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Chronic portosystemic hepatic encephalopathy refractory to medical treatment successfully reversed by liver transplantation

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Sir: Hepatic encephalopathy (HE) is a complex neuropsychologic syndrome ranging from a subclinical neurologic disorder to coma unresponsive to stimuli. HE is associated with acute or chronic hepatocellular failure, increased portosystemic shunting of blood, and metabolic changes [6]. In some patients with severe portosystemic shunting, chronic HE may be resistant to treatment with a low-protein diet and the administration of lactulose, neomycin, and branched chain amino acids [8]. Additional, and more drastic, procedures, such as surgical closure of portosystemic shunts [5], colon bypass [9], and colectomy [2] may improve HE for a while but are associated with a high perioperative mortality rate. In severe cases of chronic portosystemic encephalopathy, morphological evidence of irreversible brain damage has been found [1, 3, 10]. Liver transplantation is the most successful approach to end-stage liver disease, but in patients with irreversible cerebral damage, liver transplantation is contraindicated, as the quality of life is not improved [7]. We report on a patient with HE after a surgical portacaval anastomosis 37 years earlier who experienced full neurologic recovery following liver transplantation.

In 1955, a 17-year-old female had severe bleeding from esophageal varices as the first symptom of liver disease. History, biochemical tests, and liver biopsy revealed cryptogenic cirrhosis. A splenoportogram showed multiple varices around the esophagus. Because of severe bleeding, a surgical portacaval anastomosis was performed end-to-side in February 1956 without complications. The patient recovered completely and worked as a dressmaker for the next 30 years without ever experiencing esophageal bleeding or encephalopathy.

In 1986, 31 years after having received the portacaval shunt, the patient had her first episode of HE, grade four. She responded well to a low-protein diet and lactulose, and she experienced no further encephalopathy until 1990, when persistent subclinical encephalopathy and five episodes of grade four encephalopathy recurred. A gradual decrease in prothrombin index from 0.53 ± 6 to 0.41 ± 12 units L^{-1}, in albumin from 483 ± 51 to 398 ± 78 $\mu mol\ L^{-1}$ and in galactose elimination capacity from 25.2 ± 10 to 16.4 ± 5 $\mu mol\ k^{-1}\ min^{-1}$ were noted, together with a serum ammonium of 165 ± 12 mmol L^{-1} (normally below 26 mmol L^{-1}). The patient had problems with fine motoric movements, such as handwriting and dysarthria, and she complained of visual disturbances, persistent headache, and failure of memory. The persistent encephalopathy was evaluated by continuous reaction time [4] and neurologic examination led one to suspect that the brain dysfunction was irreversible. Several electroencephalograms revealed 4–6 Hz activity, and the visually evoked potential showed an abnormal pattern. A CT scan of the brain showed central atrophy without localized defects. In an attempt to evaluate whether the encephalopathy was reversible, an intravenous injection of flumazenil (0.5 g) was given; however, there was no effect, either clinically or on continuous reaction time.

As the patient's condition necessitated constant hospitalization, liver transplantation was performed in November 1993 without complications. A macronodular cirrhosis with a patent side-to-side anastomosis was noted during transplantation. Histological postoperative evaluation substantiated the diagnosis of cryptogenetic cirrhosis. Postoperatively, she had a dramatic neurologic recovery. Within weeks the patient had normal continuous reaction time testing, no dysarthria, headache, or disturbance of vision and she regained a normal handwritting. She is now in good clinical condition 8 months after transplantation and her brain function, as judged by her relatives, is as before she became encephalopathic. She is living a normal life as a housewife.

After a surgical portacaval anastomosis had been constructed 37 years earlier, irreversible, toxic, cerebral damage in this patient with cirrhosis and long-lasting encephalopathy could be considered to contraindicate transplantation. The patient had, however, full neurologic recovery following liver transplantation. This shows that even long-lasting and persistent portosystemic encephalopathy refractory to treatment with lactulose, neomycin, a low-protein diet, and intravenous administration of flumazenil is reversible after liver transplantation with re-establishment of a normal portal flow. Long-term HE that is unresponsive to medical treatment modalites should, therefore, not contraindicate liver transplantation.

Continuous administration of the benzodiazepine antagonist flumazenil may improve the neurologic status in some patients with chronic portosystemic encephalopathy [5]. Flumazenil, via injection or infusion, may, therefore, be an important tool in differenting between reversible and irreversible neurologic changes before liver transplantation. In our patient, the test was of no use. How-

ever, a relatively small single dosis of 0.5 mg flumazenil was used and a different result might have been obtained with a larger dosis.

In summary, the complete disappearance of encephalopathy after liver transplantation in our patient indicates that, irreversible cerebral damage does not develop despite long-lasting cerebral dysfunction due to hepatic portosystemic encephalopathy.

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Delightful hair growth after lung transplantation

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Sir: Immune-mediated mechanisms have been implicated in the pathogenesis of alopecia areata, probably with an altered T-cell regulation of the immune response [1]. Biopsy specimens show perifollicular lymphocytic infiltrates. The prognosis of this disorder is uncertain and the process can be reversed to varying extents by taking several different measures, including the administration of corticosteroids, local irritants, or photochemotherapy. Also cyclosporin, topically or orally applied, can produce regrowth of hair in some patients with alopecia areata [2].

In transplant recipients, hypertrichosis is a well-known and, especially in women, usually an unwanted, side effect of the use of cyclosporin. However, sometimes this is encountered with great delight, as is shown by the following case.

A now 49-year-old woman suffered from emphysema with progressive dyspnea and hypoxemia upon exertion. Her therapy consisted of inhaled corticosteroids (budesonide) and bronchodilators (salbutamol and ipratropium bromide), as well as systemic corticosteroids (7.5 mg daily), the latter leading to a Cushing syndrome. In the spring of 1992, alopecia areata was diagnosed with a slowly progressive, diffuse hair loss of the scalp, eyebrows, and eyelashes. There had been no change in medication and the patient did not suffer from endocrine disorders. Her father had experienced hair loss starting at age 40 and her sister had very limited alopecia areata.

The patient was treated with local application of desoximetason (Topicorte) without any effect and she progressed to alopecia universalis with complete loss of all body hair. PUVA treatment (ultraviolet A light and psoralen) had no effect, and so she started to wear a wig and to draw on eyebrows with a make-up pencil.

In April 1994 the patient underwent a bilateral lung transplantation with a good clinical result. Postoperative maintenance immunosuppression consisted of cyclosporin, azathioprine, and prednisolone. Within a few weeks she noticed progressive hair growth on her scalp and eyebrows; later, there was also regrowth of eyelashes and all other body hair. Even hypertrichosis developed.

The explanation for this renewed hair growth is probably the use of immunosuppressive therapy (cyclosporin and corticosteroids), possibly in combination with the disappearance of a state of chronic illness.

Although the patient was very happy with her lung transplantation,