tomography (CT). Follow-up MRI at between one and two months of admission revealed extensive white matter lesions with high intensity on T2-weighted images (T2WI) and fluid-attenuated inversion recovery (FLAIR) images, which extended into deep cortical layers. Additionally, linear lesions with high signal change on T1-weighted imaging developed in the superficial cortical layers, with frontal predominance. This layer appeared isointense on T2WI and high intensity on FLAIR images, suggesting laminar cortical necrosis. Two months later, linear, cavitory lesions appeared in the middle cortical layers between the aforementioned superficial laminar abnormality and deep cortex/white matter lesions. The high-intensity signals in the deep cortical layers remained contiguous with the white matter lesions. This unique type of multi-layered cortical lesion may have resulted from a complex combination of hypoglycemia and hypoxia/ischemia in the setting of adrenal insufficiency.

© 2007 Elsevier B.V. All rights reserved.

**Keywords:** Laminar necrosis; Congenital adrenal hyperplasia; Brain edema

### 1. Introduction

Cortical laminar necrosis has been identified in conditions with energy depletion and metabolic changes, including hypoxia/ischemia, epilepsy, hypoglycemia, hyponatremia, and mitochondrial disorders. The laminar pattern of distribution has been attributed to the selective vulnerability of neurons to these insults, and preferential involvement of middle to deep cortical

layers has been suggested in the case of hypoxia/ischemia [1]. On the other hand, cortical lesions in hypoglycemia and epilepsy can selectively involve the second/third and third/fourth cortical layers, respectively [1]. This differential involvement of specific layers has been discussed on the basis of histological observations; however, no such correlation has been reported using neuroimaging. In this report, we describe a serial radiological study of a patient presenting with an adrenal crisis, where differential damage of cortical layers was identified with a characteristic pattern of multi-laminae lesions in the cortical mantle.

\* Corresponding author. Tel.: +81 859 38 6777; fax: +81 859 38 6779.

E-mail address: [saitoyo@grape.med.tottori-u.ac.jp](mailto:saitoyo@grape.med.tottori-u.ac.jp) (Y. Saito).

## 2. Case report

A six-year-old girl with congenital adrenal hyperplasia developed convulsions and unconsciousness during a bout of gastroenteritis, and was admitted to our hospital. Her clinical course has been reported previously, with a focus on the neurological symptoms during her recovery phase [2]. On admission, the patient presented with clonic seizures, cyanosis, irregular respiration, and hypotension, and was immediately treated with infusions of glucose, hydrocortisone, and diazepam. Blood samples were taken after these infusions and analysis revealed the following data: pH 7.198,  $\text{PCO}_2$  40.0 mmHg,  $\text{HCO}_3^-$  14.2 mEq/L, Na 131 mEq/L, K 5.0 mEq/L, glucose 181 mg/dL, and lactate 4.5 mmol/L, AST 113 IU/L, ALT 93 IU/L, CK 607 IU/L, BUN 43 mg/dL, creatinine 1.0 mg/dL, and adrenocorticotropic hormone 1170 pg/mL (normal 4.4–48.0). Computed tomography (CT) revealed the presence of brain edema (Fig. 1A), and initial magnetic resonance imaging (MRI) showed high-signal intensity in the fronto-parietal cerebral cortex on T2- and diffusion-weighted images (DWI) (Fig. 2A and B). Restricted diffusivity was observed on apparent diffusion coefficient (ADC) mapping in these areas (Fig. 2C). Despite antihydrotic treatment including mild hypothermia therapy, brain edema worsened (Fig. 1B) on day 5 of admission, and necessitated artificial ventilation. Light and ciliary reflexes disappeared, but re-emerged by day 10 of admission.

During the recovery period, low-density areas in the frontal lobes were noted on CT (Fig. 1C). MRI at one and two months after admission revealed a progressive ventricular dilatation, and linear high-intensity signals on the T1-weighted images (T1WI, Fig. 2D) and fluid-attenuated inversion recovery (FLAIR, Fig. 2F) images in the cerebral cortex, predominantly at the bottom of sulcus (arrows in Figs. 2D and 3C). Widespread lesions with hypointensity on T1WI, and hyperintensity on T2WI and FLAIR images, were also noted in the white

matter, with pericentral gyri being spared bilaterally (Fig. 2D–F). Close inspection revealed that the lamina with hyperintensity on T1WI and FLAIR imaging showed isointensity on T2WI, and was apparently confined to the superficial thin layer of the cortex when compared to the thickness of cortical mantle on the initial imaging (Fig. 3A–E). Deep cortical layers showed hypointensity on T1WI and hyperintensity on T2WI and FLAIR imaging, and the boundary between these deep layers and the white matter had become obscured. In addition, a lamina with iso/low intensity on FLAIR imaging appeared between these high-intensity signals in the superficial and deep layers (Fig. 3E, arrowheads). Inspection of the thickness of the superficial bands (Fig. 3C–E) revealed that this middle cortical lamina showed hypointensity on T1WI that was contiguous with the deeper layers of the cortex, and isointensity on T2WI that was indistinguishable from the superficial lamina. Follow-up MRI at four and seven months after the initial event revealed that the signal intensity of this middle lamina had changed, and now displayed a pattern of hypointensity on T1WI and FLAIR images, and hyperintensity on T2WI in multiple areas (arrows in Fig. 3F–H). This type of lesion was often present at the crests of gyri, in contrast to the hyperintense lesions on T1WI in earlier studies (Fig. 2D and 3C, arrows). The hyperintensity on T1WI in the superficial lamina became ambiguous. Cortical atrophy was predominant at the bottom of each sulcus, resulting in a mushroom-like appearance of cortical gyri during this period. The lesions in the deep cortex and white matter did not show significant change during this time. Progressive atrophy of the caudate nucleus was noted, but signal change was not evident in this structure. Mild atrophy of the cerebellar cortex also appeared (not shown), but otherwise subtentorial structures were preserved.

The patient regained the ability to eat and walk by six months, but showed no interest in the surroundings, and was unable to utter meaningful words.

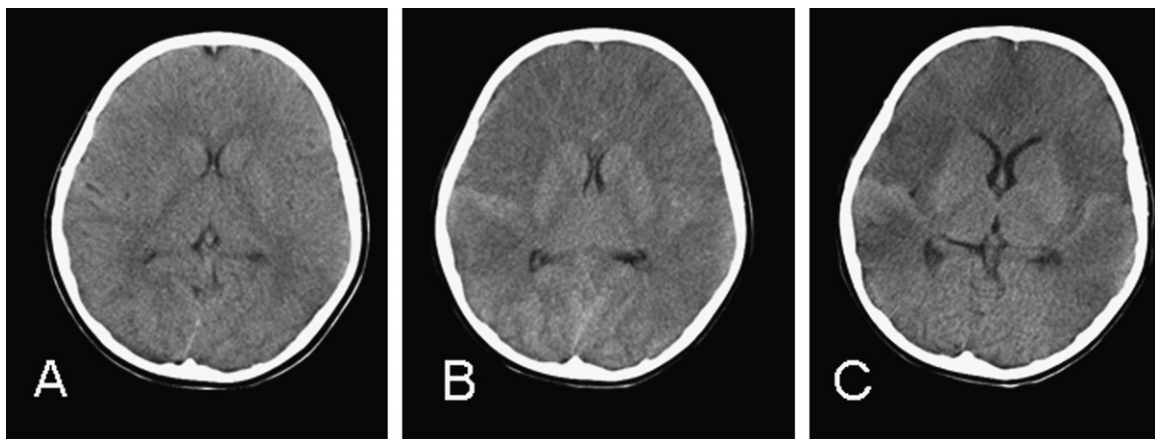


Fig. 1. Brain computed tomography (CT) of the patient. (A) Day 1. (B) Day 5. (C) Day 15 of admission.

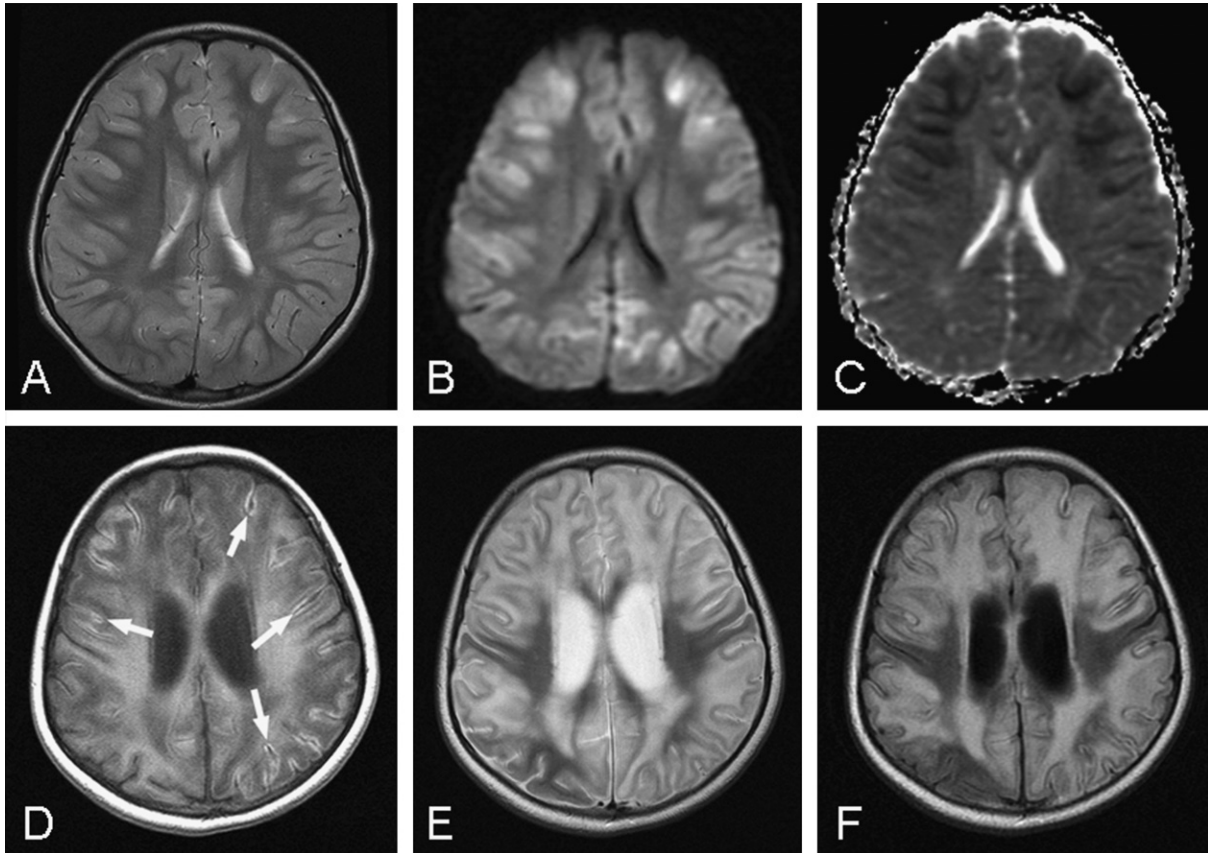


Fig. 2. Brain magnetic resonance imaging (MRI) of the patient. (A–C) Day 2. (D–F) Day 34 of admission. (A,E) T2-weighted imaging (T2WI). (B) Diffusion-weighted imaging. (C) Apparent diffusion coefficient map. (D) T1-weighted imaging (T1WI). (F) Fluid-attenuated inversion recovery (FLAIR) imaging. Arrows in (D) show the high-intensity signals in the superficial layer of the cortex.

### 3. Discussion

The linear high-intensity signals on T1WI in the superficial cortical layers in this patient, which appeared one month after the initial episode, are compatible with the finding of laminar cortical necrosis. This signal change on MRI is commonly associated with cortical laminar necrosis caused by different types of insults, and has been attributed to the presence of fat-laden macrophages or increased/denatured proteins [3,4]. Although this condition has been reported before in a rare case of hypoadrenal crisis with severe hyponatremia [5], our patient did not display significant electrolyte disturbances. The pattern of superficial distribution may rather suggest the role of hypoglycemia, which usually accompanies hypoadrenal crises and can selectively involve these cortical layers [1,6]. Release of aspartate in place of glutamate, and lack of lactate elevation due to the absence of substrate glucose, may lead to a pathology that is different from hypoxic insults [7]. Neuro-pathological reports indicate that neurons in deeper cortical layers are the most susceptible to hypoxia. However, laminar necrosis in superficial cortical layers has also been found on MRI in occasional cases of hypoxia

(see figures in [3] and [4], although there are no comments regarding which layer is involved). In turn, the superficial layer involvement in hypoglycemic encephalopathy has been exclusively identified by histological examination, and no correlation on MRI has been described. Since the presence of hypoxia aggravates the brain injury due to hypoglycemia [8], both these factors may have been acting together in the cortical lesions in our patient. In any case, further analysis is necessary regarding the intra-cortical distribution of laminar lesions in hypoxic and hypoglycemic encephalopathies, for a better understanding of brain injury in these conditions.

The second laminar lesion in the middle cortical layers appeared one month into the illness, seen as hypointensity on T1WI and FLAIR images, and isointensity on T2WI. We first regarded this lamina as relatively preserved cortical layers between the superficial laminar necrosis and the deep cortex/white matter lesion. However, this lamina progressed to form linear, cavitory lesions a few months later (Fig. 3E and H). Similar cavity formation beneath laminar necrosis has been described in patients with brain infarcts [3], and interpreted as encephalomalacia of the subcortical white matter. However, the distribution of this laminar lesion was

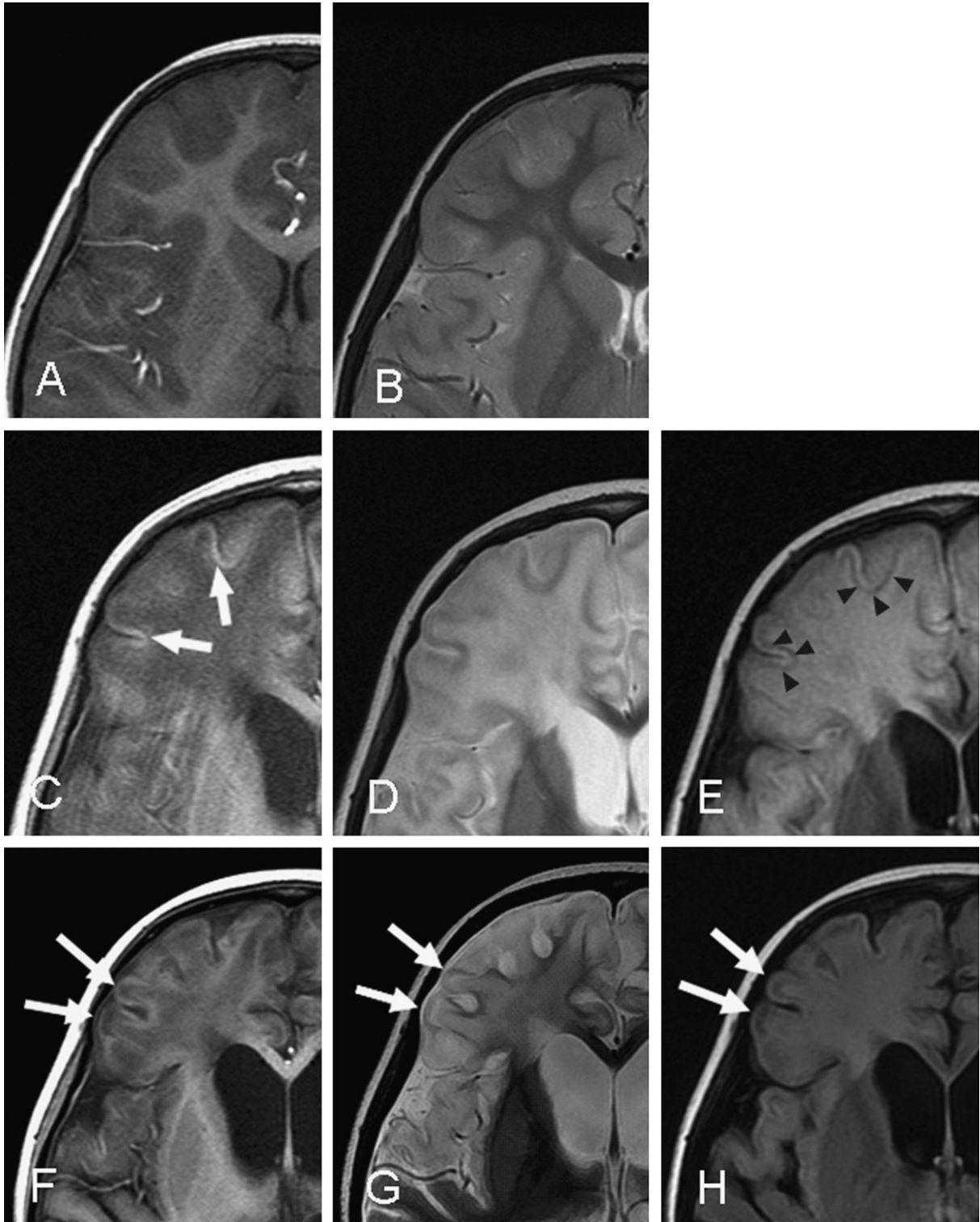


Fig. 3. Sequential MRI changes of cortical lesions. (A,B) Day 2. (C–E) Day 34. (F–H) Day 125 of admission. (A,C,F) T1WI. (B,D,G) T2WI. (E,H) FLAIR imaging. Arrows in (C) show the superficial high-intensity at the bottom of cortical sulci. Note that the high-intensity band is thin compared to the thickness of cortical mantle on submission (A,B). Arrowheads in (E), and arrows in (F–H), indicate a lamina beneath the superficial lesion in (C), indicating the formation of second laminar lesion beneath the initial cortical laminar necrosis.

different from that of the superficial laminar necrosis in our case; i.e., (1) the lesion in the present patient was predominant at the bottom of sulcus and the former

emerged at the top of a gyrus, and (2) it was present in some, not all gyri, whereas the lesions in brain infarcts showed more diffuse distribution. The distribution of

superficial laminar necrosis may be related to the fact that either hypoglycemia [6] or hypoxia/ischemia [4] can affect the cerebral cortex predominantly at the bottom of the sulcus. Apparently, there are different processes for these two types of laminar lesions. The third lamina exhibited signal changes contiguous with the white matter lesions, which may have resulted from either hypoxic [9] or hypoglycemic [10] insults. However, we could not specify the causative pathogenesis for these middle- and deep-cortical lesions.

In summary, we could identify three-layered cortical lesions on the MRI of a patient following an adrenal crisis. The combination of hypoxia/ischemia and hypoglycemia may have contributed to a complex pathogenesis, leading to this characteristic pattern of cortical lesions.

## References

- [1] Auer RN, Siesjö BK. Biological differences between ischemia, hypoglycemia, and epilepsy. *Ann Neurol* 1988;24:699–707.
- [2] Okamoto R, Saito Y, Inoue T, Maegaki Y, Nagaishi J, Ohno K. Forced mouth opening reaction: a primitive reflex released from cortical inhibition. *Brain Dev* 2006;28:272–4.
- [3] Komiyama M, Nakajima H, Nishikawa M, Yasui T. Serial MRI observation of cortical laminar necrosis caused by brain infarction. *Neuroradiology* 1998;40:771–7.
- [4] Kinoshita T, Ogawa T, Yoshida H, Tamura H, Kado H, Okudera T. Curvilinear T1 hyperintense lesions representing cortical necrosis after cerebral infarction. *Neuroradiology* 2005;47:647–51.
- [5] Shoji M, Kimura T, Ota K, Ohta M, Sato K, Yamamoto T, et al. Cortical laminar necrosis and central pontine myelinolysis in a patient with Sheehan syndrome and severe hyponatremia. *Internal Med* 1996;35:427–31.
- [6] Lawrence RD, Meyer A, Nevin S. The pathological changes in the brain in fatal hypoglycaemia. *Q J Med NS* 1942;11:181–201.
- [7] Auer RN, Benveniste H. Hypoglycaemic brain damage. In: Graham DI, Lantos PL, editors. *Greenfield's Neuropathology*. London: Arnold; 1997. p. 285–8.
- [8] de Courten-Myers GM, Xi G, Hwang JH, Scott Dunn R, Millis AS, Holland SK, et al. Hypoglycemic brain injury: potentiation from respiratory depression and injury aggravation from hyperglycemic treatment overshoots. *J Cereb Blood Flow Metab* 2000;20:82–92.
- [9] Sawada H, Udaka F, Seriu N, Shindou K, Kameyama M, Tsujimura M. MRI demonstration of cortical laminar necrosis and delayed white matter injury in anoxic encephalopathy. *Neuroradiology* 1990;32:319–21.
- [10] Mori F, Nishie M, Houzen H, Yamaguchi J, Wakabayashi K. Hypoglycemic encephalopathy with extensive lesions in the cerebral white matter. *Neuropathology* 2006;26:147–52.