Isolated Brainstem Involvement in a Patient with Hypertensive Encephalopathy

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Abstract- Hypertensive encephalopathy (HE) is one of the acknowledged hypertensive emergencies. Isolated hypertensive brainstem encephalopathy (HBE) without concomitant typical parietooccipital lesion is unusual. Patients with HBE may or may not present with symptoms attributable to brainstem and the diagnosis is challenging in an emergency setting. The most important differential diagnosis in HBE is brainstem infarction, because the goals of blood pressure treatment are different. Evidence of vasogenic edema on magnetic resonance image, i.e. absence of high signal lesions on diffusion weighted images and increased value of apparent diffusion coefficient are diagnostic indicators of HBE, but not brainstem infarction. Prompt recognition of HBE and adequately lowering blood pressure offer the best outcomes.

Key Words: Hypertension, Hypertensive encephalopathy, Brainstem, Ataxia, End-stage renal disease

INTRODUCTION

Hypertensive encephalopathy (HE) occurs in about 16% patients with hypertensive crisis[1]. Computed tomography (CT) or magnetic resonance imaging (MRI) in HE patients often shows bilateral white matter edema of the parietooccipital lobes, thus the term "reversible posterior leukoencephalopathy syndrome (RPLS)."[2-3]. Brainstem and cerebellum lesions are associated with cerebral posterior white matter change in 58% of patients with RPLS[7]. However, it is rare for HE to have isolated involvement in the brainstem without concomitant parietooccipital lesions[4-7]. In this report we describe a patient with hypertensive encephalopathy whose white matter lesions on MRI are almost restricted to the brainstem.

CASE REPORT

A 48-year-old man presented at the emergency room due to acute onset of dizziness, nausea, and unsteady gait for 2-3 days. He had past histories of poorly controlled hypertension and end-stage renal disease (ESRD) under regular hemodialysis. Examination revealed body temperature: 36.7 ˚C, pulse rate: 81/minute, respiration rate: 18/minute, blood pressure (BP): 239/130 mmHg,

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clear consciousness, mild dysarthria, and severe ataxia of his trunk and four limbs. During monitoring while in the ER his systolic blood pressure ranged between 180 and 240 mmHg, and diastolic blood pressure ranged between 100 and 130 mmHg. Emergent non-contrast CT of his brain showed diffuse brainstem swelling (Fig. 1). MRI of the brain showed high signal intensity in the pons, midbrain, and cerebellum on fluid-attenuated inversion recovery (FLAIR), increased values of apparent diffusion coefficient (ADC), but normal intensity on diffusion-weighted image (DWI). There was low signal intensity and without contrast enhancement in the same area on T1-weighted image (T1WI) (Fig. 2). MR angiography revealed normal basilar and vertebral arteries. Lumbar puncture was done to exclude brainstem encephalitis and the results were opening pressure: 270 mm cerebrospinal

fluid (CSF), white blood cell: 0/cm³, red blood cell: 3/cm³, glucose 52 mg/dl (serum glucose: 83 mg/dl), and total protein 119 mg/dl (reference: 15-45 mg/dl). The diagnosis of hypertensive brainstem encephalopathy (HBE) was made. Because the patient had a previous history of hypotensive response to intravenous forms of antihypertensive drugs, we controlled his BP using nifedipine 10 mg per os, and then gradually titrated to long-acting nifedipine (30 mg/d) and irbesartan (150 mg/d). Three days after antihypertensive treatment, his blood pressure normalized to around 160/90 mmHg. Within 2 weeks the unsteady gait and dysarthria were eliminated but he continued with residual mild dizziness. Follow-up MRI 4 months later showed only small residual faint high signal lesions in the basis pontis on FLAIR images (Fig. 3).
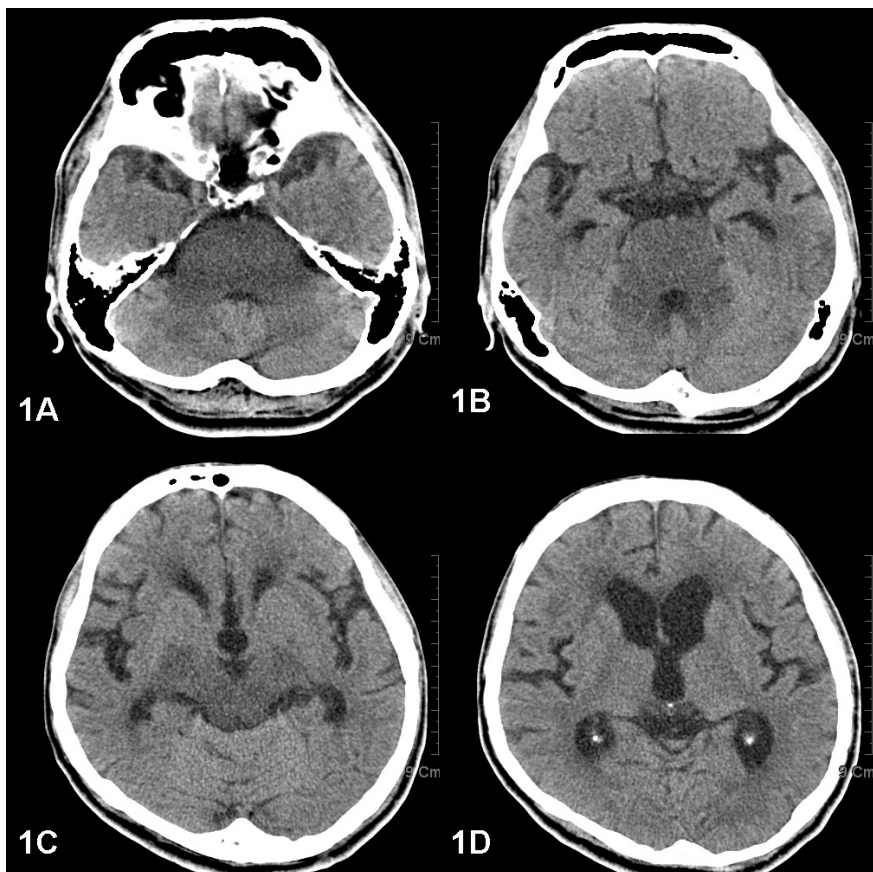

Figure 1. Non-contrast brain computed tomography (CT) showed isolated hypodensities in the whole pons (1A and 1B) and midbrain (1C) with positive pressure effect and effacement of pre-pontine and peri-aqueductal cisterns. There are no prominent hypodense lesions in the white matters of bilateral posterior cerebri (1D).
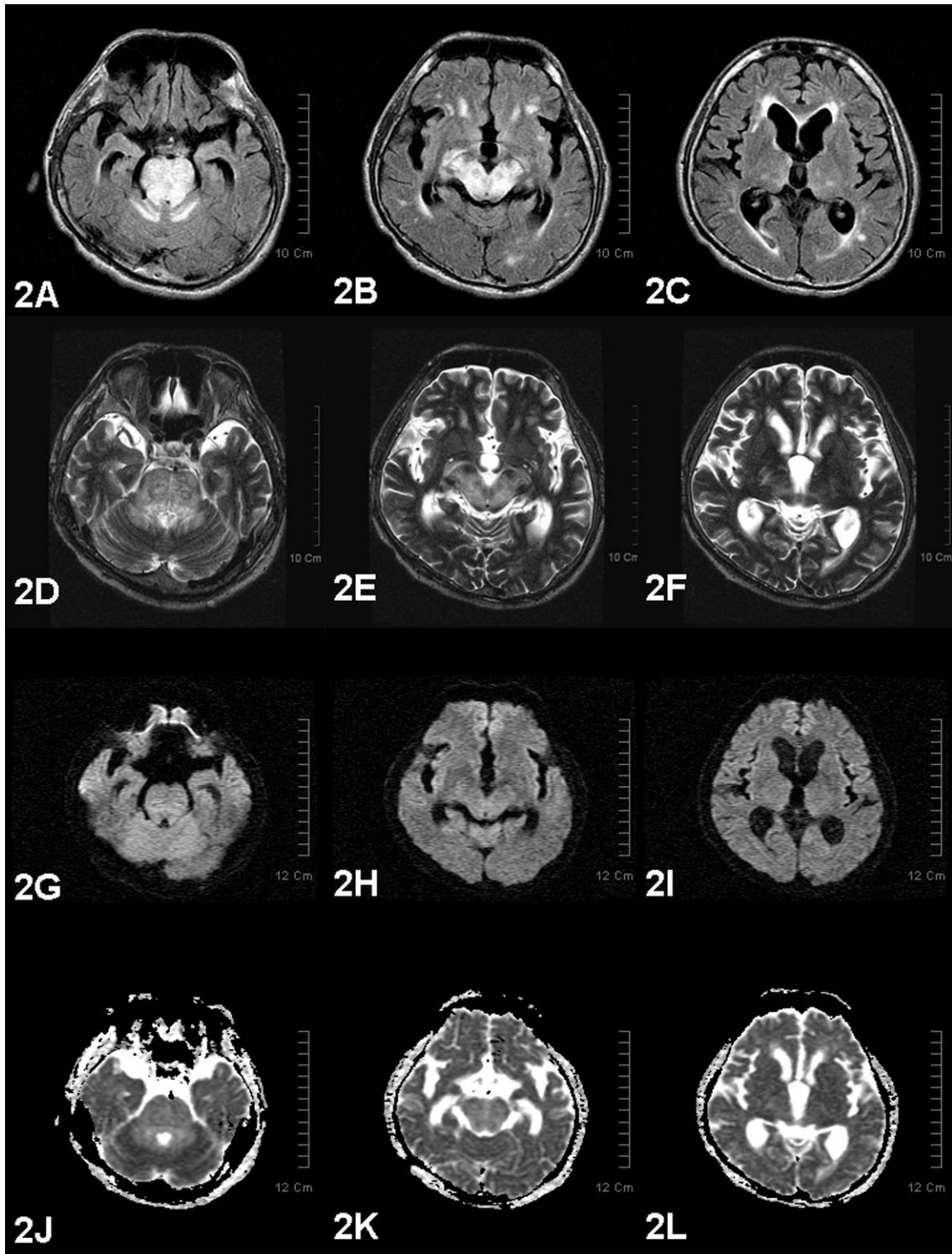
Figure 2. Non-contrast brain magnetic resonance image (MRI) showed prominent and isolated high signal intensities of whole pons and midbrain on fluid-attenuated inversion recovery (FLAIR) (2A-C) and T2-weighted image (T2WI) (2D-F); no intracellular restriction of water on diffusion-weighted image (DWI) (2G-I), but increased value of apparent diffusion coefficient (ADC) in the brainstem (2J-L).
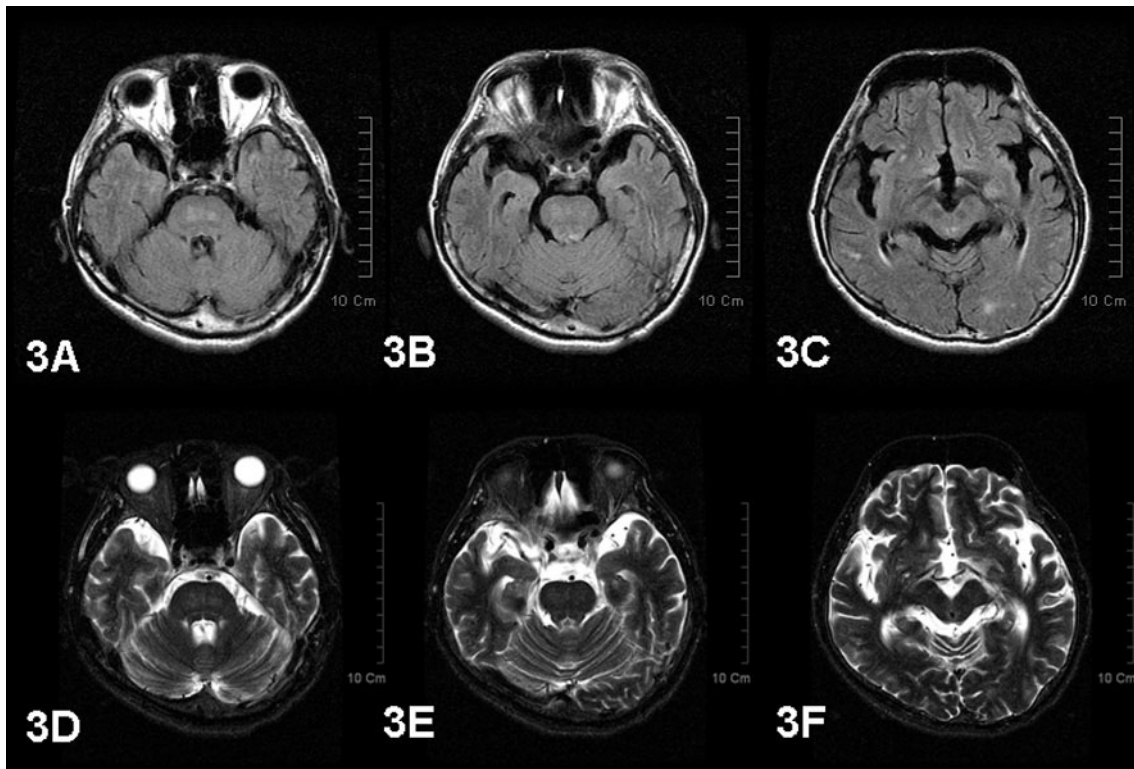
Figure 3. Non-contrast brain MRI done 4 months later showed markedly resolution of previous bright signals in the brainstem. There are only minimal and faint high signal intensities in the basis pontis on FLAIR (3A-C) and T2WI (3D-F). There is also resolution of the infratentorial mass effect.

DISCUSSION

The most widely accepted pathophysiologic mechanism of HE is vasogenic edema[8-9]. The sudden increase of blood pressure exceeds the limit of cerebral vascular autoregulation causing forced dilation with hyper-perfusion of small cerebral arterioles, dysfunction of endothelium, and leakage of fluid and protein into the extracellular space. HE has a predilection to the posterior circulation because of the sparse sympathetic innervations of the vertebrobasilar system[10-11]. HE mostly involves the posterior cerebrum rather than the brainstem because the brainstem autoregulates more effectively[13-14]. However, this patient showed an unusual presentation, which may be related to individual variation of regional autoregulation.

ESRD is the risk factor of HBE in this patient. In one review by Cruz-Flores et al.[4], two-thirds of the HE patients with involved brainstem, in addition to hypertension, had comorbidities such as renal failure. The vasoconstriction response would be poor to maintain constant blood perfusion during hypertension in a uremic state, as found in the animal model[12].

The most important differential diagnosis in this patient was the massive brainstem infarction, because the goals of blood pressure treatment are different. The MRI evidence of vasogenic edema, i.e. absence of high signal lesions on diffusion weighted images and increased value of apparent diffusion coefficient is strongly diagnostic of HBE[2-3], but not infarction. Besides, MR angiography revealed no stenosis of the vertebro-basilar arteries. Furthermore, our patient only had ataxia, mild dysarthria but no disturbance of consciousness, ophthalmoplegia, and quadriparesis, as might be expected from the striking brainstem abnormalities seen on CT and MRI. Those clinical findings are unusual in massive

brainstem infarction, but very suggestive of HBE. In the reported cases of HBE, the most common symptoms are headache, nausea or vomiting, and blurred vision, while only 23% of such patients had changes of consciousness and less than 25% had signs of brainstem dysfunction[4]. Morello et al.[15] had reported a patient with HBE who had clinically silent massive edema of the pons. This "clinical radiologic dissociation" could be explained by reversible vasogenic edema in HBE, but not irreversible cytotoxic edema and neuronal death in brainstem infarction.

The CT findings in our patient should also be differentiated with diffuse glioma, infectious rhombencephalitis, Wernicke encephalopathy, central pontine myelinolysis (CPM), and immune-mediated brainstem encephalitis[7]. The absence of contrast enhancement lesions on MRI, marked and rapid clinical and radiological improvement after only reduction of blood pressure excluded glioma. The lack of fever or other signs of infection, normal WBC and differential blood count, and no pleocytosis in the CSF analysis made infectious rhombencephalitis unlikely. Wernicke encephalopathy was ruled out because he didn't have ophthalmoplegia, amnesia, and increased signal of periaqueductal regions and medial thalami on DWI[16]. The reversibility of symptoms and image findings, and no history of rapid corrected hyponatremia also excluded CPM. Immune-mediated brainstem encephalitis mainly includes brainstem variants of acute disseminated encephalomyelitis (ADEM) and Bickerstaff's brainstem encephalitis. The absence of prior infection, vaccination, external ophthalmoplegia, alteration of consciousness, and subcortical white matter change made these disease entities less likely[17].

Prominent CSF protein elevation is less common in HBE, but uremia often increases CSF protein. According to the previous study, CSF protein elevations > 60mg/dL occur in 60% of uremic patients. Moreover, CSF protein exceeds 100mg/dL in 20% of uremic patients[18]. Therefore, CSF protein elevation in this patient can be attributed to the combined effect of HBE and ESRD.

When a patient presents in an emergency setting with a high BP and brainstem edema on brain imaging,

HBE should be differentiated from massive brainstem infarction, especially in those patients with mild symptoms. The key factors for correct diagnosis are vasogenic edema on emergent MRI and exclusion of other possibilities by history and CSF study. Prompt recognition of HBE and adequate reduction of BP offer such patients the best outcomes.

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