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Hyperammonemia in a patient with obstructive urinary tract infection due to *Corynebacterium urealyticum*

Case Report

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Abstract: A 93-year-old woman with neurogenic bladder was admitted to our hospital because of impaired consciousness. Her urine culture revealed urease-test-positive Corynebacterium urealyticum. She was diagnosed with hyperammonemia due to an obstructive urinary tract infection that was caused by urease-producing bacteria. The patient showed rapid improvement of impaired consciousness and hyperammonemia after urine analysis. It is necessary to consider obstructive urinary tract infection as a differential diagnosis of hyperammonemia, which commonly occurs in urinary tract infections owing to the presence of urease-producing bacteria. Relief from obstruction is the most important treatment for hyperammonemia caused by this mechanism.

Keywords: *Urinary tract infection • Hyperammonemia • Corynebacterium urealyticum • Dysuria*

1. Introduction

Hyperammonaemia is a recognized cause of encephalopathy characterized by episodic confusion and coma. Hepatic hyperammonemia is usually observed in cases of decompensated liver disease. However, some nonhepatic causes of hyperammonemia are severe enough to cause confusion and coma. There are numerous possible causes of hyperammonemia: gastrointestinal bleeding; portal circulation shunt; vesicorectal fistula; inherited defects of the urea cycle enzymes; transport defects in the urea cycle intermediates; organic acidurias; other metabolic causes (for example, hyperinsulinemic hypoglycemia, distal renal tubular acidosis); drugs (for example, 5-fluorouracil, asparaginase, sodium valproate, halothane, enflurane); and parenteral nutrition [1].

In addition, obstructive urinary tract infections can cause hyperammonemia; however, it is a very rare condition and has no standard treatment guidelines [1]. We report a case of obstructive urinary tract infection due to *Corynebacterium urealyticum* (*C. urealyticum*), in which impaired consciousness and hyperammonemia improved only after urine analysis.

2. Case report

The patient was a 93-year-old woman who had previously had a lacunar cerebral infarction and neurogenic bladder. Her performance status was grade 0. She had no history of alcohol consumption or chronic liver disease. A month before presentation, she had a urinary tract infection due to Escherichia coli and was treated

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with levofloxacin. She had been suffering from general malaise and urinary incontinence for several days. Impaired consciousness was observed since the day of admission, leading to emergency hospital admission. On admission, her blood pressure was 138/80 mmHg; pulse, 88/min and regular; respiration rate, 24/min; body temperature, 37.4°C; and SpO_2, 97% (no oxygen). Her consciousness level on the Japan Coma Scale (JCS) (i.e., unable to say her own name or birth date) and Glasgow Coma Scale (GCS) was I-3 and E4V4M6, respectively. The patient displayed no nuchal rigidity and no abnormal thoraco-abdominal or psychological findings. There was tenderness at the right costovertebral angle.

The laboratory findings were as follows: a white blood cell count of 10,900/μL (neutrophils, 90%); hemoglobin, 12.6 g/dL; platelets, 200.000/μL; C-reactive protein, 13.4 mg/dL; total bilirubin, 0.5 mg/dL; aspartate aminotransferase, 20 IU/L; alanine aminotransferase, 15 IU/L; lactic dehydrogenase, 173 IU/L; gamma-glutamyl transpeptidase, 20 IU/L; creatinine phosphokinase, 58 IU/L; blood urea nitrogen, 34 mg/dL; creatinine, 1.10 mg dL; Na, 138 mEq/L; K, 4.0 mEq/L; Cl, 106 mEq/L; Ca, 8.9 mg/dL; blood glucose, 138 mg/dL; hemoglobin A1c (NGSP), 5.7%; and ammonia, 263 μg/dL (standard value: 30–86 μg/dL). She tested negative for hepatitis B and C antigens. Results of the blood gas analysis (no oxygen) were as follows: pH, 7.446; $PaCO_2$, 30.1 Torr; PaO_2, 90.8 Torr; and HCO_3, 20.9 mmol/L. Urine analysis results were as follows: appearance, clear yellow with irritant odor; urine specific gravity, 1.010; urine pH, 8.5; nitrite (+); leukocyte (+); bacteria (+); magnesium-ammonium-phosphate crystals (+); urease (+). The ammonia concentration in the initial urine sample was 140 mmol/L (normal range: <40 mmol/L).

A plain-head magnetic resonance imaging revealed only the old cerebral infarction; no new infarction was found. Hence, the cause of impaired consciousness was not initially identified. Abdominal computed tomography (CT) revealed bilateral hydroureter, right hydronephrosis, and bladder wall thickening (Figure 1). There were no abnormalities in the hepatobiliary system. Blood culture results were negative. Gram staining of the urine revealed gram-positive bacilli with special tropism; further, phagocytic leukocytes against the bacteria were observed. Urine culture results revealed *C. urealyticum* (sensitive to vancomycin, teicoplanin, minocycline, and clarithromycin) $>10^5$ CFU/mL. The urease test results were positive. The isolate was definitively identified as *C. urealyticum* using the API Coryne system (bioMérieux, Marcy l'Etoile, France). Conventional methods of identification confirmed that the organism was *C. urealyticum* [2].

After admission, the patient produced 1100 mL of urine and continued to urinate well afterward. Six hours later, she became lucid (JCS, 0; GCS, E4V5M6). Serum ammonia levels normalized the following day (38 μg/dL). No magnesium, ammonium, or phosphate crystals were found in the urine. Because urease-test-positive *C. urealyticum* was found in the urine culture, the urease-producing bacteria were thought to be the cause of the obstructive urinary tract infection that led to hyperammonemia. Ceftriaxone was administrated on admission, but after obtaining the urine culture results, the treatment was switched to vancomycin, which led to the improvement of the urinary tract infection.

Because sufficient improvement of dysuria due to neurogenic bladder was not observed with oral treatment alone, intermittent self-catheterization was performed. Impaired consciousness and hyperammonemia were not observed at the following outpatient clinic visit.

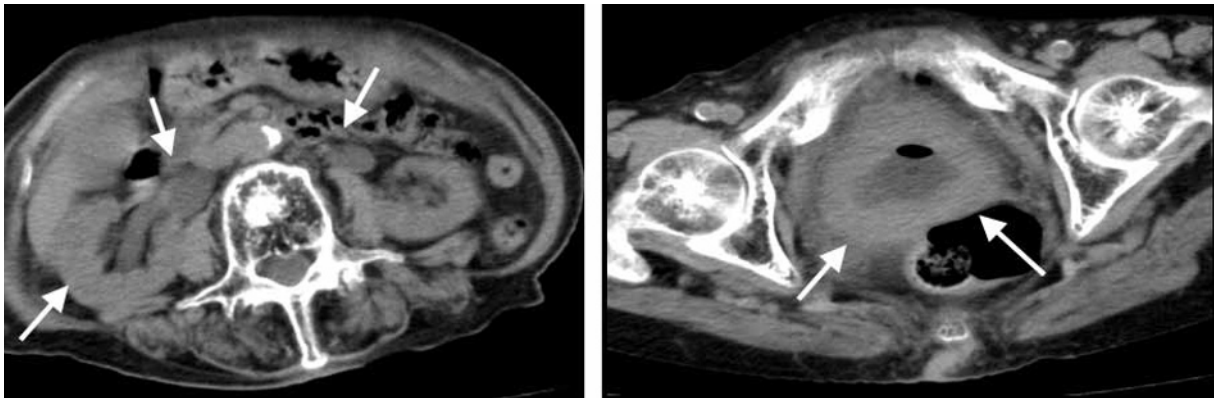

Figure 1. Plain abdominal computed tomography (CT) scan.
Bilateral hydroureter and right hydronephrosis are observed. Thickening of the bladder wall is also observed. There are no abnormalities in the hepatobiliary system.

3. Discussion

Urinary tract infections due to urease-producing bacteria are a cause of hyperammonemia, although it is a very rare condition [1].

Regarding the mechanism of hyperammonemia, a neurogenic bladder causes dysuria, which leads to increased bladder pressure. The bladder venous plexus absorbs urinary ammonia. From the iliac vein, without bypassing the liver, urine ammonia is moved to the systemic circulation from the inferior vena cava [3]. Furthermore, urease-producing bacteria in the bladder trigger hyperammonemia, thereby leading to impaired consciousness [4,5].

When urinary tract infections due to urease-producing bacteria occur, urease breaks down urinary urea to ammonium ions (NH_{4+}), leading to increased urinary pH. On the other hand, ammonium ions become fat-soluble ammonia (NH_3) in alkaline urine, which makes it easy for them to pass through the bladder venous plexus [3]. Moreover, Oliver et al described a patient suffering from hyperammonemia due to urinary retention, without a concurrent infection due to urease-producing bacteria [6].

Proteus mirabilis, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* are well-known urease-producing bacteria that cause urinary tract infections [7,8]. Although *C. urealyticum* is a relatively rare causal organism of urinary tract infections, it is reported to cause hyperammonemia in patients with urinary tract infections owing to its urease activity [1]. Results of the urine tests for ammonia and urease detection were positive. In addition, the urease tests of isolated *C. urealyticum* were positive. Therefore, we confirmed the cause of the hyperammonemia to be the urinary tract infection caused by urease-producing *C. urealyticum*.

There are no standard treatment guidelines for nonhepatic hyperammonemia caused by urinary tract infections [1]. In the present case, we did not perform reduction treatment of intestinal ammonia levels using nonabsorbable disaccharides such as lactulose and lactitol or protein control. Furthermore, ceftriaxone was administered despite its lack of antimicrobial activity against *C. urealyticum*. However, the patient exhibited rapid improvements in consciousness level and hyperammonemia. Based on the progression and mechanism of hyperammonemia in the present case, it is also important to consider relieving the obstruction when treating hyperammonemia due to obstructive urinary tract infection.

In conclusion, it is important to consider obstructive urinary tract infection as a differential diagnosis for a hyperammonemia that is particularly common in urinary tract infections due to urease-producing bacteria. Relief from obstruction is considered important for the treatment of hyperammonemia caused by this mechanism.

Conflict of interest

All authors have no financial interests to disclose and no conflict of interest to declare.

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