CASE REPORT

TRAUMA AND RECONSTRUCTIVE UROLOGY

Intermittent hyperammonemic encephalopathy after ureterosigmoidostomy: spontaneous onset in the absence of hepatic failure

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Intermittent hyperammonemic encephalopathy after ureterosigmoidostomy is a rare, but if unrecognized, potentially lethal condition. Ureterosigmoidostomy was performed in a male patient with bladder extrophy. After 35 years, he developed hyperammonemic encephalopathy. Diagnostic procedures did not reveal hepatic nor metabolic disorders. Despite administration of preventive medical treatment, several episodes recurred. A durable prevention was finally achieved by conversion into an ileal conduit.
Intermittent hyperammonemic encephalopathy can occur decades after ureterosigmoidostomy. In the case of absence of metabolic disorders and resistance to medical treatment, conversion into a urinary diversion using an ileal segment constitutes an effective *ultima ratio*.

Key Words: bladder extrophy ‹› urinary diversion ‹› ureterosigmoidostomy ‹› complications ‹› hyperammonemic encephalopathy

CASE REPORT

Primary ureterosigmoidostomy for bladder extrophy was performed in a 23 year old male patient. Osteoporosis developed two decades later and was treated successfully with bisphosphonates. Periodically, asymptomatic subclinical acidosis was treated with oral sodium/potassium citrate and bicarbonate. Otherwise, laboratory and clinical examinations during continuous follow-ups at our department were unremarkable.
However, 35 years after urinary diversion, the patient experienced recurrent episodes of disorientation, altered consciousness and epileptic seizures which led to repeated hospital admissions. Extended interdisciplinary examinations detected only a protein S deficiency. Subsequently, the patient received phenprocoumon for anticoagulation and prophylaxis of thromboembolic events.
Ten months later, he was again referred to the emergency department of our medical centre for severe deterioration of his mental status. The electroencephalogram (EEG) examination showed triphasic waves reflecting a non-convulsive *status epilepticus* (Figure 1), which was successfully treated by intravenous administration of phenytoin. The patient additionally received valproic acid (1600 mg daily) for long-term medication. Extended laboratory examinations were subsequently performed and revealed a hyperammonemic hyperchloremic metabolic acido-

sis (max. ammonia 305 μmol/l, chloride 125 mmol/l; Figure 2). Despite undergoing various diagnostic procedures, neither pre-existing acute or chronic liver failures nor congenital or acquired metabolic disorders were detected. Ultrasonic examination of the urinary tract excluded hydronephrosis or sigmoid distension. Treatment of the hyperammonemic hyperchloridemia with lactulose, paromomycin and L- carnitine decreased the ammonia serum level only temporarily. After replacing valproic acid with levetiracetam (3000 mg daily) for antiepileptic treatment, the ammonia levels declined to standard values (Figure 2).

Despite ongoing antiepileptic medication, another *status epilepticus* occurred three weeks later, again related to hyperammonia. In default of other possible etiologies, a bacterial ureolysis in the bowel was considered although the urinary tract and sigmoid colon did not show any signs of restricted urinary drainage. To verify this hypothesis, bilateral percutaneous nephrostomies were inserted (Figure 3) and 48 hours later, the elevated serum levels of ammonia and chloride indeed decreased to the normal range. The psychomotor symptoms (drowsiness, disorientation) normalized in concordance with the laboratory findings. Tentative clamping of nephrostomies resulted in the recurrence of hyperammonemia and psychomotor symptoms.

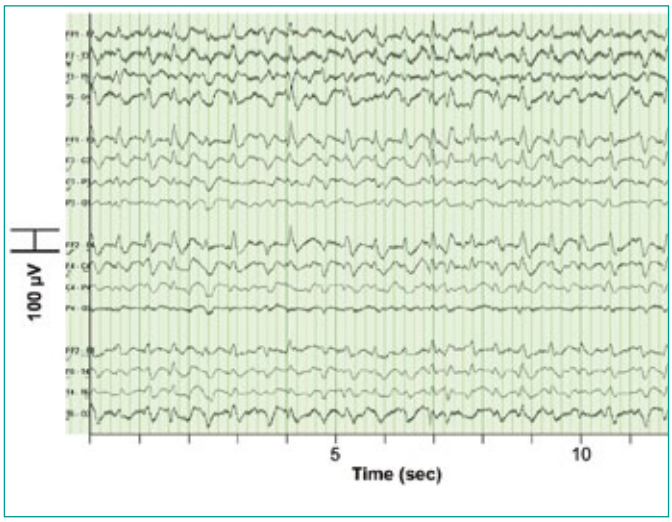

Figure 1. *Electroencephalogram (EEG). Triphasic waves indicate an acute non-convulsive status epilepticus triggered by hyperammonemic encephalopathy.*

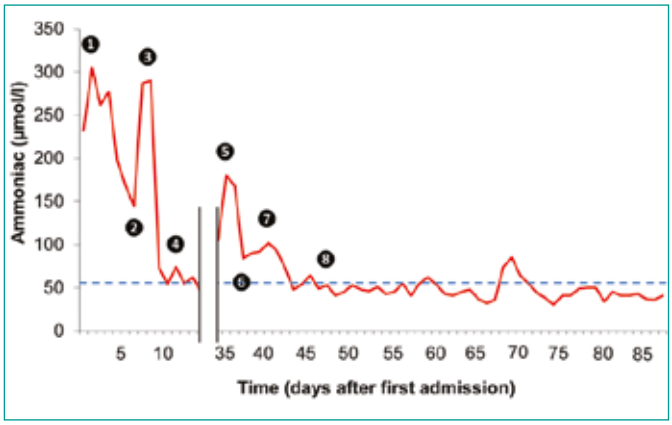

Figure 2. *Serum levels of ammonia over time. Ammonia serum level high above upper reference point at the first admission to the emergency department [1]. Administration of lactulose, paromomycin and L-carnithin only temporarily induces a significant decrease [2, 3]. After modification of the antiepileptic treatment (replacement of valproic acid by levetiracetam), ammonia levels declined to normal values in concordance with clinical symptoms [4]. Three weeks later, a recurrent episode of elevated ammonia serum levels with clinical symptoms under ongoing medical treatment [5]. Decrease of the elevated serum level 48 hours after bilateral insertion of percutaneous nephrostomies [6]. De novo increase of ammonia with neurological symptoms after clamp of nephrostomies [7]. Normal serum levels of ammonia over long-term follow-up [8]. The upper reference point of serum ammonia (<55 μmol/l) indicated by the dashed line.*

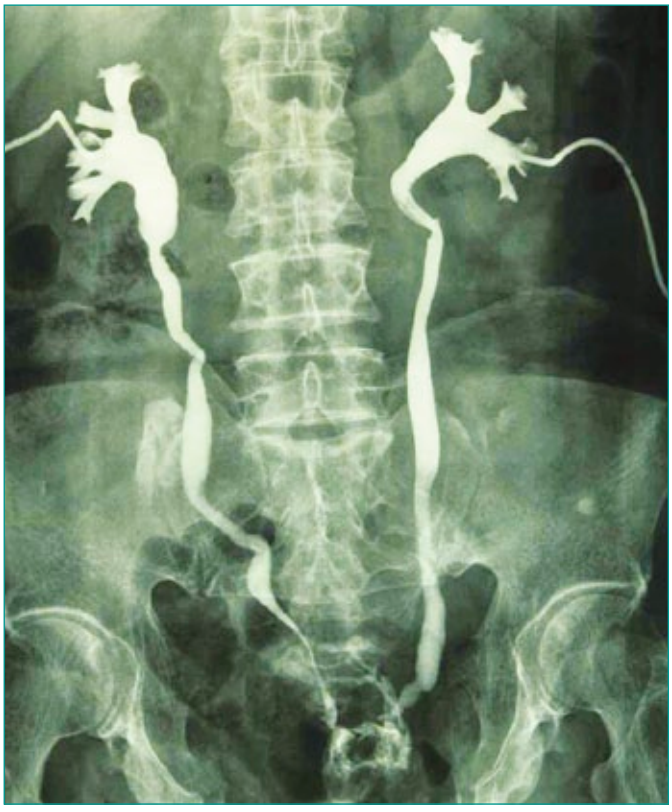

Figure 3. *Antegrade pyelography. Contrast study after insertion of nephrostomies testifies absence of impaired upper tract drainage and retention of urine in the sigmoid colon.*

Subsequently, the patient agreed to a conversion of the ureterosigmoidostomy into an ileal conduit, despite being previously satisfied with the ureterosigmoidostomy. With the exception of a postoperative subsegmental pulmonary embolism (pre-existing protein S deficiency), the patient did not suffer from further complications. Continuous clinical and laboratory monitoring was performed postoperatively and indicated normal serum levels of ammonia, as well as normal hepatic and renal function. Over the 31 months since the procedure, the patient has not presented with any further episodes of hyperammonemia, epileptic seizures or encephalopathic symptoms. Antiepileptic medication was stopped.

DISCUSSION

Ureterosigmoidostomy was first performed by John Simon in 1851 for a patient presenting with bladder extrophy [1]. This form of continent urinary diversion and its modification – the sigma-rectum pouch – are still options for primary or secondary urinary diversion in patients who are not eligible for primary bladder reconstruction [2, 3, 4].

Episodes of hyperammonemic encephalopathy after ureterosigmoidostomy are extremely rare, with only a few cases reported [5-14]. This severe neurological disorder is caused by elevated serum levels of ammonia in the post-hepatic blood circulation. After passage of the blood brain barrier, ammonia accumulates in the astrocytes where it disturbs neuronal function. The accompanying symptoms consist of somnolence, seizures and behavioral alterations [15]. In the worst case scenario, hyperammonemia can be lethal [15]. In ureterosigmoidostomy, elevated serum levels of ammonia in the portal vein can be caused by the exposure of the colon to urine [16]. Specific bacterial colonization in the colon (e.g. Proteus mirabilis) may cause fermentation of uric acid to ammonia and subsequent spill over into the blood stream. However, a reduced metabolic capacity of the liver (due to acute or chronic diseases) or portocaval shunts are generally required for pathological serum levels of ammonia in post-hepatic circulation [17]. As in the presented case, treatment with valproic acid can lower carnitine in the urea cycle and thus exacerbate hyperammonia [13] (Figure 2). Episodes of hyperammonemic encephalopathy after ureterosigmoidostomy without the presence of concomitant hepatic or metabolic failure (deficiencies of urea-cycle enzymes) are rare [7, 9-11], with only five cases reported in literature. Two of these cases had a history of previous alcohol abuse [7, 9] and the other two suffered from congenital muscular atrophy, which may also predispose to hyperammonemia [11]. The present report is the second with hyperammonic encephalopathy after ureterosigmoidostomy in the absence of additional pre-existing metabolic pre-disposition (hyperammonemia persisted after stopping treatment with valproic acid). During 31 months of follow-up, all relevant laboratory values (ammonia, chloride, natrium, base excess) were monitored at least bi-weekly and all remained in the normal range.

The exact reason for the long lag after urinary diversion until presentation of hyperammonemia remains unclear. The metabolic disorder was presumably triggered by bacterial overgrowth (bacteriogenic ureapoesis). However, it seems evident that the absorption of ammonia in the sigmoid exceeded the physiologic metabolic capacity of the liver despite the absence of hepatic or metabolic co-morbidities. Antiepileptic treatment with valproic acid, though initiated in order to treat a symptom of the hyperammonic hypercloridemia, probably additionally increased the ammonia serum level (Figure 2).

In conclusion, hyperammonemic encephalopathy after ureterosigmoidostomy is an iatrogenic problem which must be considered in the differential diagnosis of unclear mental disorders, altered consciousness and seizures. In cases of persistence and recurrence of symptoms despite medical therapy, a transient low-pressure urinary diversion which decreases bowel contact with urine should be established by bilateral insertion of nephrostomies (in our case) or by placement of a rectal tube as an emergency treatment [5]. Furthermore, a possible success of a surgical conversion into a permanently incontinent urinary diversion can be easily evaluated preoperatively. Such an irreversible surgical approach should only be performed after definitive exclusion of all other possible etiologies of hyperammonemic encephalopathy [7, 10, 11]. From both literature and our experience, this approach seems an appropriate and successful strategy in preventing further episodes of hyperammonemic encephalopathy.

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