A Case of Neuroleptic Malignant Syndrome–Prompted Myoglobin Cast Nephropathy

Abstract

Myoglobin cast nephropathy is a sequel of rhabdomyolysis, and is characterized by the release of free myoglobin in the circulation, direct proximal convoluted tubule injury, and obstruction by myoglobin cast in distal tubules. We report an interesting case of myoglobin cast nephropathy in a patient who was on neuroleptic drugs and who presented with neuroleptic malignant syndrome and acute kidney injury.

Keywords: *Myoglobin cast nephropathy, Myoglobin, Neuroleptic malignant syndrome, Neuroleptic, Pigment nephropathy*

Introduction

Rhabdomyolysis is an important cause of pigment nephropathy.[1] Neuroleptic malignant syndrome (NMS) is a life-threatening condition that occurs as an adverse reaction to antipsychotic drugs.[2] Rhabdomyolysis releases the free myoglobin in circulation, which causes direct proximal convoluted tubule injury and obstruction by myoglobin cast in distal tubules called "myoglobin cast nephropathy".[3] We discuss an interesting case of myoglobin cast nephropathy in a patient was on antipsychotic drugs and presented with fever, rigidity, breathlessness, oliguria, and acute kidney injury.

Case Report

A 48-year man on antipsychotic drugs presented with fever, abnormal tightening and posture of the body, and an episode of transient loss of consciousness over two days. It was not associated with convulsion, incontinence, headache, and visual disturbance. There was no history of diabetes or tuberculosis. He did not give a history of cough, hematuria, lower urinary tract symptoms, diarrhea, or intake of nephrotoxic drugs. He was taking quetiapine (50 mg) twice daily and chlorpromazine (100 mg) once a day for schizophrenia for the last two years. He was admitted to a local hospital and received supportive treatment for three days and was referred to us with complaints of progressive oliguria and anasarca of five days duration. A general examination revealed pallor and anasarca. His blood pressure was 160/90 mmHg, pulse rate 108/min, respiratory rate 24/min, and body temperature 101.8°F. His chest had bilateral crepitation. Cardiovascular and abdominal examinations were normal. Neurological examination was unremarkable, except for disorientation and rigidity of extremities and trunk. Papilledema and sign of meningeal irritation were negative. His urine output was about 100 ml per day. Hemogram was normal. The biochemical result showed serum creatinine at 6.3 mg/dl, elevated LDH (800 IU/L), CPK (9789 IU/L), and serum myoglobin levels (560 ng/ml). CSF analysis, EEG, and MRI brain were normal. A urine dipstick test was positive for blood, without red blood cells on microscopy. Other laboratory reports are mentioned in Table 1. Finally, after obtaining written consent, a kidney biopsy was performed with suspicion of pigment nephropathy. Renal histopathology revealed non-proliferative glomeruli. Segmental sclerosis, tuft necrosis, subendothelial/congophilic deposits, or crescent formation was absent. Tubular atrophy and interstitial fibrosis involved about 10%–12% of sampled cortex. Tubule showed prominent cytoplasmic vacuolar changes and diffuse severe acute injury with epithelial simplification and loss of brush border. A few variably sized, coarse, granular, confluent, variably pigmented cast and focally accompanied by inflammatory cell reaction was seen. Arteries showed medial thickening and subintimal sclerosis. Direct immunofluorescence was negative for the immune complex. The tubular cast was positive for myoglobin and negative for hemoglobin on immunohistochemistry staining. Electron microscopy revealed focal effacement (about 10%) of visceral epithelial cell foot processes. Electron-dense or organized deposits were absent [Figure 1]. The kidney biopsy established the diagnosis of Myoglobin cast nephropathy. A psychiatrist's advice was sought, neuroleptic drugs were discontinued, oral bromocriptine (2.5 mg) twice a day and trihexyphenidyl (2 mg) daily were started and continued for 2 weeks. He was managed with intravenous fluid, hemodialysis, and symptomatic treatment. He required a total of seven hemodialysis sessions over 2 weeks and his urine output progressively increased. His serum creatinine (0.85 mg/dl) and urine output (approximately 1500–2000 ml/day) normalized by the fourth week.

Discussion

Neuroleptic malignant syndrome (NMS) is an important cause of rhabdomyolysis However, nowadays it is rare, and the incidence has declined from around 0.2%–3.2% to 0.01%–0.02% of patients on antipsychotic drugs.[2] This condition develops due to a sudden reduction in dopaminergic neural activity and is characterized by fever, altered sensorium, muscle rigidity, and dysautonomia.[2] NMS can lead to severe rhabdomyolysis and renal failure. Characteristic laboratory of NMS includes elevated CPK and leukocytosis. Serum CPK, was elevated in our patient, and is the most sensitive marker of muscle injury.[4] Rhabdomyolysis is characterized by the breakdown of striated muscle and the release of myoglobin into circulation.[4] Serum myoglobin (560 ng/ml, normal 28–72 ng/ml) was also elevated in our cases. The serum myoglobin levels peak before serum CPK, and its metabolism is rapid and unpredictable.

Table 1: Baseline characteristics of the case at the time of hospitalization

Hematology	
Total leucocyte count	8384/mm^3 (normal 4010×10^3/mm^3)
Differential leucocyte count	N68%/L26%/E2%/M4%
Platelet count	173000/mm^3 (normal 150–400×10^3/mm^3)
Hemoglobin	12.6 gm/dl (normal 13–17 g/dl)
ESR	25 mm/hour (normal 0–15 mm/h)
Biochemistry & Serology	
Serum creatinine	6.3 mg/dl (normal 0.6–1.3 mg/dl)
Blood urea Nitrogen	41 mg/dl (normal 5–18 mg/dl)
Serum Na^+	133 mmol/L (normal 135–145 mmol/L)
Serum K^+	4.6 mmol/L (normal 3.5–5.5 mmol/L)
Serum Ca^{2+}	8.5 mg/dl (normal 8.6–10.3 mg/dl)
Serum phosphate	4.3 mg/dl (normal 3.5–4.5 mg/dl)
Serum uric acid	4.8 mg/dl (normal 2.5-7.0 mg/dl)
Serum bilirubin	1.3 mg/dl (normal 0.2–1.0 mg/dl)
ALP	346 U/L (normal <120 U/L)
SGPT	25 IU/L (normal 5×45 IU/L)
SGOT	81 IU/L (normal 5–40 IU/L)
Total serum protein	6.8 gm/dl (normal 6–8 gm/dl)
Serum albumin	3.7 gm/dl (normal 3.5–5.5 gm/dl)
RBS	98 mg/dl (normal <140 mg/dL)
LDH	800 IU/L (normal <248 IU/L)
CPK-MM	9789 IU/L (normal <171 IU/L)
Serum myoglobin	560 ng/ml (normal 28–72 ng/ml)
Serum procalcitonin	Negative
HIV/HBsAg/HCV	Non-reactive
Urine analysis	Albumin - Nil, Blood ++, RBC - 2–3/hpf, Pus Cell 6–8/hpf
Immunological markers	
ANA, PR3 and MPO ANCA	Negative
Complement C3	108 mg/dl (Normal 90–180)
Complement C4	18.1 mg/dl (Normal 10–40)
Radiology	
ECG	Normal Sinus rhythm
2D ECHO	Normal study
USG Abdomen	RK10.2 cm, LK 10.0 cm in size, grade I echogenicity, and CMD intact
Microbiology & Pathology	
Urine culture	No growth

ALP: Alkaline phosphatase, SGPT: serum glutamate pyruvate transaminase, SGOT: serum glutamate oxaloacetate transaminase, RBS: random blood sugar, LDH: lactate dehydrogenase, CPK-MM: creatine phosphokinae-muscle, ANA: antinuclear antibody, PR3: proteinase 3, MPO: myeloperoxidase, ANCA: antineutrophil cytoplasmic antibody, Echo: echocarrdiogram, RK: right kidney, LK: left kidney, CMD: corticomedullary distiction.

Myoglobin (17.8-kDa) causes renal vasoconstriction, direct injury to the proximal tubule, and after precipitation with the Tamm–Horsfall protein, it forms a myoglobin cast in the distal tubule.[3,5] Clinical and biochemical markers

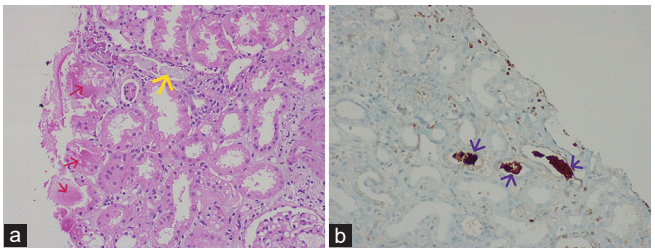

Figure 1: (a) Tubule showing prominent cytoplasmic vacuolar changes, epithelial simplification, and loss of brush border and diffuse severe acute injury. A few variably sized, coarse, granular (thick yellow arrow), pigmented cast (thin red arrows), and focally accompanied by inflammatory cell reaction. (40×, PAS). (b) The tubular cast was positive for myoglobin (voilet arrows) on immunohistochemistry staining. (40×, IHC).

suggestive of rhabdomyolysis-associated kidney injury were confirmed on kidney biopsy. NMS is a neurological emergency, and a delay in treatment can potentially lead to serious complications or death. The first step in the treatment of NMS is the cessation of neuroleptic drugs. The next step is the institution of supportive treatment like aggressive hydration to prevent kidney injury, treatment of hyperthermia, and metabolic abnormalities. In severe cases of NMS, empiric therapy with bromocriptine mesylate (dopamine agonist) and dantrolene sodium (muscle relaxant) has been used.[6] We managed our case with the cessation of neuroleptic drugs, oral bromocriptine (2.5 mg) twice a day for 14 days, oral trihexyphenidyl (2 mg) daily, intravenous fluid, hemodialysis, and other symptomatic treatment. The renal function and urine output normalized by the fourth week. Hence, timely diagnosis and prompt institution of preventive and therapeutic measures are paramount in managing NMS.

Conclusion

Myoglobin cast nephropathy was caused by rhabdomyolysis secondary to neuroleptic malignant syndrome, probably precipitated by neuroleptic drugs. Thus, reporting a case of myoglobin cast nephropathy could be helpful to clinicians engaged in the management of Neuroleptic Malignant Syndrome.

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Conflicts of interest

There are no conflicts of interest.

Prem S. Patel[1], Prit P. Singh[1], Archana[2], Om Kumar[1]

[1]Department of Nephrology, Indira Gandhi Institute of Medical Science, [2]Department of Microbiology, All India Institute of Medical Sciences, Patna, Bihar, India

Corresponding author:
Prem S. Patel, Department of Nephrology, Indira Gandhi Institute of Medical Science, Patna - 800 014, Bihar, India. E-mail: drpspdm@gmail.com

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Clinical Transplant Kidney Function Loss Due to Small Intestinal Bacterial Overgrowth

Abstract

Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome involving gastrointestinal symptoms caused by the presence of excessive bacteria in the small intestine. SIBO often leads to diarrhea and poses diagnostic and treatment challenges. Here, we report about a renal transplant recipient who experienced diarrhea-induced hypovolemic shock due to SIBO, necessitating the reintroduction of dialysis, and aim to provide insights to aid health-care providers in diagnosing and managing severe diarrhea in this specific patient group. A 14-year-old boy, who had undergone renal transplantation at the age of 2 years, experienced severe, recurring diarrhea leading to hypovolemic shock. The patient underwent volume loading and continuous hemodiafiltration. Upper gastrointestinal endoscopy findings suggested Whipple's disease. Antibiotics were initiated; however, the diarrhea did not improve. Examinations for infectious enteritis and food allergies yielded negative results. The diarrhea improved with rifaximin (RFX), but recurred repeatedly after its discontinuation. Antibiotic rotation, wherein RFX, amoxicillin hydrate and potassium clavulanate, ciprofloxacin, and RFX were administered in this order for 4 weeks each, improved the diarrhea. A lactulose breath test performed immediately before the second RFX course yielded negative results. The patient's condition was diagnosed as SIBO based on the clinical course, although the diagnostic criteria were not met. SIBO should be considered in cases of gastrointestinal symptoms in patients with transplanted kidneys. Antibiotic rotation should be considered for SIBO treatment in immunosuppressed patients.

Keywords: *Antibiotic rotation, post-kidney transplant patient, severe diarrhea, small intestinal bacterial overgrowth, immunosuppression*

Introduction

Diarrhea is the most common gastrointestinal symptom in kidney transplant patients and is often caused by infections or drugs.[1] Small intestinal bacterial overgrowth (SIBO) is a clinical syndrome characterized by gastrointestinal symptoms due to excessive bacterial population within the small intestine.[2] Herein, we report about a renal transplant recipient who experienced diarrhea-induced hypovolemic shock due to SIBO, necessitating dialysis reintroduction.

Case Report

A 14-year-old boy was admitted to our intensive care unit with hypovolemic shock secondary to diarrhea. He underwent renal transplantation at 2 years of age owing to bilateral hypoplastic/dysplastic kidneys. He had chronic diarrhea and anorexia for 2 years before admission. Upper and lower gastrointestinal endoscopy revealed no abnormalities. He was prescribed loperamide and esomeprazole based on his symptoms. After the onset of chronic diarrhea, his weight decreased from 38 to 30 kg over 2 years. Regarding chronic rejection, his transplanted kidney function, indicated by the estimated glomerular filtration rate, was 40 mL/min/1.73 m^2. The immunosuppressants administered include methylprednisolone 4 mg every alternate day, cyclosporine 120 mg/day, and mycophenolate mofetil 750 mg/day.

On admission, the patient's vital statistics included weight, 25.8 kg; height, 152 cm; body temperature, 36.5°C; blood pressure, 98/60 mmHg; heart rate, 62 beats/min; and oxyhemoglobin saturation, 88%. Clinical findings revealed drowsiness, inability to walk, sunken eyes, clear breath sounds, absence of heart murmurs, flat abdomen with increased bowel sounds, and cold limbs. Laboratory data indicated renal dysfunction, hypokalemia, metabolic acidosis, and anemia.