

## Clinical Experience of Childhood Hypertensive Encephalopathy over an Eight Year Period

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**Background:** Hypertensive encephalopathy is an uncommon neurological syndrome in children, usually with reversible clinical and neuroimaging findings. Little is known about the precipitating factors, clinical presentations, neuroimaging findings and outcomes of childhood hypertensive encephalopathy in Taiwan.

**Methods:** To characterize this syndrome, we retrospectively analyzed 12 children with hypertensive encephalopathy in a tertiary institution from 1998 through 2005. We investigated the precipitating factors, clinical findings, courses, neuroimaging characteristics and outcomes.

**Results:** Twelve patients (10 boys and 2 girls) with hypertensive encephalopathy were identified. Post-streptococcal glomerulonephritis was the most common precipitating underlying disease. Common clinical presentations included mental change (100%), seizure (91.6%), headache (66.6%), nausea or vomiting (75%), and blurred vision (41.6%). Brain imaging studies showed vasogenic edema over the bilateral parietal, occipital and parasagittal regions, or the cerebellum. All patients had a reversible clinical course.

**Conclusion:** Hypertensive encephalopathy is predominant in males, and mental change is the most common clinical presentation. Renal origin is a common precipitating factor. A characteristic lesion of hypertensive encephalopathy is occipitoparietal region edema. The overall clinical outcome is good after prompt treatment.

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**Key words:** hypertension, encephalopathy, child

Hypertensive encephalopathy is a rare neurological syndrome in children. It is associated with rapid onset of severe hypertension followed by complete recovery if promptly treated. Typical clinical findings include headache, vomiting, mental changes, seizures and visual abnormalities. This syndrome can be fatal if unrecognized and not promptly treated, therefore it should be considered as a med-

ical emergency.<sup>(1)</sup> Neuroimaging shows edema in the occipital regions, which is frequently reversible. The term 'reversible posterior leukoencephalopathy syndrome' used for this condition emphasizes the transitory nature of the dysfunction once therapy is instituted.<sup>(2)</sup> There are two hypotheses that may explain the brain edema in hypertensive encephalopathy. One proposes that infarction caused by fibrinoid

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necrosis and thrombosis of arterioles results in cytotoxic edema.<sup>(3,4)</sup> The other proposes that severe hypertension that exceeds autoregulation results in segmental vasodilatation and increased vascular permeability leading to vasogenic edema,<sup>(2,5)</sup> which is now widely accepted as the final common pathway of this syndrome. Few studies of this syndrome in children have been reported;<sup>(6,7)</sup> little is known about precipitating factors, clinical presentations, course, neuroimaging findings and outcomes of childhood hypertensive encephalopathy in Taiwan.

## METHODS

We retrospectively analyzed the cases of children (<18 years) diagnosed with hypertensive encephalopathy who were admitted to our institution from 1998 to 2005. Hypertension was defined as elevated systolic or diastolic blood pressure greater than that found in the 95<sup>th</sup> percentile for the relevant age categories.<sup>(8)</sup> There were 238 children with hyperten-

sion (154 boys and 84 girls) enrolled in this study. Patients with hypertensive encephalopathy were defined as children with hypertension who also showed mental alertness changes, seizure, headache, nausea or vomiting, and blurred vision. A chart review included obtaining information about concurrent medical illnesses, clinical manifestations, electroencephalogram (EEG), brain computed tomography (CT) and magnetic resonance imaging (MRI) findings, duration of hypertensive encephalopathy and outcome.

## RESULTS

Twelve of the 238 patients (5.0%) were identified as having been diagnosed with hypertensive encephalopathy. The 12 patients (10 boys and 2 girls) ranged in age from 8 to 17 years. All 12 patients underwent brain CT scanning, 5 underwent both CT and MRI, and 3 underwent follow-up imaging studies. Clinical details are summarized in Table 1. Most

**Table 1.** Clinical Characteristics of 12 Children with Hypertensive Encephalopathy

Age	Gender	BP (mmHg)	H/T (D)	Underlying disease	Clinical findings	Seizures (frequency)	Location	Clinical outcome	
1	9Y	M	181/101	4	PSGN	Seizure, lethargy, headache, vomiting	PS with SE (2)	Bil occipital, parietal, frontal	recovery
2	9Y2M	M	172/112	1	PSGN	Seizure, headache, mental change	CPS (1)	Normal	recovery
3	9Y6M	M	222/184	4	PSGN	Headache, vomiting, mental change, blurred vision, seizure	PS with SE (2)	Bil occipital, left parietal	recovery
4	9Y10M	M	208/146	3	PSGN	Headache, vomiting, mental change, seizure, blurred vision	CPS (2)	Bil occipital, parietal	recovery
5	10Y4M	M	163/100	2	PSGN	Vomiting, headache, seizure, mental change	CPS (2)	Bil occipital, parietal	recovery
6	11Y5M	F	211/124	14	Lupus nephritis	Headache, vomiting, seizure, mental change	GCS (1)	Normal	recovery
7	9Y6M	M	168/118	5	Lupus nephritis	Seizure, mental change, vomiting	PS with SE (1)	Normal	recovery
8	16Y7M	F	201/124	7	Lupus nephritis with ESRD	Headache, seizure, mental change	CPS (4)	Parasagittal, parietal, occipital, temporal, frontal; hemorrhagic focus over left parietal lobe	recovery
9	10Y6M	M	212/159	4	VUR with left kidney scar	Vomiting, headache, blurred vision, vomiting	-	Cerebellar vermis	recovery
10	8Y3M	M	191/109	7	Nephritis	Mental change, vomiting, seizure, headache, blurred vision	GTS (3)	Bil occipital, parietal	recovery
11	14Y8M	M	160/110	4	Essential hypertension	Vomiting, seizure, left side weakness, mental change,	GTS (3)	Normal	recovery
12	10Y	M	157/111	7	ALL during induction chemotherapy	Mental change, seizure, blurred vision	GTCS (2)	Parasagittal, frontal, temporal, parietal	recovery

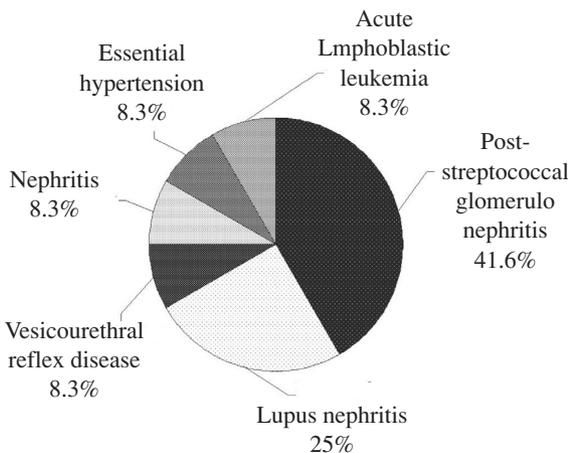
**Abbreviations:** Age YM: years months; M: male; F: female; BP: highest blood pressure; H/T(D): duration of hypertension since diagnosis; PSGN: post-streptococcal glomerulonephritis; PS with SE: partial seizure with secondary generalization; Bil: bilateral; CPS: complex partial seizure; GCS: generalized clonic seizure; ESRD: end-stage renal disease; VUR: vesicourethral reflux; GTS: generalized tonic seizure; ALL: acute lymphoblastic leukemia; GTCS: generalized tonic clonic seizure.

cases in our series were related to renal disease (Fig. 1), and post-streptococcal glomerulonephritis (PSGN) was the most common precipitating factor. Others included class IV lupus nephritis, left kidney scar as a result of previous urinary tract infection induced by grade 1 left vesicourethral reflux, nephritis, essential hypertension and acute lymphoblastic leukemia under induction chemotherapy.

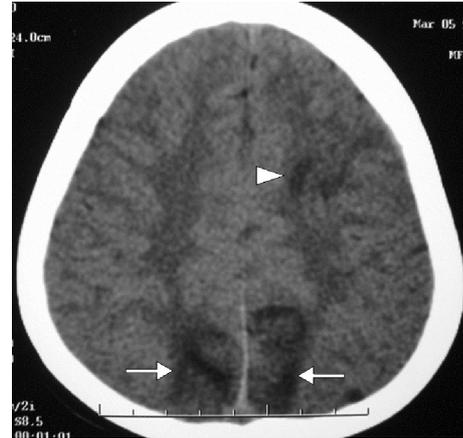
All patients had abrupt onset of severe elevated systolic blood pressure (mean  $186.5 \pm 23.4$  mmHg) with accompanying elevated diastolic blood pressure (mean  $126.3 \pm 24.5$  mmHg). The clinical presentations included mental change (100%), seizures (91.6%), nausea or vomiting (75%), headache (66.6%), visual abnormalities (41.6%) and focal neurological deficit (16.6%). Most patients experienced multiple seizures (66.6%). The seizure types were complex partial seizures in 4 patients (36.3%), generalized seizures in 4 (36.3%) and partial seizures with secondary generalization in 3 patients (27.2%).

Six patients underwent EEG. The findings on EEG included focal or diffuse delta slowing on 2 recordings, focal epileptiform discharge on 1, diffuse theta activity with focal epileptiform discharge on 1 and normal activity on 2 recordings.

Findings from brain CT of the 12 patients with hypertensive encephalopathy were normal in four patients (33.4%) but 8 patients (66.6%) had positive findings. All 8 patients presented as hypointensity lesions on brain CT (Fig. 2) with no enhancement seen on contrast-enhanced studies. Five patients



**Fig. 1** Underlying diseases in 12 children with hypertensive encephalopathy.



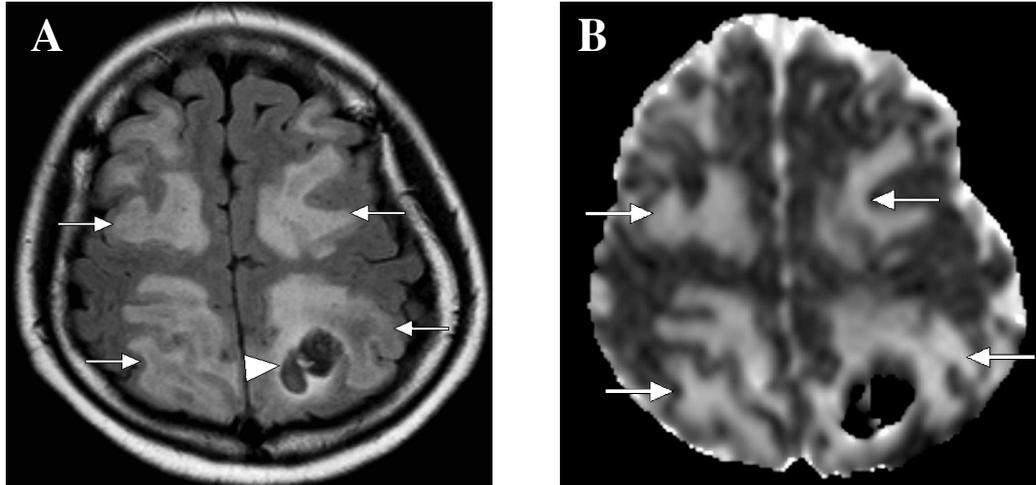
**Fig. 2** Axial non-contrast computed tomography image revealing areas of hypodensity in the bilateral parietal regions (arrows) and left frontal region (arrowhead).

underwent brain MRI, which was normal in 1 (20%), and showed focal brain edema in the white matter and adjacent gray matter in the other 4 (80%). The lesions presented as hypointense lesions on T1-weighted images (T1WI), hyperintense lesions on both T2-weighted images (T2WI) and fluid-attenuated inversion recovery (FLAIR) images (Fig. 3A), and post-contrast T1WI revealed no enhancement. Increased apparent diffusion coefficient (ADC) on diffusion imaging of these lesions (Fig. 3B) was also seen. One hemorrhagic focus was seen over the left parietal lobe of a patient with chronic hypertension due to lupus nephritis with end-stage renal disease.

All patients were treated with antihypertensive agents for hypertension and specific management for coexisting diseases. The average duration until control of the hypertensive encephalopathy was  $5.9 \pm 3.3$  days (range 1 to 14 days). Follow-up brain imaging studies were performed on only 3 patients (CT for 1 and MRI for 2) and resolution of the brain edema was noted for all 3 patients within 15 to 50 days after the initial abnormal results. Clinical manifestations improved after hypertension was brought under control.

## DISCUSSION

Unlike the adult population, in which the underlying cause for hypertension is often essential hypertension or hypertension secondary to non-renal disease, hypertension in children is often seen in associ-



**Fig. 3** (A) Magnetic resonance imaging (fluid-attenuated inversion recovery) showing hyperintensities in the bilateral parasagittal regions (arrows); one hemorrhagic focus shows hypointensity in the left parietal region (arrowhead). (B) Diffusion imaging (Apparent Diffusion Coefficient map) showing increased water diffusion in the parasagittal regions (arrows) indicating vasogenic edema.

ation with systemic disease, including renal parenchymal disease, renovascular disease, coarctation of the aorta and endocrine abnormalities.<sup>(7)</sup> In our study, 83% of cases were associated with renal disease. PSGN is more common in children than adults and may be complicated with hypertensive encephalopathy in 10% of cases.<sup>(9)</sup> The concomitant presence of azotemia may render the child more susceptible to cerebral autoregulatory dysfunction, resulting in hypertensive encephalopathy.<sup>(10)</sup>

In our series, the prevalence was 5%, which is less than the 8.8% reported in a previous study.<sup>(6)</sup> The frequency of hypertensive encephalopathy is declining because of improved recognition and therapy. Signs and symptoms that also have been reported in children with hypertensive encephalopathy include decreased level of consciousness, headache, vomiting, papilledema, cranial nerve palsies, transient hemiparesis, aphasia, apraxia, visual disturbances and coma.<sup>(11)</sup> Less frequently reported manifestations include transient loss of color vision, agitation, hallucinations, apnea and oculomotor abnormalities.<sup>(12)</sup> The syndrome may be heralded by a generalized seizure that is followed by mental changes. Seizures begin focally but usually become complex partial and generalized. Multiple seizures are more common when hypertension is not promptly controlled initially. With rapid resolution without recurrence of seizures after control of hypertension, the long-term

prognosis was good in our series and in previous observations.<sup>(13)</sup> The likely mechanism for these events was due to a number of metabolic changes known to attend seizures, including acidosis, hypoxemia and membrane alterations leading to blood-brain barrier disruption.<sup>(14)</sup>

The average systolic and diastolic pressure of the 12 patients in our series was somewhat lower than the values typically reported in adults with hypertensive encephalopathy. Cerebral blood flow increases markedly when diastolic blood pressure exceeds 145 to 164 mmHg in adult patients, suggesting the breakdown of cerebral autoregulation.<sup>(15)</sup> Normal diastolic arterial pressures are lower in children than in adults, with diastolic blood pressure by percentiles of height ranging from 80 mmHg or less at 8 year of age to 89 mmHg or less at age 17 (95<sup>th</sup> percentile).<sup>(8)</sup> Thus, children develop hypertensive encephalopathy at lower absolute pressures than adults owing to the relative 'left shift' of their range of cerebral blood flow autoregulation.<sup>(16)</sup>

As in our series, vasogenic edema on brain images was commonly bilateral and located predominantly in the posterior portions of the cerebral hemispheres, particularly the occipitoparietal lobes. The posterior predilection is thought to be related to dense sympathetic innervations of the anterior circulation that protects neural structures if blood pressure exceeds the limits of autoregulation.<sup>(17)</sup> Abnormalities

involving other cerebral areas, such as basal ganglia, brainstem and cerebellum, have been reported.<sup>(18-20)</sup> These lesions have been frequently associated with hypointensity on T1WI, hyperintensity T2WI, hypo- or iso-intense diffusion-weighted imaging, and increased diffusion on FLAIR lesions and ADC maps consistent with vasogenic edema. The syndrome resolves in most cases after the administration of antihypertensive agents, although rarely small infarcts and hemorrhages occur in patients with chronic hypertension.<sup>(21)</sup> Such hemorrhage may be due to breakdown of the blood-brain barrier from failing autoregulation that resulted in thrombosis, ischemia and infarction at the irreversible phase.<sup>(22)</sup> The treatment of underlying disease and follow-up of hypertension are important for prevention of the subsequent complications of cerebral hemorrhage and infarction. As with previous reports, neurological outcome in our series was good after well control of the hypertension.

In conclusion, hypertensive encephalopathy is a rare clinical diagnosis in children. The diagnosis should be considered when there is high suspicion of the clinical syndrome for encephalopathy in association with hypertension. The characteristic findings of brain CT or MRI studies may help in diagnosis. Management consists of recognition of this syndrome, and aggressive treatment of hypertension and underlying diseases. Neurological outcome was good after well control of the hypertension.

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## 兒童期高血壓性腦病變之八年臨床經驗分析

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**背景：**高血壓性腦病變較少發生於兒童期。由於臨床症狀與腦部影像表現往往可以恢復，所以此疾病亦稱為“可逆性腦病變”。但是若沒有及時積極有效地治療則仍可能導致死亡，所以在醫學仍視之為急症。由於此病在臺灣少見，本研究分析其致病因子、臨床表現，以及腦部影像上的病變型態，並且追蹤分析病患之預後，有助於早期的診斷以及正確的治療。

**方法：**本研究為回溯性之分析，選取從民國 87 年至 94 年期間於一醫學中心診斷為兒童期高血壓性腦病變，共 12 例。這些病例臨床上皆有高血壓且有神經學症狀，並同時接受腦部電腦斷層或核磁共振檢查。我們分析引起高血壓性腦病變的病因，並統計其臨床表現、腦波圖、腦部影像變化及預後。

**結果：**本分析共有 12 例高血壓性腦病變病患者，男性 10 例，女性 2 例，平均年齡 10.7 ± 2.4 歲（年齡層由 8 至 17 歲）。12 例患者中有鏈球菌感染後腎絲球腎炎者有 5 例（41.6%），全身性紅斑狼瘡有 3 例（25%），其他疾病則為 4 例。臨床症狀包括意識改變者有 12 例（100%），抽搐 11 例（91.6%），噁心嘔吐 9 例（75%），頭痛 8 例（66.6%），以及視覺改變 5 例（41.6%）。有 4 例患者接受腦波圖檢查並發現瀰漫性慢波為主。腦部影像分析發現有腦水腫，多發生於兩側頂葉、枕葉、額葉、顳葉、矢狀竇旁，以及小腦處，其中有 1 例在左側頂葉有出血現象。所有病患都及時接受抗高血壓藥物治療，並治療引起高血壓的根本疾病。所有病患之臨床症狀都獲得改善。有 3 例患者接受腦部影像追蹤檢查，並發現腦水腫之情形都消失或進步。

**結論：**兒童期高血壓性腦病變最常發生於男性，臨床症狀以意識改變最常見。病變部位於頂葉及枕葉最常見。若能積極有效地治療則有很好的預後。  
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**關鍵詞：**高血壓，腦病變，兒童

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