YOUR DIAGNOSIS

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Hyperammonaemic encephalopathy in a 13-year-old boy

Clinical information

A previously healthy 13-year-old boy presented with a 3-day history of nausea, vomiting and progressive weakness and lethargy. When admitted to a peripheral hospital, he was afebrile, mildly dehydrated and had a Glasgow Coma Scale of 7. Within a few hours, he became comatose and required intubation. A cerebral CT scan was normal. Plasma ammonia concentration, however, was markedly elevated with 250 µmol/l (normal 12–48 µmol/l). Renal function was mildly impaired with a plasma creatinine of 85 µmol/l (normal 45–80 µmol/l) and plasma urea of 11 mmol/l (normal < 7 mmol/l). Blood cell count showed a leukocytosis of 13.3×10^9/l with 47% neutrophils. Electrolytes, serum C-reactive protein, liver function and coagulation tests were normal. A putative diagnosis of a late-onset orni-thine transcarbamylase (OCT) deficiency was made and the patient transferred to the University Children's Hospital, Zurich.

On admission, plasma ammonia was 179 µmol/l (normal < 55 µmol/l) and glutamine 909 µmol/l (normal < 600 µmol/l). The urine was turbid; urinalysis showed leucocyturia (445 cells/µl), a positive nitrite test, bacteriuria and microhaematuria (640 cells/µl); the pH was 8. Emergency analysis of organic acids, amino acids and orotic acid in plasma and urine ruled out a primary metabolic defect. Ammonia excretion was promoted with both a catheter draining the bladder continously and forced intravenous fluids (100 ml/kg daily). Plasma ammonia decreased rapidly into the normal range (48 µmol/l) within 6 h after admission. Ultrasound revealed hyperechogenic urinary fluid, a large bladder, a dilated proximal urethra suggestive of posterior urethral valves and markedly dilated ureters and pyelons. The structure of both kidneys appeared normal. A micturition cystogram revealed remnants of posterior urethral valves and gross bilateral vesicoure-teric reflux with a left duplex system. DMSA scintig-raphy showed bilateral patchy photon defects with a differential function (right to left) of 32%:68%. Anti-biotic treatment with ceftriaxone was initiated (60 mg per kg body weight daily i. v.). When the urinary cul-ture grew *Corynebacterium pseudodiphtheriticum* (10^6 CFU/µl), therapy was changed to amoxicillin (100 mg/kg daily i. v.).

The boy was extubated after 24 h and the level of consciousness returned to normal within 2 days. At discharge 3 weeks later, neurological examination showed mild dysarthria and a limp of the right leg. MRI of the brain was normal, while an EEG showed diffuse slow waves on the left fronto-central side, but no specific features suggesting encephalitis or epilepsy. The glom-erular filtration rate, assessed as a single Cr^{51} injection clearance, was normal (99 ml/min per 1.73 m² body surface area). Six months later, the neurological exam-ination was normal.

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Diagnosis

Hyperammonaemic encephalopathy secondary to urinary tract infection with urease-producing bacteria.

Discussion

Hyperammonaemic encephalopathy secondary to urinary tract infection (UTI) with urea splitting bacteria, e.g. *Proteus mirabilis, Klebsiella oxytoca* and *Klebsiella pneumoniae and Corynebacterium group D-2,* has been reported in a few children with known underlying obstructive uropathy [1, 2, 3, 4, 5, 6, 7, 8, 9,10]. Three concurrent pathogenetic mechanisms are known to cause hyperammonaemia secondary to UTI: (1) infection with urease producing organisms splitting urea into ammonia [1, 2, 3, 4, 5, 6, 7, 8, 9,10], (2) slow passage of large urinary volumes along a large mucosal surface area [6], and (3) an alkaline urinary pH favouring diffusion of ammonia into the blood stream [3, 5, 6,7].

A few aspects of the reported patient deserve further comment. Firstly, hyperammonaemia in a previously healthy 13-year-old boy led to assume a late-onset metabolic disease as the primary diagnosis. Further investigations, however, ruled out a primary metabolic defect, intoxication or portocaval shunt, and revealed an obstructive uropathy with dilation of the whole urinary tract. While inborn metabolic diseases are rare, hyperammonaemia secondary to UTI is even rarer. Prompt urinalysis, even with a dipstix, is also part of the primary metabolic work-up. Secondly, *Corynebacterium spp.* was only reported once in a similar condition [6], the other isolated pathogens being *Proteus mirabilis* [3, 4, 7,8], *Klebsiella oxytoca* and *Klebsiella pneumoniae* [1, 2,3], *Enterococcus faecalis* [1], *Moraxella catarrhalis* [1] and *Enterobacter* [3]. Thirdly, elevated plasma glutamine points to prolonged hyperammonaemia, but normalisation of plasma ammonia within a few hours of therapy is inconsistent with a primary metabolic disorder. In the previous publications, the underlying obstructive uropathy had already been known when the hyperammonaemic encephalopathy occurred including prune belly syndrome, hydronephrosis and hydroureter, obstructive ureterocele and neurogenic bladder. Treatment included immediate intravenous administration of antibiotics and generous fluids and securing of continuous drainage of the urinary tract. All but one patient, a 6-year-old boy with hydronephrosis and hydroureter who suffered a bilateral posterior cerebral artery infarction with blindness and spastic tetraparesis [10], had a good outcome.

UTI and obstructive uropathy have to be included in the differential diagnosis of unexpected hyperammonaemia and encephalopathy, particularly if presenting beyond the neonatal period. Prompt diagnosis and treatment is crucial to prevent potential brain injury.

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