

Short communication

Blood–retina-barrier disruption accompanying blood–brain-barrier dysfunction in posterior reversible encephalopathy syndrome

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ARTICLE INFO

Article history:

Received 23 June 2014

Received in revised form 9 August 2014

Accepted 23 August 2014

Available online 29 August 2014

Keywords:

Blood brain barrier

Retina

Seizure

Posterior reversible encephalopathy syndrome

Ischemic stroke

ABSTRACT

Blood-brain-barrier dysfunction is well known to accompany hypertensive posterior reversible encephalopathy syndrome (PRES) and is considered as the culprit of vasogenic edema and cerebral hemorrhage observed as part of this syndrome. An 84-year-old female was admitted with a diagnosis of PRES in the setting of malignant hypertension. The clinical course was further complicated by ischemic stroke and seizures. Contrast enhanced fluid attenuated inversion recovery (FLAIR) studies revealed diffuse enhancement within the subarachnoid space extending to regions without evidence of cytotoxic or vasogenic edema. These findings suggestive of increased permeability were not only confined to the blood-brain-barrier, but also involved the blood-retina-barrier interface. Our observations suggest that pathologic conditions that disrupt the integrity of blood-brain-barrier might concomitantly affect retinal microcirculation, which highly resembles cerebral microcirculation both anatomically and functionally. Imaging modalities sensitive for detection of blood-brain-barrier dysfunction, such as contrast enhanced FLAIR, might be helpful in identifying these abnormalities.

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An 84-year-old female without prior history of hypertension was admitted with sudden onset of confusion and disorientation. Systolic and diastolic blood pressures at admission were 181 and 126 mm Hg, respectively, and reached to a peak of 261-mm Hg systolic and 124-mm Hg diastolic over the ensuing hours. On neurologic examination the patient was lethargic, able to follow simple commands, and had decreased verbal output with left sided hemiparesis. Cranial non-contrast computed tomography (CT) and CT-angiography studies performed with a presumptive diagnosis of stroke were normal except for a stenotic segment in the right posterior cerebral artery (PCA). Cranial magnetic resonance imaging (MRI) and MR-angiography obtained approximately 12 h after symptom onset not only confirmed the pathology in the right PCA, but also revealed patchy T2-hyperintense lesions involving the pons, medulla and cerebellum with no accompanying areas of restricted diffusion (Fig. 1 A–C). Based on the elevated blood pressure levels and imaging features excluding acute ischemic or hemorrhagic processes, but instead showing vasogenic edema involving the brain stem and cerebellum, a diagnosis of posterior reversible encephalopathy syndrome (PRES) in a setting of malignant hypertension was considered.

The patient was started on intravenous esmolol treatment and systolic blood pressure was gradually tapered to 140 mm Hg within 24 h. Despite normalization of the blood pressure the left sided weakness and drowsiness of the patient persisted and the clinical picture was complicated by secondary generalized seizures. A follow-up MRI obtained 3 days after symptom onset showed a newly developing acute ischemic lesion in the right PCA territory (Fig. 1D). More importantly there was widespread contrast enhancement of the subarachnoid space, especially prominent on fluid-attenuated inversion recovery (FLAIR) sequences, which was compatible with disruption in the integrity of blood–brain-barrier (Fig. 1E). This leakiness was not only confined to the blood–brain-barrier, but also involved the blood–retina-barrier interface, as revealed by contrast enhancement and hyperintense appearance of vitreous bodies in both globes (Fig. 1E). No papilledema was evident on fundoscopic examination; fluorescein angiography was planned in order to evaluate the integrity and permeability of retinal circulation but could not be performed due to the clinical instability of the patient. The clinical picture gradually started to improve after adjustment of anti-hypertensive and anti-epileptic regimens; the neurologic exam was within normal limits except for left homonymous hemianopia at the time of discharge. A follow-up MRI obtained 2 weeks later showed normalization of blood–brain-barrier permeability (Fig. 1F).

The failure of autoregulatory mechanisms involved in maintenance of cerebral blood flow might lead to hyperperfusion and vasogenic edema in the case of excessive elevations in systemic blood pressure.[1] Forced dilatation of cerebral arteries and disruption of the integrity of the blood–brain-barrier is considered as one of the mechanisms

Abbreviations: CT, computed tomography; FLAIR, fluid attenuated inversion recovery; MRI, magnetic resonance imaging; PCA, posterior cerebral artery; PRES, posterior reversible encephalopathy syndrome.

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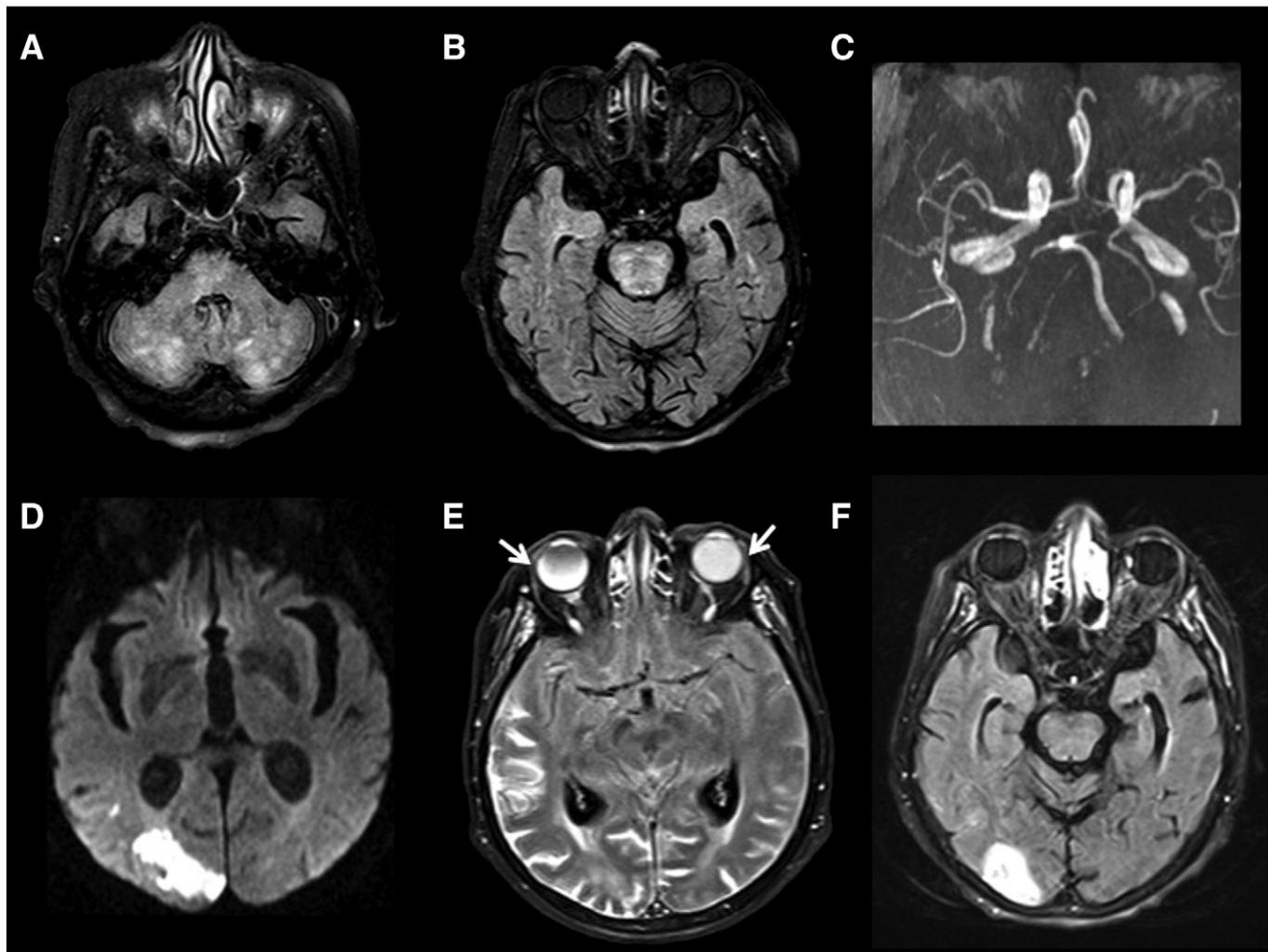


Fig. 1. Fluid-attenuated inversion recovery (FLAIR) images obtained on the day of admission revealed vasogenic edema involving the brain stem and cerebellum (A, B). Magnetic resonance angiography was normal except for a focal stenotic segment in the right posterior cerebral artery (C). Follow-up imaging obtained on day-3 showed a newly developing acute ischemic region within the right posterior cerebral artery territory on diffusion weighted imaging (D) and bilateral marked enhancement of subarachnoid space on contrast enhanced FLAIR images (E). Note also concomitant contrast enhancement in both ocular bulbs (arrows). Brainstem and cerebellar vasogenic edema, together with contrast enhancement within the subarachnoid space and ocular bulbs resolved entirely on follow-up studies obtained 2 weeks later, and only revealed a subacute infarct in the right posterior cerebral artery territory (F).

that underlie vasogenic edema observed in hypertensive PRES, which manifests as contrast enhancement within the lesions on imaging studies [2,3]. Alternatively, ischemia triggered by systemic inflammation, endothelial injury and vascular dysfunction is also suggested to contribute to vasogenic edema observed during PRES [4]. Regardless of the exact inciting pathophysiology, if we consider vasogenic edema and parenchymal hemorrhage – which not uncommonly complicates PRES – as the most downstream events during the course of blood–brain–barrier dysfunction [2,3], it is plausible to expect the presence of a large amount of cerebral tissue with more subtle impairments in blood–brain–barrier integrity during the course of sudden blood pressure elevations that have not proceeded to the phase of vasogenic edema. On the other hand it is also very well known that the blood–retina–barrier highly resembles the blood–brain–barrier both anatomically and functionally, and pathophysiological conditions affecting the cerebral circulation might lead to similar disturbances in the retinal microcirculation, as well [5]. Papilledema and retinal pathologies like detachment have indeed been described in patients with PRES as concomitant ophthalmologic manifestations related to the hypertensive episode [6,7]. Our report extends these observations by highlighting that retinal permeability might additionally be impaired in this setting.

In addition to the hypertensive episode it is highly probable that the ischemic stroke and seizures – both known to trigger focal and diffuse

disruptions in blood–brain–barrier – have contributed to the widespread increase in permeability of cerebral and retinal microcirculation observed in our patient [8,9]. Regardless of the underlying pathophysiology, imaging modalities sensitive to blood–brain–barrier disruption like contrast enhanced FLAIR are critical in identifying these abnormalities. This case once more emphasizes that blood–brain–barrier dysfunction might not be only restricted to areas with apparent lesions, but could also involve the normal appearing cerebral tissue, and even the retinal circulation.

Conflict of interest

Drs. Ozkan, Gocmen, Topcuoglu and Arsava have nothing to disclose.

Acknowledgements

None.

Authors and their contributions to the manuscript

Dr. Ozkan was primarily responsible for patient care, acquired the data and drafted the manuscript. Dr. Gocmen was the principal radiologist

involved and made critical revision of the manuscript. Drs. Topcuoglu and Arsava supervised patient care and critically revised the manuscript.

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