Postpartum Acute Kidney Failure and Hyponatremia: A Clinical Enigma

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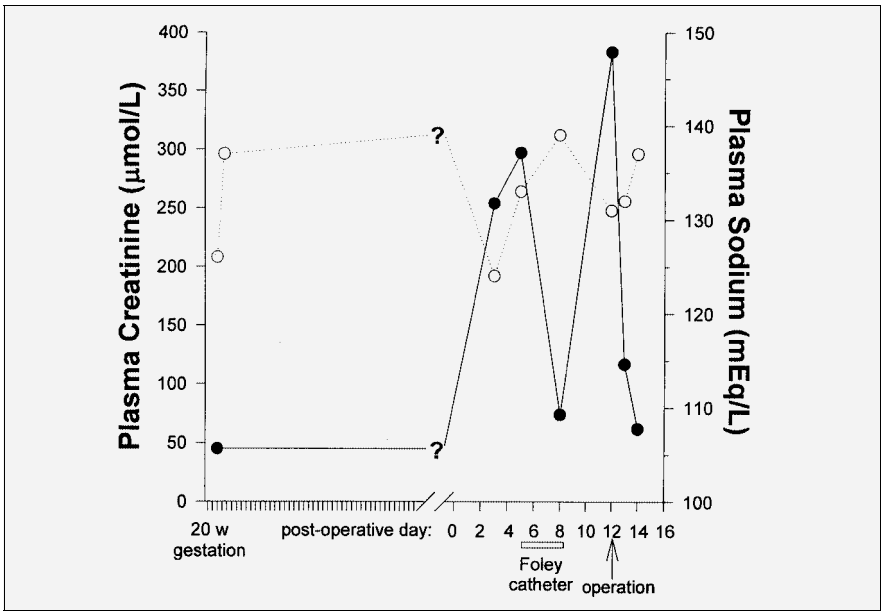
The evaluation of postpartum renal failure, without evidence for effective volume depletion or urine outflow obstruction is challenging, particularly when combined with a history of repeated bouts of hyponatremia. We report the unusual clinical presentation and diagnostic course of such a patient, who developed fluctuating renal dysfunction and hyponatremia following cesarean section.

Patient Description

Renal failure (serum creatinine and urea of 254 μmol/L and 10.5 mmol/L, respectively) and hyponatremia (sodium 124 mEq/L) were found on routine biochemical evaluation in a 30 year old primigravida 3 days after a cesarean section [Figure]. Her past medical history included uretero-vesical reflux and re-implantation of the left ureter at the age of 7, with an unremarkable follow-up. She also reported intermittent colicky abdominal pain and irregular bowel movements since adolescence, for which she underwent gastroenterologic evaluation and was diagnosed as having irritable bowel syndrome. At 20 weeks of gestation she was hospitalized for a few days because of abdominal pain. At that time creatinine was 45 μmol/L, and hyponatremia that resolved spontaneously was also noted. A short ACTH test was performed and reported to be normal. The patient admitted to having experienced a few additional previous episodes of hyponatremic dehydration during adolescence. Her late pregnancy course and delivery were unremarkable, and cesarean section was undertaken for fetal transverse position and uterine myoma.

Following surgery the patient developed paralytic ileus, was given fluids intravenously, and reported passing small volumes of concentrated urine. Her medications during hospitalization included cefamezine, meperidine, methadone and promethazine. On examination, vital signs and physical inspection were normal with the exception of absent bowel sounds and mild, diffuse abdominal tenderness and swelling. Orthostatic hypotension was absent. Hematologic evaluation revealed hematocrit 35.1%, white blood cells 10,900 and platelets 306,000/mm. Prothrombin time and partial thromboplastin time were normal, and blood smear evaluation was unremarkable. Urinary osmolality was 268 mOsm, urinary sodium 30 mEq/L and fractional tubular sodium reabsorption 98.6%. Calculated urinary/plasma urea and creatinine ratios were 8.2 and 21, respectively. Thyroid-stimulating hormone was normal, as were other plasma and urinary biochemical parameters. Urinalysis revealed +3 blood with crenated erythrocytes. There were few hyaline casts, few leukocytes, and about 10–15 round epithelial cells per low power field. Red cell casts were absent. Urinary protein/creatinine ratio was 0.15 (normal) and urine culture was sterile. Abdominal ultrasound revealed normal-sized kidneys and no signs of urine outflow obstruction. Bowel loops were dilated and there was a mild accumulation of peritoneal fluid. Other intra-abdominal and retroperitoneal structures appeared normal.



Fluctuations in plasma creatinine and sodium (filled and unfilled symbols, respectively), following cesarean section (on day 0). The timing of bladder drainage with a Foley catheter and of the urologic surgical procedure is indicated. Values on day 0 were not determined.

In order to exclude and treat occult effective volume depletion the patient was given 6 L saline over the subsequent 24 hours, but her daily urine volume was 600 ml and gross hematuria was noted. She complained of abdominal pain and swelling. Bowel movements remained absent, and progressive pedal and sacral edema developed. Plasma creatinine further increased to 298 μmol/L. For a better assessment of urine output a catheter was inserted, and quite unexpectedly, about 700 ml of urine were rapidly evacuated. At this stage, the possible diagnosis of neuroporphyria was raised, and was further supported by a weakly positive Watson-Shwartz test of a urine sample. The patient was therefore supplemented with 500 g glucose daily. Bowel movements returned and urine production remained in excess of 100 ml/hour. Though microscopic hematuria persisted, plasma creatinine decreased to 74 μmol/L within 48 hours, hyponatremia resolved [Figure] and the edema subsided.

Since the patient resumed eating and her well-being markedly improved, the intravenous lines and urinary catheter were removed. However, over the next 72 hours her condition worsened, with reappearance of abdominal pain and swelling. Oliguria was noted, hyponatremia reappeared, and creatinine rose again to 342 mol/L and continued to rise by 40 mol/L the next day. Liver function tests remained normal. Physical examination revealed moderate ascites, confirmed by a repeated abdominal ultrasound. The intraabdominal organs and retroperitoneal structures, including liver, pancreas and genito-urinary system appeared normal, as was blood flow in the vena cava, portal system, hepatic and renal veins. At this stage, paracentesis was performed, disclosing straw-colored fluid. White blood cell count and basic biochemistry were unremarkable with the exception of creatinine 1,268 mol/L (as compared to 383 mol/L and 3,750 mol/L in the plasma and urine, respectively), indicating a urinary peritoneal leak. A subsequent cystography revealed a 1 cm perforation of the bladder, which was surgically repaired. Plasma creatinine abruptly declined, plasma sodium normalized, the ascitic fluid disappeared, and the patient recovered uneventfully, supplemented with a high carbohydrate diet.

Comment

This case exemplifies the clinical presentation of two coexisting rare disease entities – acute intermittent porphyria and urinary ascites. The problem-solving process was based on the evaluation of the two main problems, namely recurrent hyponatremia and postpartum acute renal failure.

Hyponatremia was assessed to be most likely compatible with the syndrome of inappropriate antidiuretic hormone secretion. The patient's medical record of documented episodes of hyponatremia and irritable bowel syndrome that began at puberty, together with the prolonged postsurgical paralytic ileus and the presumed urinary retention, led us to consider the possibility of neuroporphyria, a rare cause of SIADH. Indeed, this diagnosis was supported by the weakly positive Watson-Shwartz test, a color reaction of urinary porphyrines produced by Ehrlich reagent. Subsequent analysis revealed that urinary porphobilinogen and uroporphirine determined in samples taken during the acute illness were markedly elevated (67 mg/24 hr, N<2 mg/24 hr, and 5,328 μg/24 hr, N<30 μg/24 hr, respectively), and a fluorometric spectrum peak was identified in the plasma (404/622 nm). Erythrocyte porphobilinogen deaminase activity, which was within the low-normal levels during her illness course (27 nmol uroporphirin/ml RBC/hr), subsequently declined to 20 nmol uroporphirin/ml RBC/hr (normal range 25–45 nmol uroporphirin/ml RBC/hr), establishing the diagnosis of acute intermittent porphyria.

Porphyrias are rare inherited disorders of heme biosynthesis [1], which differ in their clinical presentation (pure neuroporphyria, porphyria with mixed neurodermatologic manifestations, and cutaneous porphyria), the type of inheritance, and the biochemical abnormalities, characterized by elevated urinary or fecal heme precursors and the specific enzymatic defects. Lead poisoning represents an acquired form of neuroporphyria.

Neurologic manifestations of neuroporphyrias are protean and include peripheral and autonomic neuropathies manifested by muscle paralysis, unexplained abdominal pain, constipation, paralytic ileus, urinary retention, sensory neuropathy or orthostatic hypotension. Central nervous system dysfunction may manifest as altered consciousness, mental disorders, seizures, and SIADH [1]. The pathophysiology of neurotoxicity is not well understood and may reflect heme deficiency in neuronal cells or direct toxicity by intermediate metabolites or by oxygen free radicals. Attacks of neuroporphyria may be triggered by fasting, by endogenous sex hormones, or by an exhaustive list of medications – all of which were present during our patient's current illness. Additional precipitating factors are alcohol, smoking and illicit drugs. Attacks of AIP are treated by eliminating the trigger factors, and administering high oral or intravenous glucose load and, in severe cases, hematin preparations. These strategies inhibit δ-aminolevulonic acid synthase, the key enzyme initiating the chain of porphyrin synthesis.

Screening for porphyria among family members is mandatory since the phenotypic presentation of this potentially lethal disorder is heterogenous. In our patient AIP was subsequently diagnosed in an asymptomatic father and a grandfather, who had been hospitalized for prolonged periods for what seemed to be psychotic attacks that were most probably aggravated by medications he was given. The high prevalence (0.2%) of neuroporphyria reported in hospitalized psychiatric patients illustrates the low index of suspicion for this disease.

The Watson-Shwartz reaction is not a reliable screening test for porphyria owing to its low sensitivity. A timely direct determination of intermediate heme precursors in the urine and feces is required, as well as enzymatic activities whenever this diagnosis is suspected. The within-normal levels of initial porphobilinogen deaminase are misleading since acute attacks of porphyria induce enzyme pro-

SIADH = syndrome of inappropriate antidiuretic hormone secretion

RBC = red blood cells

AIP = acute intermittent porphyria

duction. Repeated samples should therefore be evaluated at stable conditions when enzyme activity is likely to be low, as illustrated by follow-up results in our patient a few months later.

Patients with inherited neuroporphyria tend to develop chronic progressive renal failure [2], perhaps related to altered autonomic control of blood pressure, as in patients with familiar dysautonomia. Acute kidney dysfunction, however, is not a feature of neuroporphyria. This led us to seek an additional coexisting disorder, especially with the reoccurrence of renal dysfunction. The diagnosis of bladder tear and urinary ascites was finally established by the determination of high creatinine concentration in the ascitic fluid.

Uroperitoneum is a rare and overlooked condition mimicking acute renal failure. Spontaneous leak of the bladder with uroperitoneum is predominantly reported in neonates with congenital anatomic defects [3], and has never been associated with porphyria-induced acute urinary retention. In adults, uroperitoneum usually occurs following abdominal trauma or surgery, and has been reported in 0.14–0.31% of cesarean sections, almost exclusively following repeated operations [4]. It is conceivable that in our patient the tear in the bladder was a surgical complication, related perhaps to the distorted anatomy caused by the previous urologic intervention at childhood, and possibly facilitated by porphyria-induced acute urinary retention.

The unusual diagnostic course illustrates a series of clinical pitfalls. We are trained to look for a single diagnosis, but in this case each of the two final diagnoses alone could not have explained all aspects of the clinical course. The diagnosis of a surgery-related complication was initially rejected due to the compelling evidence for an ongoing relapsing disease and to the preliminary clinical set-up suggesting neuroporphyria. The significance of acute renal failure that did not fit at all with this diagnosis was initially discarded, particularly in view of its prompt resolution. The search for an additional disorder was initiated only after the repeated clinical and laboratory deterioration. The erroneous diagnosis of "urinary retention," that shifted the attention of the medical team towards the diagnosis of AIP, was based on the prompt evacuation of urine following the insertion of a urethral catheter and the rapid amelioration of renal dysfunction. It is conceivable that the large urine output with a decline in plasma creatinine was in fact urinary ascitic fluids that were reallocated from the abdominal cavity, as long as the catheter was kept within the bladder, resembling a previously reported case of "renal failure relieved by a Foley catheter" [5]. Interestingly, hyponatremia is a typical overlooked electrolyte disorder of urinary ascites, presumably reflecting concomitant water reabsorption and altered free water clearance [3]. It served as a major clue to the diagnosis of AIP, but once attributed to this disorder it failed to direct us towards the diagnosis of urinary ascites.

Finally, we often fail to address quality control issues for what is obvious and frequent. We erroneously ignored the absence of distended bladder on sonography, since it did not fit with the concept of urinary retention, proposing an impact of timing of the procedure, and perhaps misinterpretation by a novice. In such a confusing situation we should have meticulously revised the ultrasound report. Was it indeed performed by a beginner? Perhaps a distended bladder was noted but not reported? What was the time interval between the sonography and catheterization? Were the 700 ml of urine truly evacuated over a short time, as reported? A better appraisal of such potential typical mistakes in clinical practice might have confirmed the prompt evacuation of a large volume of urine in the absence of a distended bladder, leading to an earlier identification of the tear in the bladder.

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References

1. Thadani H, Deacon A, Peters T. Diagnosis and management of porphyria. *Br Med J* 2000;320:1647–51.
2. Andersson C, Wikberg A, Stegmayr B, Lithner F. Renal symptomatology in patients with acute intermittent porphyria. A population-based study. *J Intern Med* 2000;248:319–25.
3. Clarke HS, Mills ME, Parres JA, Kropp KA. The hyponatremia of neonatal urinary ascites: clinical observations, experimental confirmation and proposed mechanism. *J Urol* 1993;50:778–81.
4. Rajasekar D, Hall M. Urinary tract injuries during obstetric intervention. *Br J Obstet Gynaecol* 1997;104:731–4.
5. Stebbing J, Ezra DG, Cackett PD, Greenstein AS. Ascites and apparent renal failure treated with a Foley catheter. *J R Soc Med* 1999;92:582–3.

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Capsule

Protecting damaged axons

Degeneration of axons that have been severed from their neuronal cell bodies can follow a specific course of progressive fragmentation called Wallerian degeneration. Various neurodegenerative diseases are also characterized by axonal degeneration. Araki et al. provide new insight into what directs the course of organized axonal degeneration. Analysis of a fusion protein resulting from a mutation that slows axon degeneration implicates the nicotinamide adenine dinucleotide biosynthetic pathway in this type of axonal degeneration.

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