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Original research

Delineation of microhemorrhage in acute hepatic encephalopathy using susceptibility-weighted imaging

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ABSTRACT

Introduction: Microhemorrhages (MH's) in patients with acute hepatic encephalopathy (AHE) have scarcely been described. This study set out to assess if MH's occur in characteristic locations and frequency in patients with AHE superimposed on chronic liver failure, and to determine if such findings correlate with the clinical and MRI severity.
Materials and methods: Over a 4.5-year period, AHE patients with SWI MRI were included. The maximum plasma ammonia level (PAL), number and location of "frank" hemorrhages (>5 mm size) or MH's (<5 mm) on SWI, and severity of DWI and FLAIR were recorded. Susceptibility foci in the basal ganglia were disregarded, as those changes might represent common mineralization. The presence of MH's was correlated with the MRI and clinical severity.
Results: Punctate MH foci were found in 18/38 (47.4%) patients. The most common locations were periventricular white matter (6/38 patients, 15.8%) and cerebral cortex (5/38, 13.2%). Of 47 MH's, only a tiny minority (8.5%) occurred in regions of abnormality on FLAIR or DWI. Both the MRI severity on FLAIR ($r = 0.420$, $p = 0.013$) and DWI ($r = 0.320$, $p = 0.045$) mildly correlated with clinical outcome, but the correlation was not significant after Bonferroni correction. No significant correlation was found between the number of MH's and the clinical score, clinical outcome, FLAIR severity, or DWI severity (range $r = -0.083$–0.152, $p = 0.363$–0.618). The number of MH's was not significantly different among various vasculopathies. Foci on SWI improved in two patients following liver transplantation.
Conclusion: SWI-positive foci outside of the basal ganglia (presumed MH's) are present in nearly half of AHE patients, but do not portend outcome. Regions with the most observed MH's were the periventricular white matter, cortical gray matter, and subcortical white matter.

1. Introduction

The term acute hepatic encephalopathy (AHE) encompasses a spectrum of neuropsychiatric abnormalities in patients with liver failure that have a wide range of clinical outcomes [1–5]. The pathophysiology of AHE is complex; hyperammonemia, impaired cerebral autoregulation, modulation of gamma-aminobutyric acid (GABA-A) receptors in the brain, and hyponatremia all contribute to the development of the clinical manifestations of AHE [1,2]. Clinically, the plasma ammonia level (PAL), West Haven score, and the model for end-stage liver disease (MELD) score have been used as diagnostic and prognostic clinical indicators in patients with AHE [3,4].

Numerous neuroimaging findings have been described in AHE. Classically, patients with end-stage liver disease are characterized as having high signal intensity on T1-weighted images within the globi pallidi and substantia nigra, related to manganese deposition [1,5–7]. High signal intensity on FLAIR or T2WI within the internal capsules' posterior limbs (corticospinal tracts) and cerebral white matter have also been described, perhaps related to potentially reversible edema, irreversible neuronal damage, or cerebrovascular small-vessel disease, depending on acuity [8,9]. In addition, abnormalities on both DWI and FLAIR MRI have been noted to occur

Abbreviations: (AHE), acute hepatic encephalopathy; (MH), microhemorrhage; (SWI), susceptibility weighted imaging; (GABA-A), gamma-aminobutyric acid; (MELD), model for end-stage liver disease; (PAL), plasma ammonia level.

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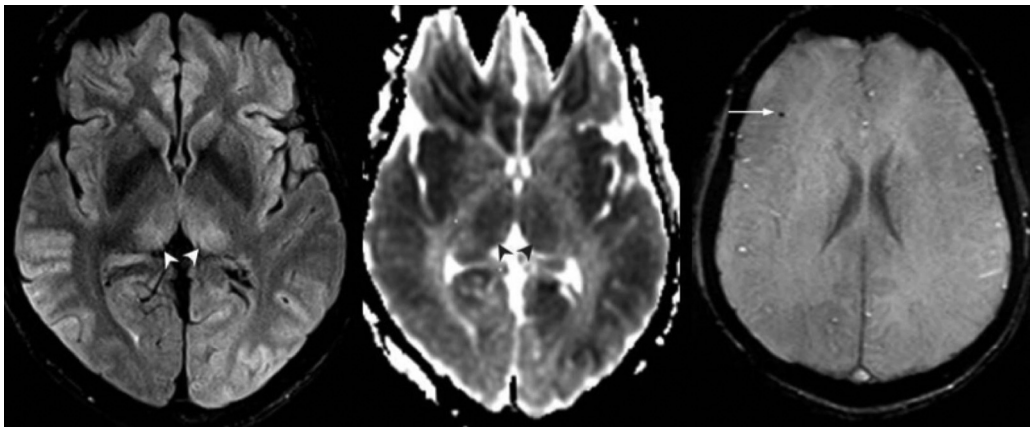

Fig. 1. A 48 year old male with acute confusion, and two MH's. A 3T FLAIR MRI (A) demonstrated bithalamic (*arrowheads*) and diffuse cortical edema, also visualized on DWI (*not shown*) and its ADC map (B); the diffuse cortical signal changes on FLAIR and DWI represent grade 4 MRI severity. On SWI (C), two frontal white matter MH's were noted (*thin arrow*). A non-enhanced CT was negative (*not shown*).

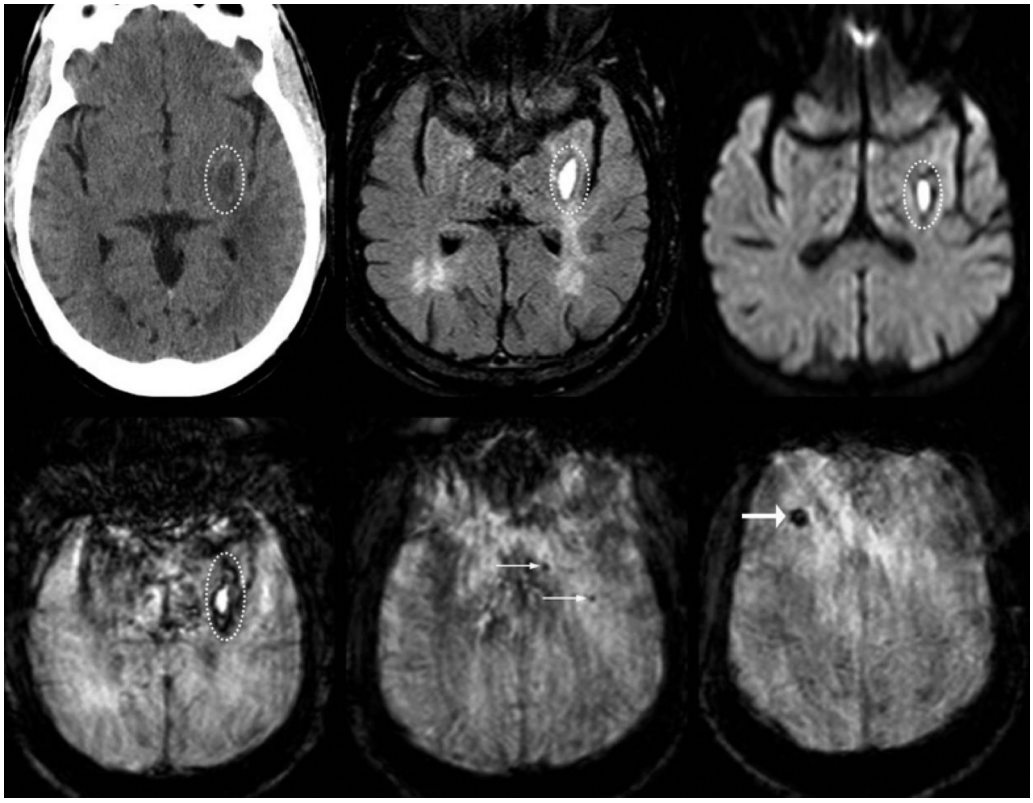

Fig. 2. A 60 year old male with acute confusion. NECT (A) showed focal left putaminal low attenuation (*circle*). FLAIR (B) demonstrated this lesion within the left putamen and chronic white matter abnormalities; restricted diffusion within the lesion (C) confirmed subacute parenchymal hemorrhage. SWI (D–E) was affected by motion but confirmed the intraparenchymal hemorrhage (*circle*). A right frontal subcortical hemorrhage (*larger arrow,* F) and punctate foci were noted (*arrows,* E); puntate foci were not called MH's due to motion.

in characteristic locations or distributions in AHE; and have been shown to be potentially reversible [9].

SWI has been established as an imaging modality that is capable of detecting MH's with a greater sensitivity than non-enhanced CT [10,11]. However, only case reports and studies of chronic liver disease have utilized this modality to assess patients with hepatic insufficiency; whereas, the extent and severity of cerebral SWI changes in patients with acute hepatic encephalopathy superimposed on chronic hepatic failure is yet to be determined [12–14]. The purpose of this study is to utilize SWI to describe the incidence and locations of punctate MH's in patients with AHE, and to determine if such findings are associated with markers of the initial clinical severity, the signal abnormalities on FLAIR and DWI, or the clinical outcome. Our hypothesis, based on scant prior studies, is that MH's will be observed in patients with AHE. However, because the physiologic cause of MH's remains unclear, we do not expect them to be located within particular areas of the brain.

2. Materials and methods

2.1. Patient selection

Institutional review board approval was obtained for this retrospective study. The medical and imaging records of all patients