CASE REPORT

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Recurrent Acute Confusional State as a Manifestation of Hypertensive Brainstem Encephalopathy

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Abstract

The brainstem variant of hypertensive encephalopathy is a rare clinical syndrome. A striking clinico-radiologic dissociation with minimal signs and symptoms of brainstem dysfunction but a prominent radiological involvement of the brainstem is the hallmark of this disorder. It is an easily treatable and largely reversible disorder. Rapid initiation of antihypertensive therapy is vital for symptomatic resolution and a good clinical outcome. We report a 56-year-old male who presented to us with severe hypertension, recurrent acute confusional states, ataxia and prominent brainstem lesions on imaging. A good clinical recovery and a near complete resolution of the brainstem hyperintensities was observed within a month of initiating antihypertensive therapy.

Introduction

Hypertensive encephalopathy is a syndrome characterised by altered mental status and/or seizures and focal neurological deficit in association with severe hypertension[1]. Radiologically, vasogenic oedema in the posterior parietal and occipital lobes is a characteristic feature of this disorder. Reversible hypertensive brainstem encephalopathy (RBHE) is a rare variant of this syndrome with lesions confined to the brainstem[2]. We report a rare case of RBHE that presented to us with recurrent episodes of acute confusional state, with or without ataxia, that showed a good response to anti-hypertensive therapy.

Case report

A 55-year-old non-diabetic, non-alcoholic male, diagnosed 6 months earlier as a case of cholelithiasis, had been receiving symptomatic treatment for recurrent episodes of pain in abdomen and vomiting which had however abated for the last three weeks. He now presented to us with a 1 week history of acute confusional state accompanied by tremulousness of the hands, gait instability and incontinence. His history revealed that in the past three months he had suffered from 2 previous short lasting episodes (3 - 5 days) of acute confusional state, the first of which had occurred three months back and the second, 2 months prior to the current episode. During both the attacks he did not have any associated neurological deficit but was found to be hypertensive. On both occasions he had received antihypertensive therapy and remained well in between the attacks without any regular medication. There was no history of fever, headache, seizures or loss of consciousness during the episodes or any other systemic illness in the past.

On general examination, pulse was regular, but his blood pressure was 220/120 mm Hg. Systemic examination was non-contributory. On neurological examination, he was conscious but agitated, inattentive, disoriented to time, place and person, talking irrelevantly and not comprehending most of the commands. There were no signs of meningeal irritation. On ocular examination fundus, pupillary size and reaction were normal. A mild restriction of ocular movements in the horizontal plane with a gaze evoked nystagmus was observed. Rest of the cranial nerves were normal. There was no obvious motor or sensory deficit or dysarthria. A severe gait ataxia with inability to stand or walk unsupported was accompanied by a prominent tremulousness and clumsiness of the hands.

In view of a history of cholelithiasis with recurrent vomitings, and three episodes of acute confusional state, with mild ocular gaze palsy and cerebellar ataxia in the current episode, a possibility of metabolic encephalopathy due to recurrent hyponatraemia was entertained. However, his routine investigations such as serum electrolytes including sodium, potassium, calcium and phosphorus, haemogram, blood sugar, liver, renal, thyroid function tests and blood thiamine levels were all normal. He tested negative for antibodies to HIV, hepatitis C virus and hepatitis B surface antigen. Work-up for vasculitis, including ANA, dsDNA, ANCA was also negative. ECG, X-ray chest and echocardiography were normal. USG abdomen and Doppler renal artery revealed a normal right kidney but a left shrunken kidney with renal artery stenosis. EEG showed a mild non-specific diffuse slowing. MRI brain revealed prominent, diffuse T2/FLAIR hyperintensities in the brainstem (pons > medulla and midbrain). Bilateral scattered

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lesions in the temporal, parieto-occipital and gangliothalamic regions were also observed.

In view of the patient having an acute confusional state, cerebellar ataxia, severe hypertension and T2/FLAIR brainstem hyperintensities in the absence of any metabolic or electrolyte derangement, a final diagnosis of hypertensive brainstem encephalopathy with recurrent acute confusional states as an unusual manifestation of this rare disorder was entertained. On antihypertensive treatment, he showed a significant clinical recovery. The acute confusional state abated within 2 weeks and the ataxia subsided by 4 weeks. A follow-up MRI done 1 month later showed near complete resolution of his brainstem hyperintensities.

Discussion

Hypertensive encephalopathy is an acute disorder of the CNS that occurs in patients with severe arterial hypertension. It typically affects people in their 50s and 60s and common presentations include: headache, nausea, vomiting, blurred vision, gait abnormalities, seizures, paresis and altered mental status or coma. Classic MRI findings include symmetric, subcortical, parieto-occipital T2 and FLAIR hyperintensities[3]. Similar lesions may also be seen in the frontal or temporal lobes in two-third of the cases and in the brainstem, cerebellum or basal ganglia in around one-third of the cases[4]. Additionally, 40% of patients may have asymmetric lesions. These lesions are hypointense on DWI images and bright on apparent diffusion co-efficient (ADC) maps, suggesting the presence of a vasogenic oedema that is potentially reversible with treatment. Restricted diffusion may however be seen in around 25% of the cases suggesting the presence of irreversible cytotoxic oedema[4].

More recently, an isolated brainstem variant of hypertensive encephalopathy without involvement of the parieto-occipital cortex has been identified on the basis of imaging. This syndrome of reversible brainstem hypertensive encephalopathy (RBHE) was first recognised by Chang and Keane in 1995. This pattern is more common in younger patients (usually 4th decade) with higher mean systolic and diastolic blood pressures of 230/140 mmHg. MRI reveals the presence of extensive, diffuse, oedematous lesions in the brainstem. A clinico-radiologic dissociation is however, an important hallmark of this syndrome[2]. Despite the striking MRI changes, clinical symptoms and signs of brainstem or cerebellar dysfunction are few and may take the form of mild headache, gait instability, confusion or hemiparesis. Our case also had severe hypertension with an acute confusional state and ataxia. Despite prominent brainstem involvement on imaging, there was no evidence of quadriplegia, cranial nerve palsies, loss of consciousness or other brainstem signs and symptoms and he showed a good response to antihypertensive therapy. Another unusual feature of our case was that he had suffered from two earlier episodes of short lasting acute confusional state associated with severe hypertension but no other neurological deficit or metabolic derangement. Even though imaging studies were not done during the previous attacks, they most probably represent a part of the spectrum of the same disorder since they had responded to antihypertensive therapy alone.

In a review of 23 patients of hypertensive brainstem encephalopathy by Cruz-Flores *et al*, the mean age at onset was around 42 years and 34% of the cases had hypertension alone[6]. Comorbid renal failure and eclampsia were common and clinical presentation included: headache (73%), nausea or vomiting (43%), blurred vision (34%), abnormal gait (26%), coma (23%), seizures (17%) and paresis (9%). Signs of brainstem dysfunction were noted in 25% cases only. MRI T2 hyperintensities were observed in pons (82%), mid-brain (70%), cerebellum (43%), deep white matter (26%), thalamus (22%), medulla (13%), occipital lobe (9%), and basal ganglia (9%). Imaging improvement was documented as early as 5 days after initiating antihypertensive therapy. De Seze *et al*[7], and Katsumata *et al*[8], have also reported MRI T2 and FLAIR hyperintensities in the occipital lobes, periventricular white matter and cerebellum besides the brainstem. In a patient presenting to the emergency, with severe hypertension and headache only, Morello *et al*, documented a clinically silent massive edema of the pons confirming the presence of a clinico-radiographic dissociation in patients with RBHE[9]. In our case, MRI brain revealed prominent, diffuse T2/FLAIR hyperintensities in the brainstem without significant suratentorial involvement. Oliverio *et al*, have reported a case of hypertensive brainstem encephalopathy related to the use of tacrolimus, an immunosuppressant agent[10].

Under normal circumstances, any rise in blood pressure, activates the sympathetic pathways to induce cerebral vasoconstriction to maintain the cerebral perfusion pressure. In patients with hypertensive encephalopathy, a sudden acute rise in blood pressure results in failure of the cerebral autoregulatory mechanisms. This leads to cerebral hyperperfusion, disruption of the blood-brain barrier (BBB) and vasogenic oedema due to extravasation of fluid, macromolecules, and red blood cells in the brain parenchyma[7]. As compared to the anterior circulation, the posterior circulation is less endowed with sympathetic innervation and thus has a limited capacity for protective vasoconstriction in response to sudden elevations in arterial blood pressure. As a consequence, the vasogenic oedema

of hypertensive encephalopathy is primarily confined to the brainstem and parieto-occipital lobes which fall within the distribution of the vertebrobasilar artery and its branches. In rare cases of hypertensive encephalopathy the vasogenic oedema may remain confined to the brainstem only, as it may serve as a buffer and absorb much of the hypertensive "tidal wave" thereby sparing the parieto-occipital regions which fall in the distal territory of the vertebrobasilar system. According to another hypothesis, the parietal and occipital lobes may sometimes have a rich sympathetic innervation via a fetal-type of posterior communicating artery (PCoA) and thereby remain protected from surges in blood pressure during episodes of malignant hypertension (Doi *et al*)[11].

The short-term goal for treating hypertensive emergency is to reduce the systolic BP by 10 - 15% within the first hour, and to 160/100 mmHg within the first 6 hours[12]. In the setting of an autoregulatory failure, rapid lowering of BP can cause or worsen cerebral hypoperfusion. For management of a hypertensive emergency, intravenous administration of short-acting agents like labetolol, nicardipine, fenoldopam or nitroprusside is recommended. Choice of the drug is determined by the associated comorbidities and drug availability.

A favourable outcome with rapid resolution of MRI changes in as few as 5 days after starting antihypertensive treatment is another key feature of RBHE. Improvement or resolution of radiographic findings after treatment often lags behind clinical improvement. Our case showed a significant clinical recovery within 2 weeks of initiating antihypertensive treatment with a near complete resolution MRI changes within a month. Although RBHE is usually reversible if treated early, irreversible neurologic sequelae can occur if the treatment is delayed.

In conclusion, an acute confusional state in the setting of hypertension and no metabolic derangement should alert the physician to the possibility of hypertensive encephalopathy/RBHE. Our case probably represents an extreme end of the spectrum of this rare disorder and presented with recurrent episodes of acute confusional state with brainstem hyperintensities. Despite a malignant appearance on neuroimaging, brainstem hypertensive encephalopathy carries a good prognosis and is usually reversible with prompt antihypertensive therapy. It therefore needs to be differentiated from other radiological mimics like brainstem infarction, pontine glioma, central pontine myelinolysis and infectious encephalitis that carry a worse prognosis.

References

1. Schwartz RB. Hyperperfusion encephalopathies: hypertensive encephalopathy and related conditions. *Neurologist* 2002; 8: 22-34.
2. Shintani S, Hino T, Ishihara S *et al*. Reversible brainstem hypertension encephalopathy (RBHE): Clinicoradiologic dissociation. *Clin Neurol Neurosurg* 2008; 110: 1047-53.
3. Hinchey J, Chaves C, Appignani B *et al*. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996; 334: 494-500.
4. Fugate JE, Claassen DO, Cloft HJ *et al*. Posterior Reversible Encephalopathy Syndrome: Associated Clinical and Radiologic Findings. *Mayo Clinic Proceedings* 2010; 85 (5): 427-32.
5. Chang GY, Keane JR. Hypertensive brainstem encephalopathy: three cases presenting with severe brainstem oedema. *Neurology* 1999; 53: 652-4.
6. Cruz-Flores S, de Assis Aquino Gondim F, Leira EC. Brainstem involvement in hypertensive encephalopathy: clinical and radiological findings. *Neurology* 2004; 62 (8): 1417-9.
7. de Seze J, Mastain B, Stojkovic T *et al*. Unusual MR findings of the brain stem in arterial hypertension. *AJNR Am J Neuroradiol* 2000; 21 (2): 391-4.
8. Katsumata Y, Maehara T, Noda M *et al*. Hypertensive encephalopathy: reversible CT and MR appearance. *Radiat Med* 1993; 11 (4): 160-3.
9. Morello F, Marino A, Cigolini M *et al*. Hypertensive brain stem encephalopathy: clinically silent massive oedema of the pons. *Neurol Sci* 2001; 22 (4) :317-20.
10. Oliverio PJ, Restrepo L, Mitchell SA *et al*. Reversible tacrolimus-induced neurotoxicity isolated to the brain stem. *AJNR Am J Neuroradiol* 2000; 21 (7): 1251-4.
11. Doi Y, Kimura F, Fujiyama T *et al*. Hypertensive brainstem encephalopathy without parieto-occipital lesion – two case reports. *Neurol Med Chir (Tokyo)* 2006; 46 (2): 75-9.
12. Vaughan C, Delanty N. Hypertensive emergencies. *Lancet* 2000; 356: 411-7.