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ORIGINAL ARTICLE

Hematuria in Children with Spinal Injury

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ABSTRACT

The presence of red blood cells (RBCs) in urine is hematuria, even in microscopic amounts alarms the patient and parents of the patient, and often prompts physician for many laboratory investigations. Hematuria can be red, dark or cola-colored, or brown known as macroscopic hematuria, and when it is not visible to the unaided eye, it is known as microscopic hematuria. RBCs in urine is one of the most important signs of genitourinary tract disease; however, it is almost never a cause of anemia, since few drops (1 mL) of blood can turn 1 L of urine into red-colored urine. Overall the physician should be alert enough not to overlook serious conditions like neoplasms and underlying bleeding disorder, to avoid unnecessary and often expensive laboratory studies. This article provides an approach to the evaluation and management of hematuria in children, and the detection of preventable and treatable conditions at the earliest to limit the disease progression, and an overall reduction in cost, energy, and anxiety. The patients are spinal cord injured patients with lower urinary tract dysfunction; special consideration of pediatric and elderly populations is presented separately. The target audience is healthcare providers who are engaged in the medical care of patients with spinal cord injury. The mandatory assessment includes medical history, physical examination, frequency-volume chart, urinalysis, blood chemistry, transabdominal ultrasonography, measurement of postvoid residual urine, uroflowmetry, and video-urodynamic study. Optional assessments include questionnaires on the quality of life, renal scintigraphy, and cystourethroscopy. The presence or absence of risk factors for renal damage and symptomatic urinary tract infection affects urinary management, as well as pharmacological treatments. Further treatment is recommended if the maximum conservative treatment fails to improve or prevent renal damage and symptomatic urinary tract infection. In addition, management of urinary incontinence should be considered individually in patients with risk factors for urinary incontinence and decreased quality of life.

Keywords: Children; Kidneys, bladder, neurogenic, injuries, spinal cord, spinal cord disorders, ; RBC cast; Red blood cells; Urine, ASIA (American Spinal Injury Association)

INTRODUCTION

Macroscopic hematuria is visible to the naked eye, but microscopic hematuria usually is detected by a dipstick test during a routine examination. Hematuria is confirmed by microscopic examination of the spun urine sediment. Microscopic examination is performed with the concentration of the urinary sediment by centrifugation. Ten milliliters of urine are spun at 2000 rpm for 5 minutes. Nine milliliters is decanted, and the sediment is resuspended, and an aliquot examined. The urine is examined by microscopy by high power field(hpf) that is 400_ magnification. Macroscopic hematuria often does not require concentration. Bright-red urine, visible clots, or crystals with normal-looking red blood cells (RBCs) suggests bleeding from the urinary tract. Cola-colored urine, RBC casts, and deformed (dysmorphic) RBCs suggest glomerular bleeding . An absence of RBCs in the urine with a positive dipstick reactionsuggests hemoglobinuria or myoglobinuria. The sensitivity and specificity of the dipstick method for detecting blood in the urine vary. When tested on urine samples in which a predetermined amount of blood has been placed, dipsticks have a sensitivity of 100 and a specificity of 99 in detecting one to five RBCs/hpf . This corresponds to approximately 5 to 10 intact RBCs/lL urine. There is no consensus on the definition of microscopic hematuria, although more than 5 to 10 RBCs/hpf is considered significant. The author and others recommend that at least two of three urinalyses show microhematuria over 2 to 3 weeks before further evaluation is performed . The American Academy of Pediatrics recommends a screening urinalysis at school entry (4–5 years of age) and once during adolescence (11–21 years of age) as a component of well child–care(1,2).

Table 1. Causes of Discoloration of Urine

Dark yellow or orange urine	Normal concentrated urine, drugs such as rifampicin
Dark brown or black urine	Bile pigments methemoglobinemia alanine, cascara, resorcinol
Red or pink urine concentration blackberries,	alkaptonuria, homogentisic acid, melanin, thymol, tyrosinosis Red blood cells (hematuria), free hemoglobin (hemoglobinuria), myoglobin (myoglobinuria), porphyrins urates in high (may produce pinkish tinge), foods (e.g. beetroot, red dyes), drugs (namely, benzene, chloroquine, desferoxamine, phenazopyridine, phenolphthalein

Adopted from Hui-Kim Yap, Perry Yew-Weng: Hematuria and proteinuria. In: Comprehensive Pediatric Nephrology(3,4).

Initial evaluation

Macroscopic hematuria: The evaluation of a child with gross hematuria differs from that of microscopic hematuria . Macroscopic hematuria of glomerular origin usually is described as brown, tea-colored, or colacolored, whereas macroscopic hematuria from the lower urinary tract (bladder and urethra) is usually pink or red. Macroscopic hematuria in the absence of significant proteinuria or RBC casts is an indication for a renal and bladder ultrasound to

exclude malignancy or cystic renal disease. Referral to a urologist is required when clinical evaluation and workup indicates that there is a tumor, a structural urogenital abnormality, or an obstructing calculus(5).

Causes of hematuria in children Glomerular diseasesRecurrent gross hematuria (IgA nephropathy, benign familial hematuria, Alport's syndrome) Acute poststreptococcal glomerulonephritisMembranoproliferative glomerulonephritisSystemic lupus erythematosus Membranous nephropathy Rapidly progressiveglomerulonephritisHenoch-Schonlein purpura Goodpasture's disease Interstitial and tubular Acute pyelonephritis Acute interstitial nephritis Tuberculosis(6).

Causes Of Hematuria In Children

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Hematologic

(sickle cell disease, coagulopathies von Willebrand's disease, renal vein thrombosis, thrombocytopenia)

Urinary tract
Bacterial or viral (adenovirus) infection–related
Nephrolithiasis and hypercalciuria Structural anomalies, congenital anomalies, polycystic kidney disease
Trauma
Tumors
Exercise
Medications (aminoglycosides, amitryptiline, anticonvulsants, aspirin, chlorpromazine, coumadin, cyclophosphamide, diuretics, penicillin, thorazine(9).

Laboratory studies: Only two diagnostic tests are required for a child with microscopic hematuria: (1) a test for proteinuria and (2) a microscopic examination of the urine for RBCs and RBC casts. Children with macroscopic hematuria require urine culture and renal imaging by ultrasound. Proteinuria may be present regardless of the cause of bleeding, but usually does not exceed 2þ (100 mg/dL) if the only source of protein is from the blood. This is especially true if the child has microscope hematuria.

Spinal Cord Injuries: A spinal cord injury is caused by trauma or disease to the spinal cord, most often resulting in paralysis (loss of strength), loss of sensation (feeling), and loss of control of bodily functions.

Causes of Spinal Cord Injuries Since 2010

• 36.5% – Vehicular accidents
• 28.5% - Falls
• 14.3% - Violence
• 9.0% - Sports
• 11.4% - Other/unknown

Paralysis, or loss of muscle strength, is the initial source of medical problems in persons with spinal cord injuries. Secondary medical problems include demineralization of bone, degeneration of the circulatory system, kidney and bladder dysfunction, pneumonia, and pressure sores (10, 11).

ASIA Impairment Scale

- ASIA A: means there is no feeling or movement below the damaged area in the spinal cord
- ASIA B: feeling, but no muscle strength, is present below the damaged area
- ASIA C: weak muscle strength is present below the damaged area
- ASIA D: strong muscle function is present below the damaged area
- ASIA E: feeling and muscle function is normal below the damaged area of the spinal cord

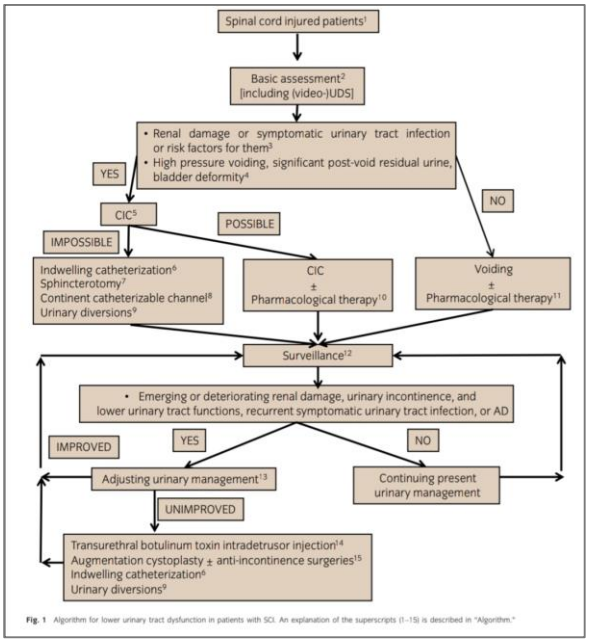

Fig. 1 Algorithm for lower urinary tract dysfunction in patients with SCI. An explanation of the superscripts (1–15) is described in "Algorithm."

How Is My Bladder Function Changed By Spinal Cord Injury?: Nerve impulses from the bladder can no longer get to and from the brain to let you sense that your bladder is full or to let you void. There are two general kinds of bladder dysfunction that can occur depending on your level of injury. Because there can be individual variations, you will probably have some tests to diagnose your particular bladder type (12, 13).

These types of bladder dysfunctions are described next.

•**Upper motor neuron bladder (reflex or spastic bladder)** In this condition, the bladder tends to hold smaller volumes of urine than before SCI. Just like your other muscles may have spasms and contract on their own, so can the bladder muscle. The result is that you may have frequent, small urinations without control. This bladder type is common in most spinal cord injuries above the sacral level. This type of urination generally happens with elevated bladder pressures and is a significant cause of urinary tract infections (UTIs).

• **Lower motor neuron bladder (flaccid bladder)**In this condition, the bladder muscle has lost its ability to contract and can be easily stretched. Therefore, large volumes of urine can be held by the bladder at low pressure. Because

the muscle cannot contract, urine leaves the bladder only when it is overfilled. The urine "spills over" out of your bladder into your urethra like a glass that is too full of water. The bladder type is common when SCI affects the sacral level of the cord (cauda equina injuries)(14,15,16).

How Do IE**mpty My Bladder After S**CI**?:** If you have an incomplete injury, you may eventually regain all or some voluntary control of your bladder. If you have a complete injury, one or a combination of the following bladder emptying techniques will become part of your bladder management program.

Catheterization: A catheter is a small rubber or plastic tube inserted into the bladder to drain urine.

Stimulated voiding: We call this "tapping." The tapping is done on your abdomen over your bladder. A Lower Motor Neuron bladder may empty with firm pressure over the bladder called crede (creh-DAY), or during straining or bending forward.

Spontaneous voiding: sphincterotomy and wearing an external collecting device will keep you dry.

DIAGNOSTIC ALGORITHM AND MANAGEMENT

Medical History: Information on trauma is usually available. It is important to emphasize that, in children, even minor trauma can result in extensive genitourinary tract damage..

Physical Examination: Signs of blunt or penetrating trauma should be located, when there is a history of trauma. Genitalia should always be examined and, in cases of trauma, signs of contusion, hematoma, or lacerations should be identified. Lesions of the genitalia without a clear history of trauma should raise the suspicion of child abuse. When a genitourinary mass, such as rhabdomyosarcoma, is part of the differential diagnosis, a rectal examination should be performed also. Examination of the abdomen demonstrating tenderness of the flank could lead to the diagnosis of a urinary tract infection or stone disease; abdominal, retroperitoneal, and pelvic masses are relatively easier to palpate in young children than in adults as the abdominal wall layers are less developed.

Laboratory Tests: Urinalysis should verify the existence of red blood cells. The concomitant presence of red blood cells, proteins, nitrites, and positive leucocytes esterase assay is pathognomonic for urinary tract infection; urine culture will provide the final diagnosis. Urinary casts and protein will direct us toward the diagnosis of renal glomerular and parenchymatic diseases. Urine microscopy can also identify crystals that may appear in stone disease. also serum urea, creatinine, and electrolytes should be tested.

Evaluation and Management: Trauma patients should be managed according to their hemodynamic status and concomitant injuries. In stable children with trauma, the gold standard for imaging is CT. If urethral or bladder trauma is suspected, urethrocystography should be performed. Abdominal masses should be evaluated with ultrasound to differentiate between cystic/hydronephrotic masses and solid masses (17,18,19).

Clinical Approach in Approaching a Child with Hematuria: should be asked about recent trauma, exercise, passage of urinary stones, recent respiratory or skin infections and intake of medications like NSAIDS and calcium or vitamin D, or traditional medicines. It is worth asking about family history of hematuria, hypertension, renal stones, renal failure, deafness, coagulopathy, jaundice and hemolytic anemias.

Physical examination: Vital parameters like blood pressure, temperature, heart rate and breathing pattern should be always noted first. Presence of high blood pressure, low urine output and edema prompt the clinician to think on lines of acute nephritic syndrome, while hematuria with skin rashes or arthritis may indicate systemic lupus erythematosus or Henoch-Schonlein nephritis or collagen vascular disease. However, ill-look, fever, vomiting, or loin pain may point to pyelonephritis. Palpable abdominal masses with hematuria should be looked for the presence of tumor, polycystic kidney, or hydronephrosis; however, IgA nephropathy, thin membrane disease, Alport's syndrome may present with recurrent hematuria only.

When to Refer for Hematuria: Referral to a pediatric nephrologist for evaluation of hematuria is warranted when accompanying factors are present that increase the risk for renal parenchymal disease or significant resulting morbidity. This includes the presence of hypertension, which may signify the presence of glomerulonephritis, and may require treatment with antihypertensive agents to avoid both acute (i.e. hypertensive encephalopathy) and chronic (i.e. left ventricular hypertrophy, dilated cardiomyopathy) sequelae. The presence of proteinuria, particularly nephrotic range proteinuria, and certainly renal dysfunction may herald a sufficiently destructive lesion (i.e. crescentic or rapidly progressive glomerulonephritis due to PIGN, IgAN, HSP Nephritis or other less common lesions [i.e. membranoproliferative glomerulonephritis, pauci-immune vasculitis such as granulomatosis with polyangiitis]). With such cases, prompt referral to a pediatric nephrologist is indicated for diagnostic renal biopsy and definitive management with immunosuppressive therapy. Identification of renal cysts in the context of hematuria may benefit from referral to nephrology, largely to provide guidance to the family as to the most likely etiology among the array of cystic kidney diseases, the risk of any associated extra-renal manifestations, and expectations of long-term outcome. Finally, if nephrolithiasis is identified through the workup of microscopic or gross hematuria, once acute management has been completed by a pediatric urologist, referral to nephrology is appropriate to initiate a metabolic workup and then devise a comprehensive stone risk mitigation plan with dietary and pharmacological interventions. Referral to a pediatric urologist is warranted particularly if there is evidence of structural pathology causing microscopic or gross hematuria and if the identified pathology has a surgical treatment (i.e. hydronephrosis, renal mass, obstruction or renal colic from urolithiasis). In addition, the pediatric urologist may also offer additional diagnostic tools such as cystoscopy if the clinical features are consistent with lower-tract bleeding(20).

Management of Hematuria: After it is learnt from the history, physical examination and lab tests that condition does not need any immediate intervention, the parents and older children must be reassured and advised for the stepwise plan of action. However, clues like history of recent upper respiratory tract infection, trauma, recent

exercise, menstruation, sore throat, skin infection, painful micturition, increased frequency, urgency, enuresis, urine color, abdominal and costovertebral angle pain, family history hematuria, deafness, hypertension, coagulopathy, calculi will be very helpful in appropriate management of hematuria. Dipstick test and microscopic urinalysis should be repeated weekly within 2 weeks after the initial specimen. If the hematuria resolves, no further tests are needed . If hematuria persists, with more than 5 RBCs/HPF and no evidence of hypertension, edema, oliguria, or proteinuria on at least two of three consecutive samples, determination of the serum creatinine levels and ultrasonography for the presence or absence of stones, tumors, hydronephrosis, structural anomalies, renal parenchymal dysplasia, medical renal disease, inflammation of the bladder, bladder polyps, and posterior urethral valves, should be performed. The cost effectiveness of renal ultrasonography for evaluation of an asymptomatic child with microscopic hematuria is equivocal though . If there is no proteinuria, no RBC casts, no edema and oliguria, no hypertension, normal serum creatinine along with normal renal and bladder ultrasonography, reassurance to parents and patient with regular follow-up is advised. However, parents' and sibling urine should be tested with dipsticks , to rule in/out the familial causes of hematuria. Going for detailed investigations including invasive renal biopsy is still debatable in asymptomatic hematuria; however, for prognosis, insurance purposes and genetic counseling, renal biopsy has been recommended by some researchers .

CONCLUSION

Hematuria in children has a wide differential diagnosis, mandating different approaches and management compared to adult patients. Family history, concomitant symptoms and signs, physical examination, urinalysis, and blood tests may direct us towards an accurate diagnosis. Most of the disorders that may cause hematuria are "nonsurgical, nonurological" diseases and should be managed by a pediatrician. In a minority of cases, invasive diagnostic procedures will need to be performed. Primary diagnostic imaging using ultrasound is widely used, the breadth of kidney and urinary tract pathology that leads to either gross or microscopic hematuria is vast, and a careful history and physical examination as well as focused laboratory investigation may provide sufficient insight as to the likely culprit of hematuria, either reassuring the clinician as to the suitability of expectant management, or spurring them on to facilitate referral to subspecialty care. As such, the crux of management of many causes of hematuria may be to determine when it is time to refer, more than what treatments to initiate one's self. To this end, the patient's primary care provider is often an integral team member in ensuring that renal and urological pathology with significant morbidity is addressed in a timely fashion(20,21).

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