

Acute Confusion in an Elderly Woman with Rendu-Osler-Weber Disease

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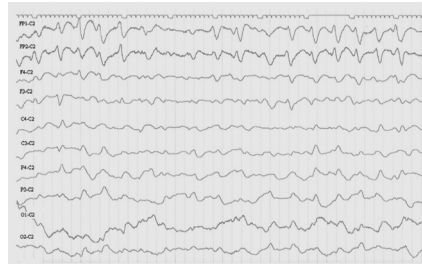
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Hereditary hemorrhagic teleangiectasias – Rendu-Osler-Weber disease – is an autosomal dominant disorder with incomplete penetrance. The prevalence is estimated to range from 1:3.500 to 5.000. Two mutant genes encoding for proteins that bind to the transforming growth factor-beta are involved in the pathogenesis of this disease; however, up to 30% of cases are due to spontaneous mutations [1].

The hallmark of the disease is a defect in the vessel walls of the microvasculature with teleangiectasias and arteriovenous malformations of the skin, mucous membranes, gastrointestinal and urinary tract, lungs and central nervous system. The skin teleangiectasias appear during childhood and enlarge later, involving mostly the face (lips, conjunctiva and retina), hands and nails. The main complications of the disease are due to rupture of the abnormal walls of the teleangiectasias and bleeding into various organs, resulting in epistaxis, hemoptysis, intestinal and urinary tract bleeding [1]. We report here a patient with Rendu-Osler-Weber disease who presented with an acute confusional state and where the clue for the diagnosis was an electroencephalography record.

Patient Description

A 75 year old woman was admitted due to acute confusion. Two days previously she complained of dizziness and had become withdrawn, confused and drowsy. The patient and her son suffered from Rendu-Osler-Weber disease with recurrent epistaxis leading to chronic anemia. Physical examination was unremarkable, with blood pressure 105/80 and pulse rate 108/minute. The patient was lying with eyes open; she did not respond to verbal or visual

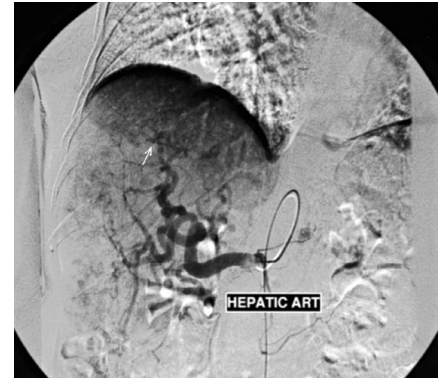


[A] EEG record shows generalized slowing and triphasic waves.

stimuli and reacted semi-purposefully to pain. Neurologic examination revealed an intermittently increased tone of the limbs and a bilateral extensor toe response. There were no signs of meningeal irritation or involuntary movements.

Blood examination revealed normal glucose, urea, creatinine, sodium, calcium, magnesium, total protein, albumin, uric acid, alkaline phosphatase, transaminases, lactate dehydrogenase, amylase and thyroid-stimulating hormone. Hypokalemia 3.4 $\mu\text{mol/ml}$ was corrected promptly. Coagulation factors, vitamin B12, folic acid and blood gases as well as hepatitis serology were normal. A blood count showed signs of chronic iron deficiency anemia with hemoglobin 9.4 g/dl.

A brain computed tomography scan demonstrated only an old lacunar infarct in the left basal ganglia and the chest X-rays were normal. A lumbar puncture yielded normal laboratory results except for an increased lactate level – 2.89 mmol/L (normal 1.1–2.4 mol/L). An electroencephalogram that was performed to rule out a non-convulsive epileptic state revealed widespread triphasic waves, more frontally, on the background of a generalized slowing [Figure A]. Consequently,



[B] Angiography of the hepatic artery demonstrates teleangiectasias and arteriovenous shunts.

hyperammonemia of 104.8 $\mu\text{g/dl}$ (normal 11–48 $\mu\text{g/dl}$) was found.

Abdominal sonogram revealed multiple tubular structures in the liver, which demonstrated high velocity turbulent flow on color Doppler, and the hepatic artery was strikingly dilated. Similarly, the hepatic veins were markedly dilated, whereas the portal vein was normal in caliber. Angiography of the celiac, splenic, superior mesenteric and common hepatic arteries demonstrated multiple vascular lesions of different sizes in the liver and spleen, compatible with teleangiectasias and intrahepatic arteriovenous shunts [Figure B]. On gastroscopy, teleangiectasias without evidence of active bleeding were found in the stomach and duodenum. On the third day of hospitalization, hemoglobin decreased to 8.3 g/dl and melena was detected.

Tranexamic acid as an antifibrinolytic agent was administered for 5 days. The patient was further treated with a low protein diet, neomycin 1 x 3 g and lactulose

suspension. Clinical improvement occurred 2 days after initiation of the treatment. The ammonia level decreased to 39 $\mu\text{g}/\text{dl}$. The patient was discharged on the eighth day of hospitalization.

Comment

The classical nervous system complications of Rendu-Osler-Weber disease are brain or spinal cord hemorrhage. Vascular malformations can also cause focal neurologic signs due to local pressure as they enlarge, even in the absence of bleeding. Remote central nervous complications of this entity are usually consequences of pulmonary arteriovenous fistulas accompanying the disease; thus brain abscess, embolic stroke and air embolism may occur. The presentation of Rendu-Osler-Weber disease with hepatic encephalopathy is rare even among patients with documented hepatic involvement [2].

Portal systemic encephalopathy in these patients occurs due to arteriohepatic, arterioportal venous or portohepatic shunts [3], following a precipitating factor such as increased dietary protein, constipation, gastrointestinal bleeding, electrolyte

disturbance, or exposure to certain drugs. The trigger for encephalopathy in our patient was probably an occult intestinal bleed.

The diagnosis can be difficult since the neurologic signs can vary and the finding of a typical tremor (asterixis) may be absent. The clue to the diagnosis in our patient was an EEG that showed triphasic slow waves. This finding is not specific, but it is highly characteristic for metabolic encephalopathies. Subsequently, high ammonia blood levels were detected while other liver tests were normal.

In our patient a hepatic encephalopathy first manifested at an old age, without previous major complications of the disease. Early recognition of the condition is crucial before irreversible brain damage occurs. The diagnosis can easily be confirmed by ultrasound and the patient can be successfully treated without sequelae. Moreover, recurrences can be prevented by a low protein diet and avoidance of known precipitating factors. In cases with impaired liver function, portal hyperten-

EEG = electroencephalogram

sion and high cardiac output, embolization of hepatic arteries or liver transplantation can be considered [4].

References

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