Case Report

SAGE Open Medical Case Reports

Hiccups: You got to be kidney me!

SAGE Open Medical Case Reports
Volume 8: 1–4

DOI: 10.1177/2050313X20962641
journals.sagepub.com/home/sco
SAGE

Viva Nguyen[1], Khaled Deeb[1] and Ranga Rathakrishnan[2]

Abstract

Hiccups are usually benign processes that most people experience with spontaneous resolution. However, persistent hiccups with a duration greater than 48 h may prompt a thorough workup for structural, infectious, or inflammatory disorders. Moreover, toxic-metabolic states, including renal dysfunction and/or uremia, have also been identified as sources of hiccups. We present a 62-year-old male with persistent hiccups that developed acute, worsening renal function. Workup for a possible intrinsic renal disease process was negative. Ultimately, a kidney biopsy was performed, demonstrating acute tubular injury with oxalate crystals and interstitial fibrosis. Dialysis was initiated with resolution of the hiccups, and kidney function improved over an extended period of time.

Keywords

Hiccups, acute renal failure, kidneys, oxalate crystals, noni

Date received: 15 June 2020; accepted: 7 September 2020

Introduction

Hiccups are common, typically transient, and almost experienced by everyone. Involuntary, intermittent, and spasmodic contractions of the diaphragm and intercostal muscles are the mechanics behind a hiccup. Prolonged hiccups can affect quality of life by interrupting eating, drinking, sleeping, ultimately leading to malnutrition, weight loss, and dehydration.[1] Hiccups lasting greater than 48 h are rare and may be caused by a serious illness. Little is known about overall incidence or prevalence of prolonged hiccups. The aim of this case report is to demonstrate that a benign initial presentation of an everyday occurrence such as a hiccup may be a small glimpse into a more serious disease process, such as acute kidney failure.

Case report

A 62-year-old male with medical history of coronary artery disease status post stent placement, hypertension, hyperlipidemia, asthma, and previous nephrolithiasis presented to the emergency department (ED) with a 1-day onset of violent hiccups. Hiccups started in the evening, without any particular triggers. He admitted to a brief cessation of hiccups for about 10 min following one episode of nonbloody emesis, before relentless return and lasting throughout the night. His hiccups persisted until the morning of admission, which interfered with his sleep and prompted his visit to the ED. He denied fever, chills, night sweats, weight changes, dysuria, recent frothing of urine, gross hematuria, changes to frequency of urination, and/or change in urine color. Outpatient medications included albuterol inhaler, atorvastatin, budesonide/formoterol inhaler, carvedilol, ticagrelor, insulin glargine, losartan, and metformin with no recent changes in any medications or recent usage of oral or intravenous corticosteroids. Upon further inquiry, the patient admitted to chronic use of nonsteroidal anti-inflammatory drugs (NSAIDs), ingestion of about 2–4 tablets of ibuprofen products per day for several years due to chronic lower back pain. The patient denied use of tobacco, alcohol, or illicit drugs. There was no family history of renal disease and no recent surgeries. Physical examination was unremarkable with no evidence of suprapubic or costovertebral tenderness. On admission, he was found to have a creatinine of 2.7 (baseline is 1.0). Ultimately, patient was admitted for the persistent hiccups and acute kidney injury (AKI).

[1]Internal Medicine Resident, University of Miami JFK GME, Atlantis, FL, USA
[2]Department of Internal Medicine, Hospitalist, West Palm Beach Veterans Affairs Medical Center, West Palm Beach, FL, USA

Corresponding Author:
Viva Nguyen, Internal Medicine Resident, University of Miami JFK GME, 180 JFK Drive Suite 210, Atlantis, FL 33462, USA.
Email: vhn5@med.miami.edu

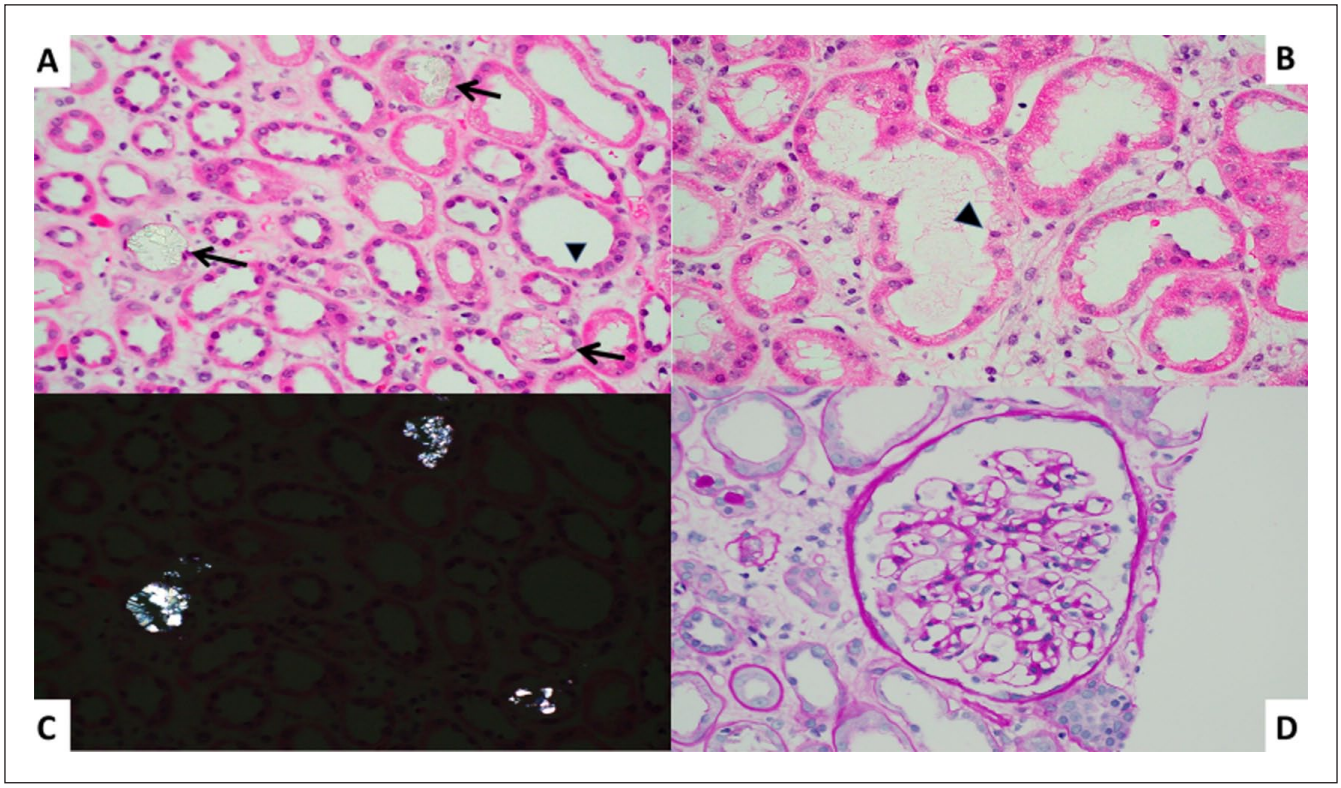

Image 1. (A) Flattened tubular epithelium with apoptotic nuclei, cytoplasmic injury, and absent brush border (arrowheads). Calcium oxalate crystals are demonstrated in the tubular lumen (arrows). (B) Acute tubular necrosis and cellular and interstitial changes, similar to those in image (A). (C) Intratubular calcium oxalate crystals with polarized light. (D) Glomerulus with mild diabetic glomerulosclerosis and tubular changes.

Initial urinalysis was not indicative of a urinary tract infection or obstruction with no urinary casts seen; urine toxicology screening was negative. Workup for autoimmune, glomerular, malignancies, vasculitis, infectious, and inflammatory diseases for the acute kidney failure were negative (e.g. antinuclear antibody, complement levels, hepatitis panel, immunoglobulin levels, HIV, serum kappa/lambda, eosinophils, erythrocyte sedimentation rate, c-reactive protein, anti-glomerular basement membrane antibodies). Renal ultrasound at admission demonstrated multiple renal cysts but no evidence of calculi or hydronephrosis. Chest X-ray demonstrated no acute cardiopulmonary disease or masses. Later, computed tomography of the abdomen and pelvis without contrast showed no bilateral nephrolithiasis, hydronephrosis, hydroureter, or obstructing calculus in the ureter. There was a cyst at the upper pole of the left kidney measuring 2.1 cm and fullness in bilateral renal pelvis and lower pole collecting system bilaterally.

The AKI was presumed likely due to chronic NSAIDs usage. The patient was started on intravenous (IV) fluids for the AKI and received lorazepam, prochlorperazine, baclofen, gabapentin, and omeprazole to alleviate the hiccups. Hiccups improved but persisted despite medications given in the ED. Patient was later switched to chlorpromazine to limit nephrotoxicity, and calcium was replenished. Over the course of the patient's hospital stay, the creatinine trended upward, peaking at 10.00 on hospital day number 6. Nephrology was consulted, and hemodialysis was initiated due to electrolyte abnormalities and continued decline in renal function. Kidney biopsy was determined necessary, as the workup for the etiology in this acute disease process was not evident. The kidney biopsy revealed (Image 1) acute tubular injury with several intratubular oxalate crystals, minimal diabetic glomerulosclerosis, and mild to moderate interstitial fibrosis. Kidney function improved after 3 dialysis sessions within a span of 4 days.

Discussion

Hiccups, or singultus, are common, typically transient, and almost experienced by everyone. Most hiccup episodes last less than 48 h, and studies have shown a greater prevalence in men.[2] Hiccups lasting longer than 48 h are rare and may be caused by a serious disease process. Etiologies of prolonged hiccups include structural, infectious, or inflammatory disorders that affect the central nervous system or the vagus or phrenic nerves and their branches.[3]

Our patient presented in the ED due to these persistent, violent hiccups that disturbed his sleep. In most simple cases, this patient would have mostly like been discharged home with some oral medications and advised to follow up with his primary care physician. However, patient was admitted to the hospital due to an AKI with a creatinine of 2.7, initially believed due to his chronic use of NSAIDs.

Originally, the hiccups were seen as a benign entity due to the duration of symptoms lasting less than 48 h initially.

Despite initiation of baclofen, gabapentin, and omeprazole, patient's hiccups persisted for greater than 48 h. Physical maneuvers were performed with the patient, including breath holding, Valsalva maneuvers, and pulling the knees to chest to relieve pressure on the diaphragm.[4] No relief was provided. Chest X-ray revealed no acute process, and no masses or hemidiaphragm were noted. With worsening renal function, the hiccups were believed to have been caused by toxic-metabolic components, including renal impairment, hyponatremia, and hypocalcemia seen in our patient.[5] The pathogenesis of hiccups lasting more than 48 h is uncertain; it is believed that the trigger is a component of the reflex arc involving the phrenic nerves related to the glottis and inspiratory intercostal muscles.[6] Patient was later switched to chlorpromazine to limit nephrotoxicity, as this medication does not require renal adjustments compared to baclofen and gabapentin.

Despite IV fluids, the acuity of the worsening creatinine was alarming. Patient's creatinine was at baseline (1.0) 3 months prior to this admission. Fractional excretion of sodium (FENa) was calculated to be 2.7% on day of admission, indicating an intrinsic process causing the renal failure. Workup for intrinsic renal disease was conducted. Autoimmune, glomerular, malignancies, vasculitis, infectious, and inflammatory diseases for the acute kidney failure were negative. Hemodialysis was initiated, with improvement in creatinine after 4 days and 3 dialysis sessions. With no clear etiology of the acute renal failure, a renal biopsy was performed with results shown in Image 1. Further investigation into the patient's diet revealed that the family liked to use herbal supplements. Patient's electrolytes improved, and hiccups resolved following the initiation of dialysis.

Common agents that are known to cause intratubular crystal-induced obstruction include acyclovir, sulfonamide antibiotics, ethylene glycol, megadose vitamin C, methotrexate, and protease inhibitors.[7] Specifically for oxalate crystals, oxalate deposition in the kidneys can be contributed to primary hyperoxaluria, ethylene glycol poisoning, secondary hyperoxaluria due to pancreatic insufficiency/inflammatory bowel disease/bowel resection/gastric bypass, orlistat therapy, and high doses of vitamin C.[8,9] High doses of vitamin C, whether from fruits or vitamin supplements, metabolize into oxalate, an insoluble compound.

The family admitted to having noni trees in their backyard and have been eating the noni fruit and juice for an extended period of time. Noni juice, from the fruit *Morinda citrifolia*, is believed to provide some protection against tobacco-induced DNA damage, blood lipid and homocysteine elevation, and systemic inflammation.[10] It is believed that the noni fruit has high contents of oxalic acid and vitamin C that combines with calcium to form oxalate. Patient was ultimately discharged home, with outpatient hemodialysis and an appointment with a dietician to limit oxalate intake. Diet and avoidance of nephrotoxic agents were discussed extensively with the patient, in the hopes of the patient not requiring long-term dialysis.

This case is consistent with other published case reports in regard to patients' presentation with hiccups with underlying renal disease from renal abscess, hydronephrosis, or uremia. A 65-year-old male presented with hiccups for a month with an underlying renal cyst, with the hiccups resolving after drainage of the cyst.[11] An 82-year-old male presented with hiccups for 2 months with an underlying giant hydronephrosis, with resolution of the hiccups after drainage of the hydronephrosis.[12] Numerous dialysis patients presented with intractable hiccups from ingesting star fruit (*Averrhoa carambola*), who had varying levels of consciousness from potential neurotoxicity and nephroxicity of the fruit.[13] This case report is a valuable presentation of hiccups and renal disease, which can be used as a reference for the approach to treat treatment-resistant hiccups, induced by supplements other than medicinal drugs.

Conclusion

This case report demonstrates that what appears to be a benign presentation, such as hiccups or incidental finding of kidney dysfunction, can be the early phase of a life-threatening disease process. The recognition of a hiccup in the history, physical, and basic laboratory studies should alert a healthcare professional to conduct further investigation. As always, herbal medications and supplements should be inquired for every patient due to potential health side effects. The impact of missing such benign presentations of more serious disease processes could potentially be detrimental to the patient, as well as increase healthcare costs with resulting emergent procedures or admissions to the intensive care unit.

Acknowledgements

The authors thank Eduardo de la Flor Weiss, MD, FCAP, Pathologist, West Palm Beach Veterans Affair, Florida, USA, for the renal biopsy images and descriptions.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

ORCID iDs

Viva Nguyen https://orcid.org/0000-0002-8971-5197
Khaled Deeb https://orcid.org/0000-0002-9131-9505

References

1. Jeon YS, Kearney AM and Baker PG. Management of hiccups in palliative care patients. *BMJ Supp Palliat Care* 2018; 8(1): 1–6.
2. Lee GW, Kim RB, Go SI, et al. Gender differences in hiccup patients: analysis of published case reports and case-control studies. *J Pain Symptom Manage* 2016; 51(2): 278–283.
3. Souadjian JV and Cain JC. Intractable hiccup. Etiologic factors in 220 cases. *Postgrad Med* 1968; 43(2): 72–77.
4. Petroianu GA. Treatment of hiccup by vagal maneuvers. *J Hist Neurosci* 2015; 24(2): 123–136.
5. Hosoya R, Uesawa Y, Ishii-Nozawa R, et al. Analysis of factors associated with hiccups based on the Japanese Adverse Drug Event Report database. *PLoS ONE* 2017; 12(2): e0172057.
6. Samuels L. Hiccup; a ten year review of anatomy, etiology, and treatment. *Can Med Assoc J* 1952; 67(4): 315–322.
7. Perazella MA. Crystal-induced acute renal failure. *Am J Med* 1999; 106(4): 459–465.
8. Hoppe B, Beck BB and Milliner DS. The primary hyperoxalurias. *Kidney Int* 2009; 75(12): 1264–1271.
9. Bhavani R, Nandhini S, Rojalakshmi B, et al. Extract on treatment of ethylene glycol and ammonium chloride induced kidney disease. *Int J Pharma Sci Res* 2014; 5(6): 249–256.
10. West BJ, Deng S, Isami F, et al. The potential health benefits of noni juice: a review of human intervention studies. *Foods* 2018; 7(4): 58.
11. Garrigues P, Giovansili B, Villard F, et al. Kyste rénal responsable d'un hoquet. *Presse Med* 2007; 36(2I): 239–242.
12. Liao XX, Yang JH and Xing NZ. Intractable hiccup due to giant hydronephrosis: a rare case report and literature review. *Int J Surg Case Rep* 2020; 67: 134–138.
13. Chang JM, Hwang SJ, Kuo HT, et al. Fatal outcome after ingestion of star fruit (*Averrhoa carambola*) in uremic patients. *Am J Kidney Dis* 2000; 35(2): 189–193.