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Correspondence

Cerebral autoregulation in a fulminant hepatic failure patient who underwent liver transplantation

Dear Editor,

We report the case of a 47-year-old woman diagnosed with fulminant hepatic failure (FHF). Over a two-week period, the patient had jaundice and Grade 4 encephalopathy associated with coagulopathy and renal failure. On admission, the patient underwent endotracheal intubation and mechanical ventilation, fulfilling the clinical criteria for liver transplantation. The patient underwent urgent liver transplantation and was monitored before and after transplantation by transcranial Doppler (TCD). Norepinephrine was infused to increase the mean arterial blood pressure by approximately 20 mmHg in order to calculate static cerebral autoregulation (CA) according to Tiecks et al. [1] Values > 0.6 indicate preserved CA. In the case reported, cerebral blood flow (CBF) velocity showed lower values prior to transplant, high values immediately post-transplant, and a tendency to normalize within 48–72 h (Fig. 1). Loss of CA was demonstrated before transplant; CA recovery was seen on the 3rd day after transplant. Unexpectedly, deterioration of CA was noted on the 5th day after transplantation, coinciding with hepatic artery thrombosis. The patient underwent liver retransplantation, and restoration of CA occurred 48 h later (Table 1).

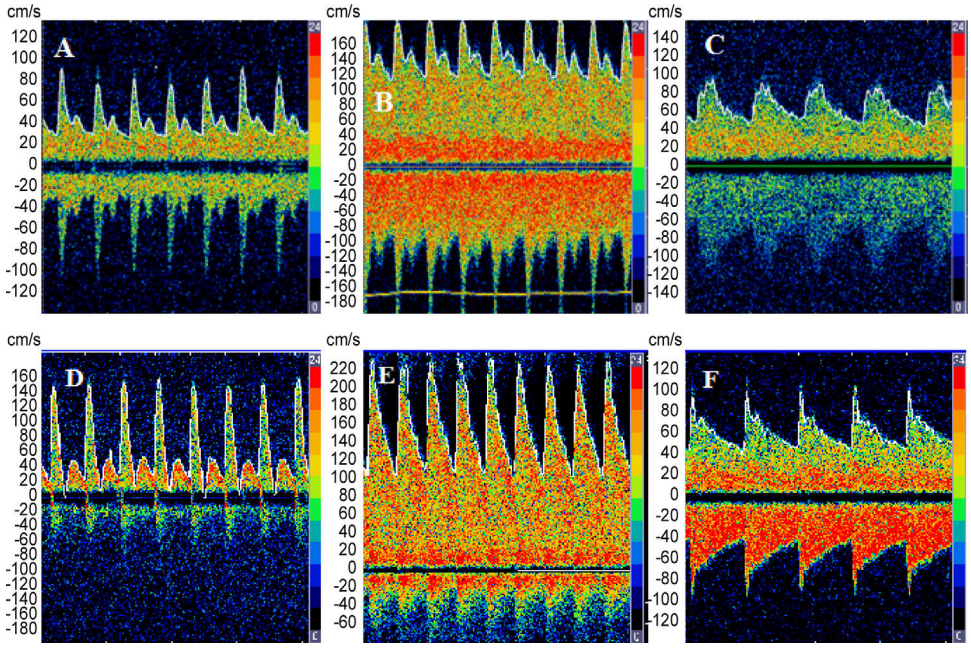

Fig. 1. Transcranial Doppler: (A) before liver transplant; (B) 1st day after transplant; and (C) 3rd day after liver transplant; (D) 4th day after transplant; (E) 5th after transplant and (F) 7th after transplant.

Table 1
Performance of systemic and haemodynamic parameters (CBFV and CA) before and after transplantation (tx) liver in FHF.

	Before tx	1st day after tx	3rd Day after tx	5th Day after tx	7th day after tx and 2nd day after new liver tx
ABP (mmHg)	108	102	120	107	106
Heart rate	119	95	73	69	93
PCO_2 (mmHg)	45	34	36.7	36	36.5
Haemoglobin (g/dl)	11.8	10.8	10.7	12.1	10.8
Temperature (C)	37	36	36.5	36.1	37
CBFV MCA maximum (cm/s)	45	145	66	161	63
CA index MCA maximum (cm/s)	0.25	0.33	0.92	0.30	0.70

ABP: arterial blood pressure; pCO_2: partial pressure of carbon dioxide; CBFV: cerebral blood flow velocity; CA: cerebral autoregulation; MCA: middle cerebral artery.

Cerebral autoregulation refers to the inherent cerebrovascular physiological mechanisms that keep CBF relatively constant despite wide variation in arterial blood pressure levels. These mechanisms act to protect the brain from the harmful effects of oligaemia and hyperaemia due to decreased and increased perfusion pressure, respectively [2–3]. Loss of CA in FHF can be explained by the dysfunction of cerebral arterioles, leading to vasodilation, associated with metabolic derangement and toxic substances released from the necrotic liver [4], but the actual pathophysiological mechanism remains unknown. Both loss of CA and hyperaemia have been considered important factors for the worsening of hepatic encephalopathy, brain swelling, and unfavourable outcomes. The present case raises the possibility that CBF dynamics and CA capacity can be restored shortly after recovery of liver function [4]. TCD can be a useful method for real-time monitoring of FHF patients in terms of CBF velocity and CA. Improvement of CA can be directly associated with recovery of liver function; for this reason, CA may be a marker of liver function, as suggested by this case. Future studies should determine the dynamic behaviour of CA. Such evaluation can help elucidate the pathophysiology of FHF and enable better therapeutic management of patients.

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No expression of HBV-human chimeric fusion transcript (HBx-LINE1) among Vietnamese patients with HBV-associated hepatocellular carcinoma

Dear Editor,

Hepatitis B virus (HBV) related hepatocellular carcinoma (HCC) is the most common malignancy among males in Vietnam and annually approximately 500,000 new HCC cases are diagnosed worldwide [1]. The rates of progression to liver cirrhosis (LC) in chronic HBV carriers are estimated to be 10% per year [2], and the risk of HCC development in chronic HBV carriers is significantly higher compared to that in uninfected individuals [1]. Chronicity of HBV infection results from persistence of the viral minichromosome (cccDNA) and the integration of HBV DNA into human genome contributing to pathogenesis/carcinogenesis of HBV infection has been widely described [3]. HBx-LINE1 is believed to be a chimeric viral and human long non-coding RNA (lncRNA) that induces tumor formation by promoting Wnt signaling and promotes HCC-related injury by sequestering liver-specific microRNA-122 expression [4–6]. Nevertheless, Integration of HBV in the cell genome in HCC is still poorly understood and the exact mode of HBx-LINE1 in HCC development needs to be defined in more detail [7]. Recently, a whole-transcriptome sequencing study utilized HBV-positive HCC cell lines and indicated common transcription of a viral-human chimera in response to HBV genome integration (HBV-human chimeric fusion transcript; HBx-LINE1) [8]. In this study, HBx-LINE1 was described to occur in 23.3% of HBV-associated HCC tumors and the authors also suggested that HBx-LINE1 might be an independent prognostic factor predicting shorter survival of HCC patients [8]. However, a later study conducted in France did not confirm these findings and found complete absence of these fusion transcripts in 50 HBV-associated HCC patients [9]. The reasons for such a discrepancy in detecting HBx-LINE1 chimeric transcripts remain to be explained.

Vietnam has a high prevalence of hepatitis B and 8.6 million people are reported to be HBsAg positive. An estimated 8.8% of women and 12.3% of men are chronically infected with HBV [10]. In recent years, there is a growing incidence of HBV-associated HCC and increasing mortality [10]. In the context of the growing incidence of HBV-related HCC mortality, we tried to determine if HBx-LINE1 might be used as a prognostic marker for HCC.

Fresh HCC tumor tissue and matched serum samples from 119 unrelated Vietnamese HBV-infected patients with HCC in the 108 Military Central Hospital, Hanoi, Vietnam, between 2014 and 2016 were screened for the presence of the HBx-LINE1 transcript. Patients were characterized based upon pathohistological findings and clinical and laboratory manifestations (hepatomegaly, splenomegaly, hyperbilirubinemia, elevated levels of aspartate aminotransferase (AST) and alanine transaminase (ALT), HBV-specific serology, alpha-fetoprotein). All HCC patients were positive for HBsAg and negative for antibodies against HCV and HIV. Blood samples were collected from all HCC patients and serum was immediately separated and stored at −70 °C until further analyses.

In brief, total RNA was isolated from 200 μl serum and from matched dyads of liver biopsy tissues with Trizol reagent (Life Technologies). 500 ng of total RNA were used for reverse transcription (RT) by RevertAid First Strand cDNA Synthesis Kit (ThermoFisher