
CASE REPORT

Computed Tomography of Hypoxic-ischaemic Brain Injury in Infants, Children, and Adults: Three Illustrative Cases and Literature Review

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ABSTRACT

Global hypoxic-ischaemic injuries to the brain are devastating and result in high mortality and morbidity in both children and adults. We report three cases from different causes of hypoxic-ischaemic injury to the brain in these age-groups. Computed tomography plays an important role in the diagnosis and acute management of this condition. Diffuse hypodense changes with effacement of the cerebrospinal spaces, decreased cortical gray matter attenuation with loss of normal gray-white differentiation, the 'reversal sign' and 'white cerebellum sign' can all be discerned by computed tomography. However, such changes can be subtle and may mimic other conditions such as subarachnoid haemorrhage and dural sinus thrombosis. Magnetic resonance imaging, including conventional T1- and T2-weighted images, diffusion-weighted imaging and proton spectroscopy are accurate and useful modalities for further evaluating hypoxic-ischaemic brain injury in cases with no overt computed tomography abnormalities. To facilitate prompt patient management, recognition of differing imaging features in infants / young children versus older children / adults is crucial for radiologists and clinicians.

Key Words: Child, preschool; Hypothermia, induced; Hypoxia-ischemia, brain; Tomography, X-Ray Computed

中文摘要

替缺氧缺血性腦損傷的嬰兒、小童及成人作電腦斷層掃描： 三個病例報告及文獻回顧

尹宇瀚、岑承輝、盧成璋、李仲啟、施雅倫、朱志揚、賈亦尊、鄭志成

缺氧缺血性腦損傷無論對小童或成人的破壞性都很大，導致高罹病率及死亡率。本文報告三宗因不同成因而導致缺氧缺血性腦損傷的病例。電腦斷層造影對於分析及緊急處理這類腦損傷扮演著很重要的角色。瀰漫性低密度改變伴有腦脊髓液空間消失會令皮層灰質密度衰減，繼而使灰質 / 白質失去正常的密度差異。電腦斷層造影可以顯示「反轉徵」及「白色小腦徵」。可是這些變化可以極細微，可能被誤以為是蛛網膜下腔出血和腦靜脈竇栓塞。磁力共振影像（包括常規的T1加權及T2加

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Submitted: 16 Aug 2010; Accepted: 22 Nov 2010.

權)、彌散加權成像及氫質子磁振頻譜都能準確地評估一些缺氧缺血性腦損傷而又無明顯異常CT的病人。要盡快處理病者，臨床醫生和放射科醫生必須要認識嬰兒/小童以及年青人/成人不同的放射學徵狀。

INTRODUCTION

Global hypoxic-ischaemic injuries to the brain are devastating and result in high mortality and morbidity in children and in adults, for whom computed tomography (CT) plays an important role in diagnosis and acute management. CT changes, however, may be subtle and can mimic other conditions such as subarachnoid haemorrhage and dural sinus thrombosis. Recognising the specific features is crucial for prompt patient management.

CASE REPORTS

Herein, we report three cases of hypoxic-ischaemic brain injury resulting from different causes.

The first patient was a four-month-old baby girl born full-term by normal spontaneous delivery with no previous neonatal problem. She presented with sudden collapse and cardiac arrest, after her father noticed that she was lying in prone position with her face down when asleep. She was sent to the hospital, resuscitated and admitted to the Paediatric Intensive Care Unit. Later, non-contrast CT of the brain was performed. The CT showed the ‘reversal sign’ with loss

of gray-white matter differentiation in both cerebral hemispheres (Figure 1a). The midbrain was hypodense and the cerebellum, pons, and medulla were relatively hyperdense. The radiological features were consistent with global hypoxia (Figure 1b).

The second patient was a 16-year-old girl with Down’s syndrome who suffered choking after food intake (five pieces of “dim sum”) and collapsed. Resuscitation was initiated and she was sent to the Accident and Emergency Department and had subsequent non-contrast CT brain.

The third patient was a 41-year-old schizophrenic man who attempted suicide by hanging. He was transferred to the Accident and Emergency Department and resuscitated. Later, non-contrast CT of the brain was performed.

The images of the second and third patients showed similar findings, namely: diffuse hypodense changes in the brain and cerebellum, more marked over the thalami and midbrain, which suggested hypoxic brain injury

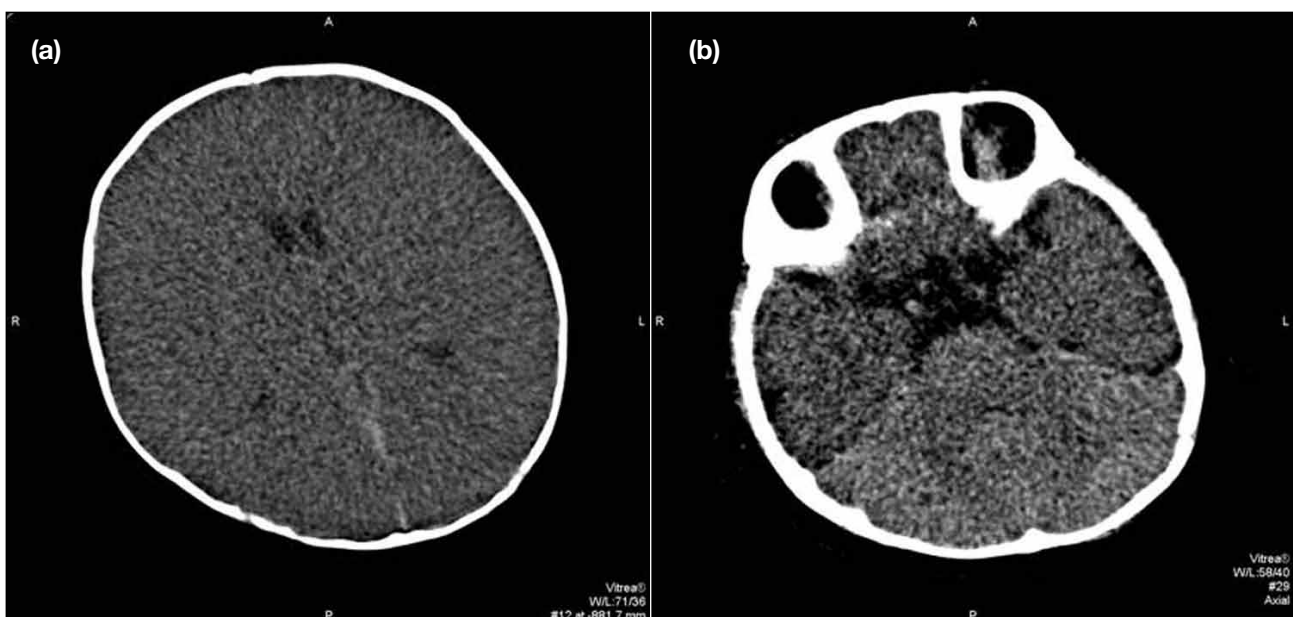


Figure 1. A four-month-old baby girl presented with sudden collapse and cardiac arrest when sleeping prone. Non-contrast axial computed tomographic scans of the brain show (a) loss of gray-white matter differentiation in the cerebral hemispheres bilaterally, with diffuse hypodense changes, and (b) the ‘reversal sign’ with the cerebral hemisphere and midbrain being hypodense, and the cerebellum, pons, and medulla being relatively hyperdense.

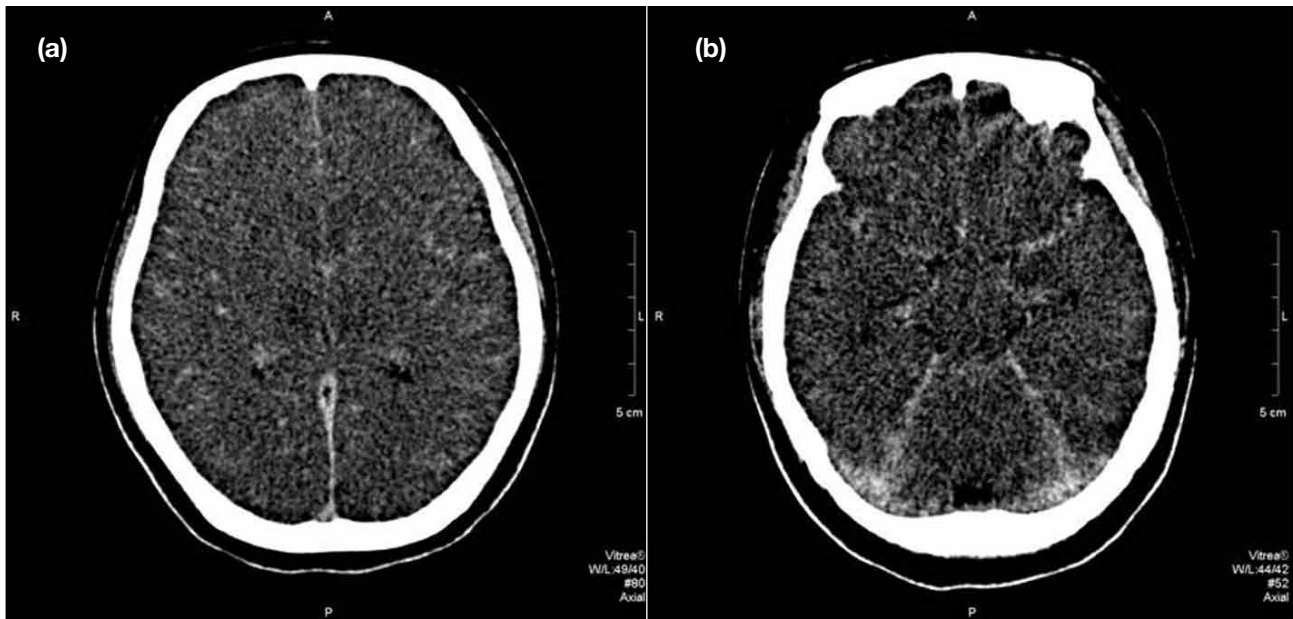


Figure 2. A 16-year-old girl with Down's syndrome suffered from choking and collapse after food intake. Non-contrast axial computed tomographic scans of the brain show (a) diffuse hypodense changes suggestive of hypoxic brain injury, more evident over the thalami and midbrain, and (b) apparent hyperdensities over the cisterns, falx cerebelli and vascular structures mimicking findings of acute subarachnoid haemorrhage and dural sinus thrombosis.

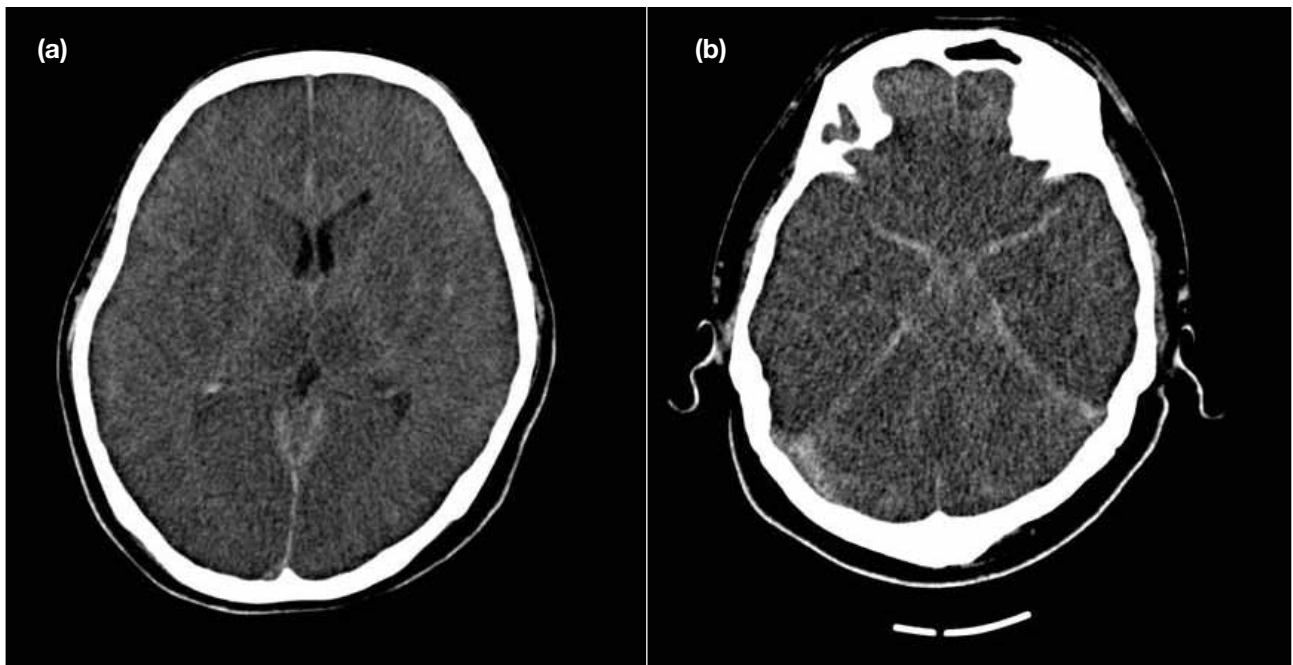


Figure 3. A 41-year-old man with schizophrenia who attempted suicide by hanging himself. Non-contrast axial computed tomographic scans of the brain show (a) diffuse hypodense changes suggestive of hypoxic brain injury, more prominent over the thalami, and (b) apparent hyperdensities over the cisterns, falx cerebelli and vascular structures mimicking findings of acute subarachnoid haemorrhage and dural sinus thrombosis.

(Figures 2a, 3a). Notably, there were hyperdensities over the cisterns, falx cerebri, falx cerebelli and vascular structures, which mimicked findings encountered in acute subarachnoid haemorrhage and dural sinus

thrombosis. The imaging appearance was actually accounted for by the relative hypodensity of the brain parenchyma that formed a contrasting background (Figures 2b, 3b).

DISCUSSION

Treatment of hypoxic-ischaemic injury to the brain mainly relies on supportive care designed to avoid ongoing injury immediately following the causative insult. Promising recent neuroprotective strategies including hypothermia and administration of excitatory amino acid antagonists are under investigation, and may further restrict the extent of brain injury, but the window of effectiveness for such interventions is limited, rendering early recognition of the injury essential.^{1,2}

The radiological patterns of hypoxic-ischaemic insult to the brain are different between older children and adults, as opposed to infants and young children.³ Selective vulnerability to hypoxic ischaemic injury is dependent on the maturity of the brain.^{4,5}

In infants and young children, asphyxial events are more common, resulting in hypoxaemia and brain hypoxia. Prolonged hypoxaemia affects the heart and a reduced cardiac output results in brain ischaemia. The brain insult due to asphyxia is therefore the consequence of ischaemia superimposed on hypoxia. The 'reversal sign' — reversal of the normal attenuation of gray and white matter — is revealed by CT in these patients. This appearance is believed to be related to the distension of deep medullary veins due to partial obstruction of venous outflow as a result of an elevated intracranial pressure caused by diffuse oedema. The 'white cerebellum sign' is attributed to diffuse oedema and hypoattenuation of the cerebral hemispheres with sparing of the cerebellum and brainstem, resulting in apparent high attenuation relative to the cerebrum. It has been described as a component of the reversal sign. This phenomenon is possibly related to redistribution of blood to the posterior circulation during anoxic events. Both signs are indicative of severe injuries and a poor prognosis.^{6,7}

In adults, hypoxic-ischaemic brain injuries are usually due to cardiac arrest or cerebrovascular disease leading to secondary hypoxaemia. In older children, drowning and asphyxiation are the common causes.⁵ Mild-to-moderate global ischaemic brain injury typically leads to infarction of watershed areas. In this population, severe insults predominantly affect the deep gray matter nuclei, basal ganglia, thalami, cerebral cortices, cerebellum, and hippocampi. The predominance of gray matter injury is attributed to gray matter being more active metabolically than white matter (due

to synaptic activity); gray matter contains most of the dendrites with postsynaptic glutamate receptors that are most susceptible to the effects of glutamate excitotoxicity. Cerebellar injury is also more common in older patients. The relative immaturity of Purkinje cells in young infants, which are sensitive to ischaemic damage, appears to confer a protective effect on the cerebellar cortex.^{8,9} Other consequences of hypoxic-ischaemic injury to the brain revealed by CT include decreased cortical gray matter attenuation with loss of normal gray-white differentiation, diffuse oedema with effacement of cerebrospinal spaces, and decreased basal ganglia attenuation bilaterally. The 'reversal sign' and the 'white cerebellum sign' that are more typical in young children may also be seen in adults, and signify severe injury and a poor prognosis.

Magnetic resonance (MR) imaging is an accurate imaging modality for further evaluating hypoxic-ischaemic brain injury.

For infants and young children, conventional T1- and T2-weighted images can be unremarkable up to about 2 days after the insult. If imaged after 48 hours, diffuse basal ganglia and cortical signal abnormality that represents oedema is usually seen in T2-weighted images. Diffusion-weighted imaging is a sensitive means of detecting insult in the first 24 hours, when conventional T1- and T2-weighted images may be unremarkable. Hyperintense signals in the posterolateral lentiform nuclei and thalami involving the ventrolateral nuclei may be seen early on after the injury. Progressive involvement of remaining basal ganglia tissue and the cortex is typically noted in the following 48 hours.¹⁰

In older children and adults, conventional T1- and T2-weighted images can also appear normal; abnormalities being very subtle. Increased signal intensity and swelling of injured gray matter structures in T2-weighted images can be seen in subacute settings after 48 hours and may persist until the second week. Residual hyperintensity over the basal ganglia in T2-weighted images and areas of high signal intensity in the cortex suggesting cortical necrosis in T1-weighted images may be seen in the chronic stages post-injury. Diffusion-weighted imaging is again the earliest modality to become positive during the first 24 hours. It shows up as increased signal intensity in the cerebellar hemispheres, basal ganglia, cerebral cortex, thalami, brainstem, and hippocampi.⁸

If a negative diffusion-weighted MR image in the first 24 hours seems implausible, a follow-up scan should be performed after two to four days, when diffusion abnormalities tend to be greatest.¹⁰ Evaluation by proton MR spectroscopy may also be considered. When performed in the first 24 hours after a hypoxic-ischaemic event, this modality is more sensitive and more indicative of severe injury, whilst conventional and diffusion-weighted MR imaging may yield false negatives or underestimate the extent of injury. In general, elevation of lactate and glutamine-glutamate, and decreased N-acetylaspartate are worrisome spectroscopic findings. These abnormalities correlate with a grave prognosis, including persistent vegetative state or death.¹¹

An imaging protocol should be implemented as different modalities have their pros and cons. Despite being more readily available, convenient, and readily performed shortly after the insult, CT is less sensitive for detecting the extent of injury as compared to MR imaging. Presence of ionising radiation is another concern about CT. On the other hand, performing MR studies may be logistically difficult due to limited availability in hospitals other than tertiary centres, as well as the need to transfer, monitor, and sedate patients.¹² A generally accepted algorithm for older infants, children, and adults with suspected hypoxic-ischaemic brain injury is to start with a non-contrast CT. If findings are positive, usually no additional MR imaging is deemed necessary. In patients with negative CT findings, MR should be performed for further evaluation.³

CONCLUSION

Hypoxic-ischaemic injury to the brain are life-threatening, often confers high morbidity, including profound long-term neurological disability. Diffuse hypodense changes with effacement of cerebrospinal spaces, decreased cortical gray matter attenuation with

loss of normal gray-white differentiation, the 'reversal sign', and the 'white cerebellum sign' are features seen in CTs of the brain. MR imaging, including conventional T1- and T2-weighted images, diffusion-weighted imaging and proton spectroscopy are accurate and useful modalities for further evaluating hypoxic-ischaemic brain injury, especially in patients with negative CT findings. It is important for radiologists and clinicians to recognise the differences in imaging findings between infants / young children and older children / adults, which would facilitate prompt patient management.

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