Foamy Urine and Sickled Cells

Margaret Prat Huntwork, MD, MSEd
Tulane / Ochsner Residency Program
New Orleans, LA
Red Stick Pediatric Potpourri

presented by

The Louisiana Chapter of the American Academy of Pediatrics
Red Stick
Pediatric Potpourri

presented by

The Louisiana Chapter
of the
American Academy of Pediatrics
Red Stick
Pediatric Potpourri
presented by
The Louisiana Chapter of the American Academy of Pediatrics
Foamy Urine and Sickled Cells

Margaret Prat Huntwork, MD, MSEd
Tulane University Health Sciences Center
New Orleans, LA
History of Present Illness

A 19 year-old girl with known sickle cell disease (Hgb SS) presented with one day of lower back and bilateral thigh pain.

Symptoms were typical of her usual pain crisis.
Review of Systems

- “Foamy” urine.
- Facial swelling.
- Decreased appetite.
- One episode of vomiting.
- Feels dizzy when standing up rapidly.
- No shortness of breath, no cough, no fever, no chest pain, no focal weakness.
Past Medical History

- Hemoglobin SS Disease, with history of vaso-occlusive crises, but no acute chest, stroke, avascular necrosis, or any other known complications.

- Crigler-Najjar Type 2

- Two recent ER visits for vaso-occlusive crises, and one recent hospitalization for pneumonia.
Additional History

- No surgeries.
- Family history significant for sickle cell trait.
- Lives with her mother, is studying to be a respiratory therapist.
- Denies alcohol, drug use, tobacco use.
Medications

- Folic acid
- Amoxicillin
- Tylenol with codeine
- Phenobarbital
- Chart review: she had received ten doses of ketorolac over the past month, at ER visits, clinic visits, and from her last hospital admission.
Physical Exam

- T: 97.5  HR: 108  RR: 12  BP: 116/74  O2: 100%
- +Orthostatic hypotension
- HEENT: Mild scleral icterus
- CV: tachycardic, regular rhythm
- Pulm: clear to auscultation
- Abd: nontender, no organomegaly
- Ext: Anasarca present, including periorbital and facial edema, edema of hands and feet. Full ROM of extremities, no tenderness to palpation.
Laboratory Studies

- Complete blood count demonstrated a white blood cell count of 18,000 per mm3, hemoglobin of 5.7 mg/dL (baseline is ~7), and a reticulocyte count of 10%.

- Chemistry was significant for a blood urea nitrogen of 43 mg/dL, a creatinine of 3.6 mg/dL (baseline is 0.5 mg/dL). Bicarbonate level was 17 mmol/L.

- Liver function tests revealed an albumin of 1.3 g/dL and a total bilirubin of 3 mg/dL (baseline is ~2).

- Urinalysis showed a protein greater than 500 mg/dL. Spot urine protein-to-creatinine ratio was 27. (Nephrotic range proteinuria is greater than 5.)
Diagnosis

- Given the patient’s elevated creatinine, high urine protein-to-creatinine ratio, hypoalbuminemia, and generalized edema, she was diagnosed with acute kidney injury due to nephrotic syndrome.

- What is the etiology of the patient’s nephrotic syndrome: is it secondary to sickle cell disease or another cause? Or is it a primary nephrotic syndrome?
Nephrotic Syndrome: A Differential diagnosis

- Primary Glomerular Disease
  - FSGS
  - Membranous Nephropathy
  - Minimal Change Disease
  - Membranoproliferative GN

- Secondary to a systemic disease
  - DM
  - Hepatitis
  - Sickle Cell
  - SLE
  - Amyloidosis
  - Cryoglobulinemia
Miscellaneous Labs

- Complement levels were normal, making immune complex disease causing membranoproliferative nephropathy less likely.
- ANA was negative, making SLE causing membranous nephropathy less likely.
- Hepatitis and syphilis serologies were negative, ruling out infection causing a membranous nephropathy.
Renal Biopsy

- Light microscopy demonstrated focal segmental glomerulosclerosis.
- Electron microscopy revealed widespread areas of complete podocyte effacement.
- There was not enough tissue to perform immune staining.
She was ultimately diagnosed with focal segmental glomerulosclerosis with notable podocyte effacement. 

FSGS is a known complication of sickle cell disease. 

So, it doesn’t matter that the patient got 10 doses of ketorolac over the past month?
Discussion
Discussion Outline

1. Why this patient is a set-up for renal injury.
2. Sickle cell disease and nephrotic syndrome.
3. NSAIDs and nephrotic syndrome.
1. A Set-Up for Renal Injury?

- Our patient had multiple risk factors for development of acute kidney injury:
  - presence of sickle cell disease
  - recent pneumonia
  - state of volume depletion
  - history of multiple vaso-occlusive crises in a short time span
  - too many doses of ketorolac in the last month
2. Sickle Cell Disease and Nephrotic Syndrome

Vaso-occlusive Crisis

- Sickle cell crisis is associated with a decrease in creatinine clearance with return to baseline demonstrated around four weeks after the episode, suggesting a mechanism of transient glomerular dysfunction during acute episodes.
2. Sickle Cell Disease and Nephrotic Syndrome

Sickle cell disease can cause a nephrotic picture entirely on its own.

- Altered regulation of vasoconstrictive and vasodilatory cytokines cause decreased systemic resistance and increased renal blood flow.

- Increased renal blood flow causes hyperfiltration at the glomerular level.

- Hyperfiltration results in an increased GFR and lower serum creatinine.

- Chronic glomerular hyperperfusion can lead to glomerular injury or glomerulosclerosis thus leading to development of proteinuria.

- While the renal cortex is hyperperfused, the medulla is hypoperfused. A hypertonic, hypoxic, acidic environment sickles RBCs, slows flow in the vasa recta, and can cause infarcts resulting in painless hematuria.
3. NSAIDs and Renal Injury

- Acute kidney injury resulting from NSAID use is well documented in the adult literature.

- In children, NSAID-induced acute kidney injury often occurs in conjunction with other comorbid conditions (i.e. sickle cell disease, volume depletion) which likely increase a patient’s susceptibility to the nephrotoxic effects.
3. NSAIDs and Renal Injury

- NSAIDs inhibit cyclooxygenase and decrease prostaglandin production.

- Prostaglandins mediate vasodilation of the afferent arteriole. Decreased prostaglandin production causes decreased renal blood flow, decreased GFR, and this can cause ischemic injury and acute tubular necrosis.

- In the case of glomerular disease, NSAIDs cause acute kidney injury and minimal change disease as a direct toxic effect of therapy.
3. NSAIDs and Renal Injury

- Acute kidney injury (hemodynamically-mediated or acute tubular necrosis)
- Acute interstitial nephritis
- Nephrotic syndrome (minimal change disease or membranous nephropathy)
- Hyponatremia
- Hyperkalemia/type 4 renal tubular acidosis
- Hypertension/edema
- Acute papillary necrosis
- Chronic tubulointerstitial nephritis/analgesic nephropathy
- Uroepithelial malignancy
NSAIDs and Sickle Cell

- NSAID use is a common practice in acute episodes of vaso-occlusive crisis associated with sickle cell disease. They are on many pre-printed order sheets for sickle cell pain crises.

- Ketorolac has an opiate-like efficacy and the additional benefit of being parenterally administered.

- Use of NSAIDs has decreased risk of respiratory depression and other central nervous system adverse effects. There is also a lower addictive potential.

- NHLBI states that, “due to the need for more safety data, the current recommendation is that ketorolac should not be used by any route or combination of routes for longer than 5 days in a given month because of the increased risk of toxicity.”
Our Patient

NSAIDs causing AKI and nephrotic syndrome

Glomerular injury due to sickle cell nephropathy

Volume depletion

Multiple consecutive vaso-occlusive crisis
What to do now?

In a patient with frequent vasoocclusive pain crises, clinicians should carefully monitor frequency and dosing of NSAIDs because there is risk for developing nephrotic syndrome and acute renal failure in the sickle cell population.
Special Thanks

- Dr. Yosypiv
- Dr. El-Dahr
- Dr. Singleton
- Dr. Chavan
- Dr. DeBord
- Dr. Meghan Howell and Dr. Jessica May
Red Stick Pediatric Potpourri

presented by

The Louisiana Chapter of the American Academy of Pediatrics
References


