

## Untethering an unusual cause of kidney injury in a teenager with Down syndrome

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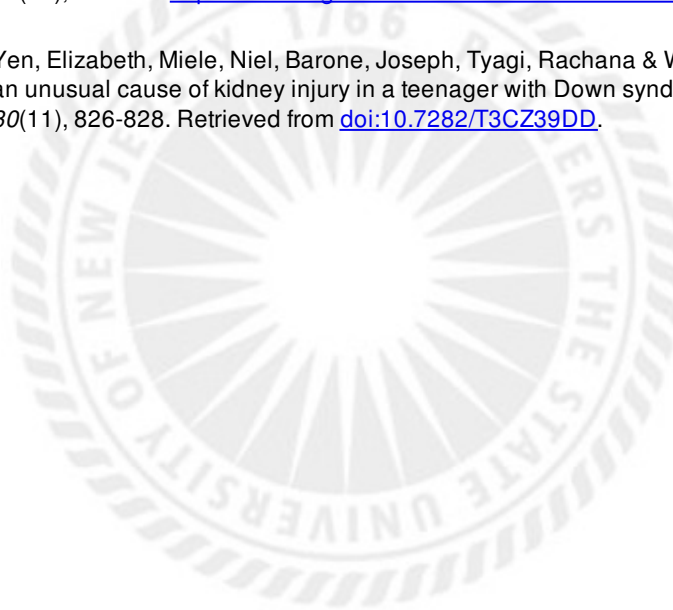
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### Background:

Acute kidney injury (AKI) (previously known as acute renal failure) in children could be detrimental—if not fatal—without prompt management. Three causes of AKI are prerenal, intrinsic, and postrenal disease. Prerenal disease is by far the most common etiology of AKI in children. Conditions that could result in prerenal disease include hypovolemia (bleeding, GI or GU losses) and decreased renal circulation or perfusion (shock, heart failure). Intrinsic renal disease includes any damage to the renal parenchyma, and may result from toxins, drugs, glomerular disease. Postrenal disease refers to an obstruction—congenital or acquired—to the lower urinary tract. Some of the causes that may lead to postrenal AKI include renal calculi, clots, neurogenic bladder, and medications causing urinary retention. We report a case of AKI resulting from a postrenal process that is secondary to tethered cord and an ongoing chronic kidney disease (CKD) and highlight the importance of understanding and searching for the pathophysiology and etiology in managing a case.

### Case:

A 16-year-old female with Down Syndrome was referred to the emergency department by her pediatrician for evaluation of suspected kidney injury. Three weeks prior to arrival, she was diagnosed with streptococcal pharyngitis and treated with a 10-day course of Amoxicillin. Despite the treatment her mother stated that the patient “was still not right,” exhibiting increased fatigue, decreased appetite, and increased thirst. The patient was also noted to “bear down and push hard” when urinating. There was no urinary frequency, urgency, color change, nor was her urine malodorous. She developed mild abdominal distention thought to be due to her chronic constipation. Repeat rapid strep was negative. Blood tests, done in part at the mother’s request, showed normal complete blood count (CBC), and complete metabolic panel (CMP) with serum potassium of 5.4 mEq/L, blood urea nitrogen (BUN) of 48 mg/dL, and creatinine (Cr) of 6.17 mg/dL. Based on the results, the patient was referred to the ED for further evaluation and management.

On physical examination, the patient appeared comfortable. She was afebrile, not tachycardic or tachypneic. Her oxygen saturation was at 97% on room air. Blood pressure was 157/98. Mucous membranes were dry. A midline abdominal mass was palpated from the periumbilical to the suprapubic areas. On palpation, she demonstrated discomfort. There was no CVA tenderness or midline deformity. She had hypertrichosis—facial hair above the upper lip and fine hair on bilateral arms and lower back, but not true stigmata of a tethered cord. The patient’s strength was 5/5 with intact sensation throughout. She was able to walk but with flexed posture, complaining of low back pain. She was able to answer simple questions appropriately and carry limited conversations. The rest of the examination was unremarkable.

Repeat laboratory tests in the ED confirmed an elevated BUN/Cr of 49/5.6 (mg/dL), phosphorus 5.2 mg/dL, uric acid 8.1 mg/dL. The rest of CMP was within normal range. Urine analysis showed specific gravity of 1.006 with normal protein/creatinine ratio. Urine osmolality was 232 mOsm/kg. On abdominal ultrasound, bladder was distended with an estimated 950mL of urine pre-void. Post-void, there was an estimated 550mL of urine. There was hydronephrosis on bilateral kidneys, with increased echogenicity and no stones or cortical thinning. After placement of a foley catheter, 540mL of urine immediately drained. Her blood pressure post drainage decreased to 132/85.

The patient continued to put out approximately 2.5 liters of urine during the next 12 hours. Her BUN/Cr normalized to 12/0.8 (mg/dL) within 4 days, and her blood pressure came down to 110/78 within this period as well. Further inquiries were performed to discover the underlying etiology of her obstructive uropathy. Abdominal x-ray showed a moderate amount of stool in the recto-sigmoid area, not large enough to cause urinary obstruction. A lumbar spine MRI without contrast demonstrated a low-lying conus medullaris (at the L2-L3 level) suspicious for tethered cord, with no evidence of thickened filum terminale, lipoma, or diastomyelia. In addition, a moderate central stenosis at C2-C3 levels due to a right disc herniation was noted, as well as mild spondylotic changes in the lower thoracic spine. There was no Arnold-Chiari malformation, syrinx or cord signal changes.

With the tethered cord as a likely cause for the patient's urinary retention, a laminectomy and filum sectioning was performed. Post operatively, due to behavioral issues, she was unable to tolerate intermittent catheterization. A repeat ultrasound prior to discharge demonstrated normal appearing kidneys with no hydronephrosis. She was discharged with an indwelling foley catheter. Repeat CMP showed normal BUN and Cr values. At her urology follow up appointment a month later, her foley was successfully removed. Another ultrasound showed prevoid bladder volume of 200mL and postvoid volume of 25mL, indicating a much improved bladder emptying capacity.

To complete her evaluation, a cystoscopy and urodynamic study was performed 3 months later. The study showed that she had a normal appearing urethra without lesions, diffuse bladder wall thickening (8mm) and a trabeculated bladder with diverticulum, and normal appearing orifices bilaterally. Her urodynamic study showed a greater-than-normal compliance of the bladder. It did not find uninhibited detrusor contractions, and there was no EMG discoordination.

### Discussion

This case highlights an acute-on-chronic kidney injury in an adolescent with Down Syndrome. She presented with an elevated serum creatinine level, oliguria, and hypertension, all of which are signs of AKI. Without any preceding history of prior kidney injury and urinary tract abnormalities, her current renal function abnormality is more likely of an acute type. In addition, the fact that her kidney function normalizes within days further supports the acute nature of her kidney injury.<sup>1</sup> Despite AKI, however, our patient seems to have an underlying chronic kidney disease (CKD) that predisposes her to having AKI. She has been having long-standing constipation, and a tethered cord on the MRI confirms the underlying cause of her obstructive uropathy.

Tethered Cord Syndrome (TCS) is a condition in which the filum terminale, the anchoring segment of the cauda equina, is prevented from hanging freely within the spinal canal. This stems from different growth rates between the vertebral column and the spinal cord. Such tethering leads to neurological symptoms, mainly the upper motor neuron deficits. They include bladder and bowel dysfunction, scoliosis, foot deformities, progressive back and lower leg pain, weakness, and other sensorimotor disturbances.

The etiology of TCS in adolescents and adults is rather different from that in infants and children. TCS in older population stems either from an undiagnosed congenital tethering or from

acquired causes such as lipoma, dermoid cyst, lipomeningocele, spinal stenosis, trauma, adhesion, etc. Multiple neurological problems may occur, with lower back pain remains the most common symptom.<sup>2</sup> These neurologic symptoms tend to progress in a slower and more insidious fashion compared to those in the congenital/childhood population. Urinary symptoms such as increased frequency and residual urine may appear within a few years of the onset of vague lower back pain and/or numbness in the lower extremities.

It is widely accepted that congenital/childhood TCS will benefit from early surgical interventions. Surgical intervention for TCS in the adolescent and older population, however, has been a topic of ongoing discussion. Mainly, the timing of the surgery has been debated. Some opt to intervene once the structural abnormalities are found in the imaging, even before bladder symptoms appear, yet some wait until patients become symptomatic.<sup>3,4,5,6,7</sup> The decision to surgically intervene for our patient was made in light of her worsening renal function. Despite the fact that foley catheterization relieved her obstruction, the more important and evident underlying etiology was her newly diagnosed TCS. Her progressive back pain, chronic constipation, and bladder dysfunction were the reasons why surgery was offered to the family and was performed.

Our patient's postsurgery ultrasounds demonstrated resolved hydronephrosis, but diffuse bladder wall thickening of 8mm (normal range up to 3mm). The trabeculated bladder and diverticulum on cystoscopy are findings consistent with urinary retention in the setting of her insidious neurogenic vesicourethral dysfunction.<sup>8</sup> With this discovery, it is concluded that patient's acute kidney injury stems from an ongoing neurogenic bladder resulting in severe urinary retention and hydronephrosis. It may take several more months or years before her bladder anatomy and function resolve. It is difficult to predict the amount of time that has elapsed until the development of bladder wall thickening and trabeculation in our patient.

Treatments for neurogenic bladder causing urinary retention include behavioral modifications (physical-psychological therapy with voiding diary), electrical stimulation therapy (biofeedback), clean intermittent catheterization (CIC), indwelling catheterization, and more invasive surgeries such as urethral stents, urethral sphincter resection or sphincterectomy, urinary diversion creating a stoma, etc. At the present time, it was decided that due to her Down Syndrome, it is in patient's best interest to have her parents closely monitor her voiding patterns and to work with patient in a structured manner such that her voiding pattern is regulated. Indwelling catheter, CIC, or surgical option is deferred at this point.

Chawla and Kimmel<sup>9</sup> emphasized the bidirectional nature of AKI and CKD. A single event of AKI may directly lead to an end-stage renal disease, and it certainly increases the risk of CKD. It is a misnomer to think that a survivor of AKI has a limited event and will not need to be followed up further. The authors proposed an integrated approach to the long-term care of patients with kidney disease and "consideration of the state of diminution in GFR as a clinical entity" instead of separating AKI and CKD. They asserted that the distinction between AKI and CKD may be artificial. As such, our patient will be closely followed and monitored. Specialists involved in her care (urologist, nephrologist, neurosurgeon) will continue to monitor her long-term, both clinically and with multiple laboratory studies, further imaging and urology studies.

One thing to be yet determined is whether or not she has re-tethering of her TCS. A repeat imaging (MRI) is necessary in the near future.

#### Lessons for physicians:

Several lessons arise in the management of this case. The fact that our patient had polydipsia and polyuria might be an early sign of concentrating defect (renal tubular dysfunction). As reported by her mother, the patient was “thirsty all the time.” Such signs should prompt physicians to further evaluate renal function.

Secondly, when adolescents present with any complaints of lower back pain, leg pain, it is important to consider TCS in the diagnosis. As pointed out by Giles<sup>10</sup> “the possibility of functional tethered cord syndrome should be considered when adolescent patients present with unexplained [and vague] lumbar, buttock, and leg symptoms.” He further insisted that physicians should think about TCS “even when repeated lumbar reports after MRI state there are no features of tethered cord or other dysraphic disorder, laboratory tests are normal, and routine neurological tests for deep reflexes, plantar response, pinprick sensation, and vibration sensation are normal.”

Thirdly, despite the resolution of AKI, it is of utmost importance that patients have long-term follow up due to the increased risk of development of CKD. AKI and CKD is a continuum rather than a separate entity, and the dichotomization of the two will limit thorough investigations and is likely to be detrimental to the patients.

Finally, when physicians encounter patients with chronic illness or with cognitive limitations, it is important to take into account family’s concerns, questions, and requests. As we strive to gather the most accurate history from our patients, often times we lack the advantage of having the daily observations and findings that the families have. It is therefore crucial to always collaborate with families while maintaining a sharp diagnostic thinking and judgment.

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