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ACQUIRED (NON-WILSONIAN) HEPATOCEREBRAL DEGENERATION

Neurology

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ABSTRACT

Acquired (Non- Wilsonian) hepatocerebral degeneration is common in patients with large porto-systemic shunts and usually does not respond to therapy for hepatic encephalopathy. The neuropsychiatric changes include apathy, psychomotor retardation, memory failure and deficits in attention and concentration suggestive of a subcortical dementia. The pathogenesis of the disease is not known but diversion of portal blood in to the systemic circulation appears to underlie the condition. It is conceivable that both Wilson's disease and AHD are characterised by an early stage neuropathological process mainly affecting the basal ganglia, where MRI detectable hepatocerebral degeneration is slowly reversible and liver transplantation can rapidly improve neurological symptoms.

KEYWORDS

Hepatocerebral Non-Wilsonian Manganese Encephalopathy

Introduction:
Liver diseases give rise to variable degrees of neurological impairment ranging from hepatic encephalopathy caused by the toxic effects of ammonia on the brain to a chronic progressive encephalopathy called acquired hepatocerebral degeneration characterised by Parkinsonism, cognitive decline and movement disorders. The disease appears after one or more episodes of hepatic coma or it begins insidiously following a decline in hepatic function [1,2].

Pathogenesis:
The pathogenesis of the disease is not known but diversion of portal blood in to the systemic circulation appears to underlie the condition [2]. The disease is common in patients with large porto systemic shunts and usually does not respond to therapy for hepatic encephalopathy [2,3]. The neuropsychiatric changes include apathy, psychomotor retardation, memory failure and deficits in attention and concentration suggestive of a subcortical dementia [2].

The neuroimaging and pathological distinctions between chronic acquired hepatocerebral degenera-tion (AHD) and genetic hepatolenticular degenera-tion (Wilson's disease) are well elucidated and applied worldwide. In the inherited form there is a metabolic dysfunction which leads to copper deposition in basal ganglia. Consequently, the disease causes parkinsonism, dystonia, and abnormal movements that include athe-tosis and chorea [4]. In the acquired form, akinetic-rigid symptoms were prevalent [5,6]. Even so, the disease displays a wide spectrum of symptoms, and it is not rare that pa-tients present other signs and symptoms such as cho-reoathetosis and dystonia [7,8]. In AHD physiopathology, manganese deposition in basal nuclei appears to be a key factor [9-11]. The neuropathological changes observed in non-Wilsonian hepatocerebral degeneration include diffuse astrocytic hyperplasia, microcavitation and zonal necrosis of the deeper parts of the cerebral cortex and the lenticular nuclei with loss of nerve cells in the cerebral cortex, putamen, thalamus, cerebellar cortex and dentate nuclei [2,3]. A neurotoxic substance from the portal circulation bypasses hepatic metabolism and enters in to the systemic circulation traversing the blood–brain barrier [2]. Manganese is one such potential neurotoxin that could accumulate in the mitochondria of the globus pallidum damaging the glial cells and disrupting their energy metabolism [2].

Relation to hepatic encephalopathy:
The question of whether of HE is completely reversible is controversial, and some neurological deficits may persist [12,13]. However, until now there is no consensus about whether repeated HE episodes constitute a key factor in AHD development. Some reports did not find any relationship between HE and AHD [5,7]. However, other studies showed a direct relationship between the number of episodes and the probability of AHD occurrence [14,15], and some authors prefer the diagnosis of chronic hepatic encephalopathy for patients with a chronic liver disease and long-term neurological signs and symptoms and without apparent signs of manganese deposition in the brain [16].

Magnetic resonance (MR) imaging of the brain in patients with chronic hepatic failure stemming from a variety of causes reveals hyperintense signal on T1-weighted sequences, primarily in the lenticular nuclei [17-20]. The cause of this signal change is unknown. Experience with MR imaging in AHD is much more limited, and pathologic correlation is generally not available.

The most common cause of hyperammonemic encephalopathy is acute hepatic dysfunction, and other etiologies include portosystemic shunt surgery, drugs (e.g., sodium valproate, asparaginase therapy, or chemotherapy), infection, hypothyroidism, multiple myeloma, and post-lung or bone marrow transplantation [21]. Although the imaging findings of acute hyperammonemic encephalopathy are well described in children with inborn errors of metabolism [22], the radiologic findings of acute hyperammonemic encephalopathy in adults are less well described.

In the case reports by Stracciari et al [2], there were significant impairment in visuospatial attention and motor sequencing. The movement disorders include severe bradykinesia, rigidity, postural instability, postural tremor and orobuccolingual dyskinesias.2 Acquired hepatocerebral degeneration may be associated with myelopathy and spastic paraplegia [2]. Polymicrocavitation of the cortex and adjacent internal capsule along with loss of axons in the corticospinal tracts of the spinal cord occur [2,3] MRI of the brain shows lesions in the lenticular nuclei and midline cerebellum [3].

Role of liver transplantation:
Despite the different pathogenesis, the similarities between AHD and Wilson's disease are remarkable for pathological lesions and clinical and neuroradiological presentation [23,24]. Liver transplantation has been reported to reverse neurological manifestations in most patients with Wilson's disease [25]. Liver transplantation in AHD is confined to two cases. A cirrhotic patient with improved chronic cognitive and motor disorders after liver transplantation was described in 1970 [26]. Twenty years later, Powell et al reported a case of successful liver transplantation in AHD. Their patient had a significant improvement in intellectual functions and chronic neurological signs early after surgery. Findings confirm these positive results and also documents that neuroradiological abnormalities are reversible. It is conceivable that both Wilson's disease and AHD are characterised by an early stage neuropathological process mainly affecting the basal ganglia, where MRI detectable hepatocerebral degeneration is slowly reversible and liver transplantation can rapidly improve neurological symptoms. The

duration of the disease does not seem to be a crucial factor, as patients with long standing encephalopathy may also recover after liver transplantation both in AHD [3], and in Wilson's disease [25]. This conclusion has pathogenetic and therapeutic implications: the presence of signs and symptoms of chronic hepatocerebral degeneration, both in Wilson's disease and in the acquired non-Wilsonian form, should not be considered a contraindication for liver transplantation and surgery may be the elective treatment for the neurological syndrome.

Renjen et reported a case of acquired hepatocerebral degeneration (AHD) which responded very well to liver transplantation [27]. The patient underwent liver transplantation within 2 weeks of admission and postoperatively he showed a steady improvement in cognitive functions. He was discharged in a stable condition with improvement in speech, bradykinesia and reduction in the intensity of tremor [27]. Neurological improvement following liver transplantation occurs gradually over the course of 1 month to 1 year. The duration of the response following transplantation is not known but favourable outcomes in excess of 6 years following transplantation have been documented [27].

It is noteworthy that significant improvement in the neuropsychiatric syndrome has been defined following prolonged lactulose usage and by Freund et al. [28], using a branched chain-enriched amino acid diet. The neuropathological changes observed in non-Wilsonian hepatocerebral degeneration include diffuse astrocytic hyperplasia, microcavitation and zonal necrosis of the deeper parts of the cerebral cortex and of the lenticular nuclei, loss of nerve cells in the cerebral cortex, putamen, thalamus, cerebellar cortex, and dentate nuclei, and loss of axons in the corticospinal tracts in the spinal cord with fibrous gliosis [29].

Conclusion:

- In AHD physiopathology, manganese deposition in basal nuclei appears to be a key factor.
- All cases of hepatocerebral degeneration are not owing to Wilson's disease; other causes should be looked for.
- Patient with non-Wilsonian hepatocerebral degeneration do fairly well after liver transplantation.

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