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Case report

Degeneration of the corticospinal tract following portosystemic shunt associated with spinal cord infarction

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Summary. The clinicopathological aspects of a case of myelopathy that followed the creation of a surgical porto-caval shunt for hepatic cirrhosis and oesophageal varices are presented. Degeneration of the lateral corticospinal tracts associated with diffuse bilateral ischaemic changes of the spinal gray matter and proliferation of Alzheimer type 2 glia in the brain and brain stem were the most prominent findings. The association of corticospinal tract degeneration and ischaemic lesions of spinal gray matter in absence of any anatomical cause of spinal cord infarction suggests that a modification of the spinal blood flow caused by creation of portosystemic shunts might be the basic pathogenetic mechanism of this complication of severe liver disease.

Key words: Myelopathy – Cirrhosis – Portosystemic shunt – Spinal cord infarction

Introduction

The occurrence of spastic paraplegia following the creation of portosystemic venous shunts is considered to be a rare complicance of severe liver disease. Up to now no more than 50 cases have been reported but detailed pathological observations were available on only 13.

We report an additional case of "post-shunt" myelopathy in a patient with hepatic cirrhosis in whom the neuropathological examination disclosed degeneration of the corticospinal tracts associated with diffuse infarction of the spinal gray matter. A review of the pathological data available in the literature and a discussion on the pathogenesis of this disorder on the basis of these pathological findings is presented.

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Case report

The patient was a 60-year-old alcoholic male with hepatic cirrhosis. He underwent a surgical porto-caval shunt after several episodes of bleeding from oesophageal varices. From that time, he was followed as out-patient for several episodes of mild encephalopathy, controlled by conventional medical treatment. Thirteen months later he was admitted because of a severe episode of confusion and drowsiness and treated by means of selective aminoacids solutions. Laboratory data included the following values: total bilirubin 1.45 mg/dl; SGOT and SGPT 17 and 18 (normal values <12); cholesterol, 110 mg/dl; alkaline phosphatase, 18 U/l (normal values <28); albumin, 253 g/dl; γ-globulin, 1.98 g/dl; blood ammonia, 116 μmol/l (normal values <35); HBV markers were negative.

After the acute episode he complained of increasing difficulties with the gait which rapidly progressed to a spastic paraplegia. A complete neurological evaluation showed signs of marked spastic paraparesis and exaggerated deep tendon reflexes with bilateral ankle clonus. Plantar responses were flexor. Dysarthria and mental deterioration were present. All sensor modalities were intact. Ophthalmic examination was negative for Kayser-Fleisher ring and ceruloplasmin levels were normal.

The difficulty in walking progressed until he became bed ridden. The terminal period was characterized by a further episode of encephalopathy with progressive deterioration of the mental state and biochemical data. During this period the arterial blood pressure was about 110/70 mmHg; no acute drop of blood pressure occurred until 1–2 h before death. The patient died eight months after the acute episode and 21 months after the surgical porto-caval shunt.

General pathological findings

Postmortem examination disclosed a perforated duodenal ulcer and bilateral pneumonia.

The liver weighed 800 g and displayed diffuse finely nodular cirrhosis. The porto-caval shunt was patent. There was mild left-ventricular hypertro-

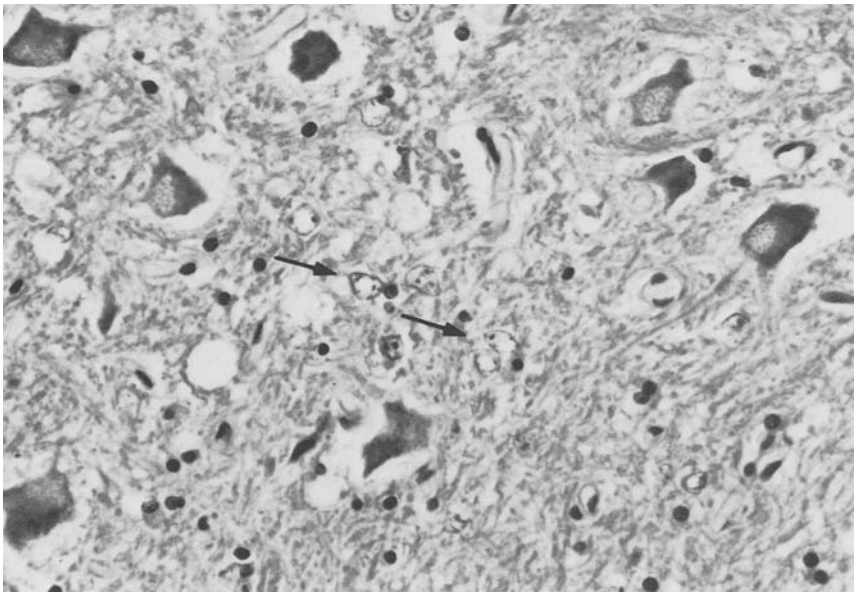

Fig. 1. Proliferation of Alzheimer type 2 glia (*arrows*) in cerebellar dentate nucleus (H.E. ×400)

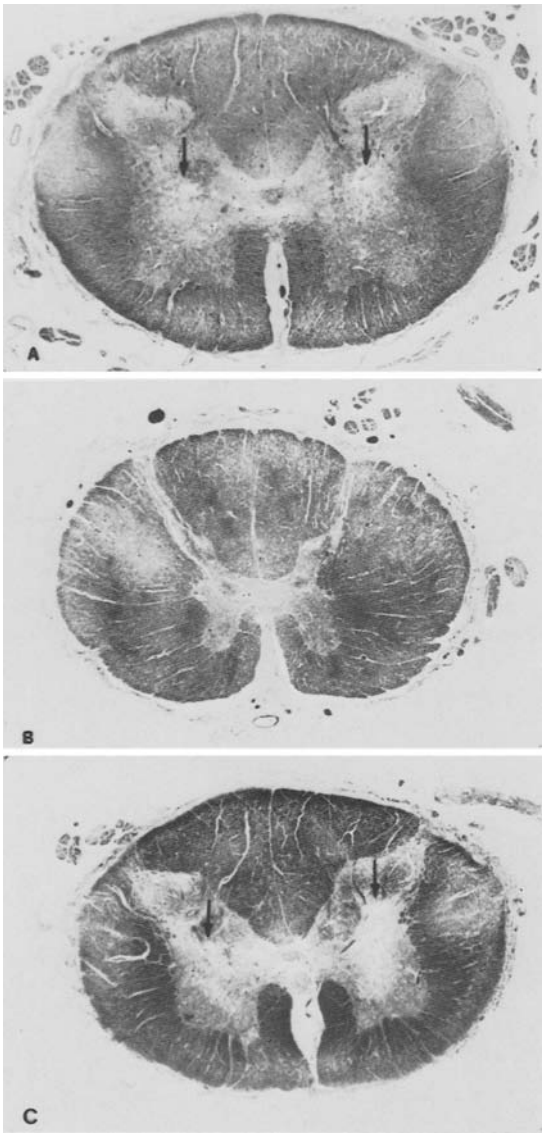

Fig. 2A–C. Spinal cord.
A cervical.
B thoracic. **C** lumbar. There is pallor of the area occupied by the lateral corticospinal tract and symmetric softening with cavitation of grey matter (*arrows*). (Luxol Fast Blue/H-E ×6)

phy and pulmonary emphysema. The aorta showed mild aterosclerosis and the orifices of intercostal arteries were patent. Features of dissecting aneurysm of the aorta were absent. Gross and microscopic examination of the kidney, thyroid, adrenal, pancreas showed no significant abnormalities.

Neuropathological findings

The brain weighed 1,400 g and showed no macroscopic abnormalities.

Microscopic sections obtained from each lobe, basal ganglia and brain stem showed the presence of large glial cells with clear vesicular nuclei

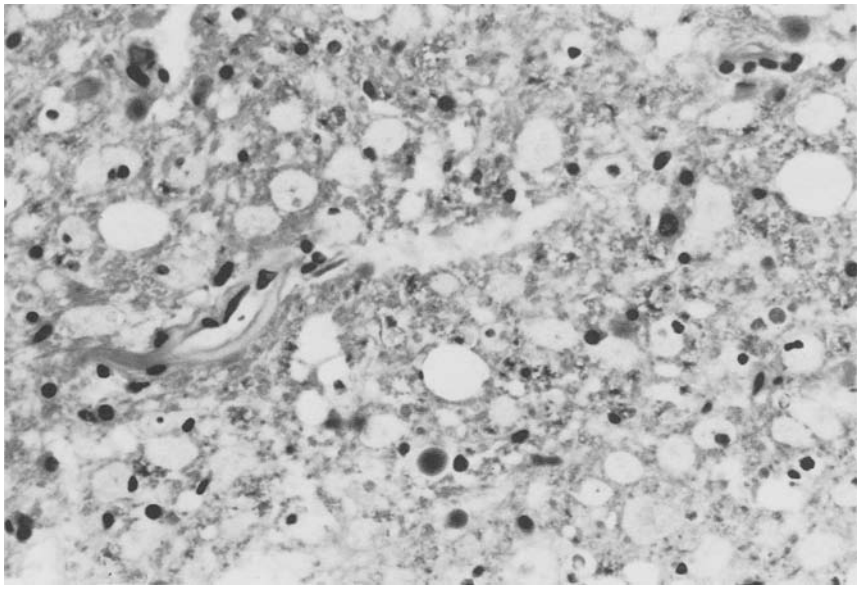

Fig. 3. Corticospinal tract in the thoracic spinal cord. There are numerous lipid-laden macrophages and scattered reactive astrocytes (H-E ×400)

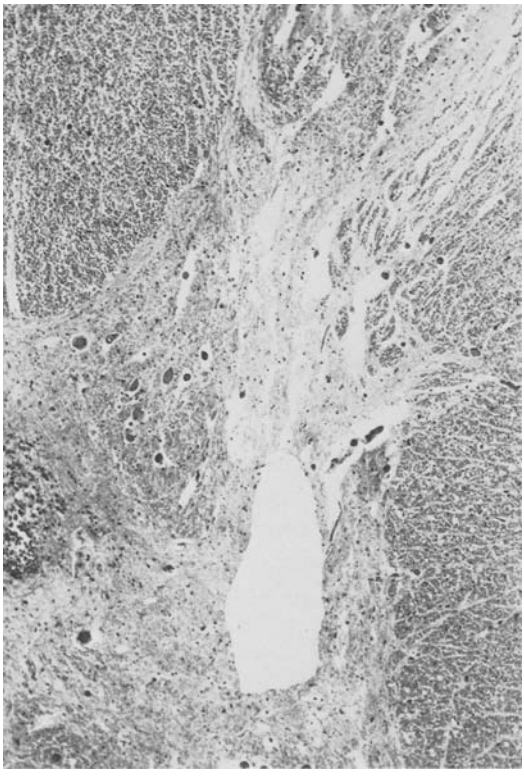

Fig. 4. Lumbar cord. Ischaemic changes of the grey matter with neuronal loss and cavitation (H-E ×100)

and very scanty cytoplasm corresponding to Alzheimer type 2 glia (Fig. 1). These large astrocytes were present in great numbers throughout the cerebral cortex, cerebellum and brain stem. They were absent in the spinal cord. With the exception of the presence of Alzheimer modifications there were no other pathological changes. No ischaemic loss of neurons was observed in the hippocampus or cortex. Examination of the cerebellum revealed a loss of Purkinje cells associated with proliferation of Bergmann's glia in the vermis. Examination of the brain stem revealed no pathological changes in the red nuclei and dorsal motor nuclei.

Spinal cord

Sections stained for myelin showed symmetrical loss of fibers in the lateral columns in the regions occupied by the lateral corticospinal tracts. The fiber loss started in the lower cervical segments and extended to the sacral segments (Fig. 2). The demyelinated area of the lateral columns contained numerous macrophages and scattered reactive astrocytes (Fig. 3). Rare perivascular lymphocyte infiltrates were present. Longitudinal sections of this area stained for axons by Bodian stain revealed marked loss of these structures. The spinal gray matter showed bilateral softening of the central portion of the horns which extended similarly to the corticospinal tracts, the degeneration sparing the lower lumbar and sacral segments. The morphology of the gray matter lesions varied from neuronal loss with slight reactive gliosis in the thoracic segments to bilateral central cavitation in cervical and lumbar segments (Fig. 2, 4). Histological examination of the arterial and venous spinal vessels showed no changes.

Discussion

In their review of the literature, Gauthier and Wildi (1975) reported 35 cases of encephalomyelopathy following portosystemic shunts. Following this paper we found 2 more cases (Budillon et al. 1979; Hoyumpa et al. 1979). Detailed neuropathological findings are available in only 14 cases, including this one. Review of these cases shows that liver cirrhosis was a constant pathological finding, except in one case in which chronic aggressive hepatitis was reported. The portosystemic shunts were spontaneous in four, surgically created porto-caval in eight, and surgically created lienorenal in two. The interval between the creation of the shunt and the onset of symptoms varies between 3 and 23 months, with a mean of 10.5 months.

The most common neuropathological finding in the brain was the presence of Alzheimer type 2 glia diffusely scattered throughout cerebral hemispheres and cerebellum. The pathological finding in the spinal cord common to all reported cases was symmetrical degeneration of the lateral corticospinal tracts associated with degeneration of the ventral corticospinal tracts in 7 cases; this tract was preserved in our case. The posterior colums disclosed a slight demyelination in 3 cases and the spinocerebellar tract in 2. Both tracts were uninvolved in the present case.

The pathogenesis of "shunt myelopathy" is still obscure. Two time-honored theories on the pathogenesis of this disorder have been reported. The first, based on the observation of intact axons in the corticospinal tract suggested a process of "primary demyelination" in which the noxa affects the myelin sheaths and spares the axons (Zieve et al. 1960). However, the finding of marked rarefaction of the axons observed in our case and in 8 of 11 cases in which specific histological studies of the axis cylinders were made is against a process of primary demyelination in the affected tracts (Lefer and Vogel 1972).

The second is based on the observations of reduction of Betz cells in the pre-Rolandic areas in two cases (Pant et al. 1963, 1968). These authors suggested that the disease process afflicted these neurons primarily and that the abnormality first becomes manifest in the distal axons as a progressive "dying-back" process. However, the absence of any reduction in number of the Betz cells and the cessation of demyelination in the cervical segments of the spinal cord in this and in other cases, makes the acceptance of such a theory difficult.

The role of the portosystemic venous shunt in the pathogenesis of this disorder is emphasized by the observation that hepatic encephalopathy in uncomplicated cirrhosis or other diseases causing liver failure results in pathological changes only within the brain and brain stem. However, in hepatic cirrhosis complicated by spontaneous or surgically induced shunts, pathological changes can be observed in the spinal cord. Lefer and Vogel (1972) suggested that the mechanism by which the porto-caval shunt might cause long tract degeneration is related to the presence of compounds normally detoxified by the liver, which reach the brain and spinal cord and cause injury to the axis cylinders, nerve cell bodies and myelin.

The present case differs from the previously reported post-shunt myelopathies in the presence of necrosis of the spinal gray matter associated with corticospinal degeneration. Infarction of the spinal cord is rarely related to severe episodes of hypotension. Usually, paraplegia occurrs suddenly a few hours after the acute episode (Henson and Arson 1967). In our patient the onset of paraplegia occurred about 13 months after surgery. This is too long a period of time to relate the spinal cord lesion to a severe hypotension during the surgical procedure. Moreover, no hypotension was observed in the terminal period apart from an acute drop of blood pressure 1–2 h before death. The exclusion of any marked and prolonged episodes of hypotension is supported by the pathological examination of the brain, which did not disclose ischaemic loss of neurons in the neocortex and hippocampus. The loss of Purkinje' cells in the vermis is probably related to patient's alcoholism more than to ischaemic damage.

Selective necrosis of the spinal gray matter has been reported in patients with dissecting aneurysm of the aorta or atheromatous emboli arising from severely atherosclerotic aortas occluding small spinal arteries (Kepes 1965; Herrick and Mills 1971). In our case the aorta does not show either severe atherosclerosis with ulcerated atheromas or wall dissection.

A temporal relationship between corticospinal degeneration and ischae-

mia of the gray matter is difficult to establish. The histological pattern suggests that the ischaemic damage of the spinal gray matter was a burned-out process, while corticospinal degeneration was not. However, while repair of neuronal necrosis requires a short time only (Lindenberg 1982), repair of degeneration of the long tracts might be a very long process. Indeed, in 8 of 13 autopsy cases of post-shunt myelopathy reported in the literature the presence of macrophages associated with variable degrees of gliosis has been described independent of the range of time between first neurological symptoms and death (Gauthier and Wildi 1975). Thus, it cannot be excluded that both events occurred simultaneously.

Although the association of spinal gray matter infarction and corticospinal tract degeneration might occur co-incidentally, the absence of any obvious causes of spinal cord infarction and the extension of the ischaemic lesions to the same segments involved by corticospinal tract degeneration suggests that haemodynamic factors may play an important role in the pathogenesis of post-shunt myelopathy. The porto-caval shunt may cause a derangement of spinal cord blood flow with consequent hypoxic damage to the nervous tissue. The effects of this haemodynamic change may be enhanced by the presence of circulating toxic substances normally cleared by the liver (Norenberg 1977).

Studies on haemodynamic modifications induced in the spinal circulation by porto-systemic shunts are necessary to understand the mechanism of this rare complication of severe liver disease.

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