

REVIEW ARTICLE

RENAL AND URINARY TRACT NEOPLASIA IN THE DIFFERENTIAL DIAGNOSIS OF GROSS HAEMATURIA IN CHILDREN: A NARRATIVE REVIEW

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ABSTRACT

Gross haematuria is an uncommon but alarming presentation in children and its cause is benign in the overwhelming majority of cases. Neoplasia accounts for approximately 1% of paediatric series, yet it is the aetiology that carries the greatest cost when overlooked. This narrative review examines the place of renal and urinary tract tumours in the differential diagnosis of paediatric gross haematuria. PubMed was searched for studies addressing the aetiology of gross haematuria in children and the clinical presentation of paediatric renal and bladder neoplasms. The spectrum of tumours is strongly age dependent: congenital mesoblastic nephroma predominates in the neonatal period, Wilms tumour accounts for 80 to 85% of childhood renal tumours with a peak between 3 and 4 years and renal cell carcinoma overtakes Wilms tumour in adolescence. In Wilms tumour, gross haematuria occurs in about 18% of patients at presentation and is usually accompanied by a palpable abdominal mass. Haematuria becomes the dominant sign when the tumour involves the collecting system, as in ureteral extension and in intrapelvic and botryoid variants. In the lower tract, rhabdomyosarcoma is the commonest malignant bladder tumour of childhood and urothelial neoplasms, though rare, present characteristically with painless gross haematuria. Absence of a palpable mass does not exclude malignancy and empirical treatment of presumed urinary tract infection is a recognised source of diagnostic anchoring. Renal and bladder ultrasonography is the appropriate first-line investigation. A sterile urine culture, or recurrence of haematuria after treatment, should prompt imaging before resolution is assumed.

Introduction

Gross haematuria is not common in children, but it rarely goes unnoticed: blood visible in the urine invariably worries families and almost always prompts medical attention. Its causes are benign in nearly all cases. In a series of 342 children and adolescents assessed over 10 years, the leading aetiologies were benign urethrorrhagia, trauma, urinary tract infection (UTI) and congenital urological anomalies and no cause was identified in around one third of patients.¹ In that same series, malignancy accounted for approximately 1% of cases, comprising three low-grade bladder transitional cell carcinomas and a single Wilms tumour (WT).¹

This distribution creates a particular clinical hazard. A diagnosis occurring in roughly one of every hundred children is frequently overlooked and the remaining diagnostic hypotheses are both more probable and more readily treated. Empirical antibiotic therapy for presumed UTI in a child with haematuria and

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ABBREVIATIONS

CCSK - Clear cell sarcoma of the kidney,

CMN - Congenital mesoblastic nephroma,

CT - Computed tomography,

ED - Emergency department,

RCC - Renal cell carcinoma, RMS - Rhabdomyosarcoma, US - Ultrasonography,

UTI - Urinary tract infection, WT - Wilms tumour.

leucocyturia is a defensible decision, particularly in an emergency setting, but it closes the diagnostic loop prematurely if the result of the subsequent urine culture is never acted upon, either because it is not actively checked by the team, which is common in an emergency department (ED), or because symptoms are intermittent and appear to improve initially.

This review addresses the place of renal and urinary tract neoplasia in the differential diagnosis of gross haematuria in children. Although it is a rare diagnosis, it is essential not to miss a case of neoplasia, because early diagnosis is decisive for a good clinical outcome. The paper summarises which tumours present with haematuria and at what age, identifies the circumstances in which haematuria becomes the dominant or isolated sign and proposes a narrow and feasible criterion for imaging investigation.

Materials and Methods

A narrative review was conducted. PubMed was searched for English-language publications addressing two domains: the aetiology and evaluation of gross haematuria in children and the clinical presentation of paediatric renal and bladder neoplasms. Search terms combined "gross haematuria", "macroscopic haematuria", "children", "Wilms tumour", "nephroblastoma", "renal neoplasms", "bladder

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neoplasms" and "delayed diagnosis". Clinical series, national study group reports, narrative and systematic reviews, clinical practice guidelines and illustrative case reports describing atypical presentations were considered. Reference lists of retrieved articles were hand-searched. Given the rarity of several entities discussed, case reports and small series were retained where they provided the only available description of a presentation pattern. No formal quality appraisal or quantitative synthesis was performed and the review is not intended as a systematic review.

Use of Artificial Intelligence:

Claude Opus 5 was used to assist with the translation of the manuscript from Portuguese into British English to facilitate readability. It was also used to assist with manuscript formatting in accordance with the journal's author guidelines and character counting. The authors reviewed and approved the final manuscript and take full responsibility for its content.

Results and Discussion

How often is gross haematuria caused by a tumour?

Published paediatric series consistently place malignancy at the bottom of the frequency list. In the largest single-institution review available, four of 342 children had neoplasm.¹ Earlier and subsequent series report comparable patterns, with infectious, structural, traumatic and glomerular causes predominating.^{2,3} The clinical implication is not that tumours can be disregarded, but that their detection depends on deliberate consideration rather than on statistical likelihood.

The spectrum of renal tumours is age dependent

Renal tumours account for approximately 7% of childhood malignancies and WT represents 80 to 85% of them.⁴ The remainder comprise a heterogeneous group, each accounting for only 2 to 4%.⁴ Age is the single most useful discriminator (Table 1). Congenital mesoblastic nephroma (CMN) predominates in the neonatal period and is the commonest benign renal tumour of childhood. Malignant rhabdoid tumour of the kidney presents at a mean age of around 11 months and is distinguished by its association with synchronous intracranial tumours. Clear cell sarcoma of the kidney (CCSK) peaks between 2 and 4 years, with male predominance and has a propensity for bone metastasis. Renal cell carcinoma (RCC) gains proportional importance in adolescence, representing more than half of renal malignancies between 10 and 15 years of age.

Benign lesions also matter, because several present with haematuria rather than with a mass. Angiomyolipoma, characteristically associated with tuberous sclerosis, contains macroscopic fat and may bleed. Ossifying renal tumour of infancy is exceptionally rare, but gross haematuria is its commonest presenting symptom, frequently in the absence of any palpable abdominal mass.

Wilms tumour: when haematuria comes first

The classic presentation of WT is an asymptomatic abdominal mass, detected by a caregiver or during

routine examination and present in around 80% of children at diagnosis. Gross haematuria occurs in approximately 18% of patients at presentation and microscopic haematuria in about 24%.⁵ Haematuria as the sole initial complaint, without a palpable mass, is therefore clearly uncommon and readily attributed to more frequent conditions.

The circumstances in which haematuria dominates are largely explained by tumour involvement of the excretory tract. In a National Wilms Tumor Study Group review of 45 children with ureteral extension, an event occurring in approximately 2% of patients, gross haematuria was the initial manifestation in 22 and was identified as a significant clue to collecting system involvement.⁶ The same mechanism underlies the intrapelvic and botryoid variants, in which the tumour occupies the pelvicalyceal system with minimal parenchymal invasion; in these forms haematuria is reported at presentation in the great majority of patients, in contrast with the classic form.^{7,8} Recognising this association is useful in two directions: haematuria as an isolated first sign should raise the possibility of collecting system involvement and preoperative identification of ureteral extension is surgically relevant, since transecting tumour within the ureter carries a risk of local spill and residual disease.⁶

Lower urinary tract tumours

Bladder tumours are rare in the first two decades of life, with urothelial neoplasms reported at an incidence of 0.1 to 0.4%.⁹ Rhabdomyosarcoma (RMS) is the commonest malignant bladder tumour of childhood.⁹ Across paediatric bladder neoplasia, painless gross haematuria is the predominant presenting symptom, followed by dysuria, whether isolated or recurrent and abdominal US is typically the first investigation, confirming the lesion in most patients.⁹ Urothelial carcinoma in childhood is characteristically superficial and low grade, but it has been described in children with persistent gross haematuria whose complaint was initially dismissed.¹⁰ Urinalysis and urine culture are mandatory to exclude concomitant infection, which may coexist and mask the underlying lesion.

Clinical features that should raise concern

Several features recur in the literature as reasons to broaden the differential diagnosis (Table 2). A palpable abdominal or suprapubic mass, hypertension, constitutional symptoms or a known tumour predisposition syndrome are self-evident indications for prompt imaging investigation. Less obvious and more relevant to everyday practice, are three negative findings frequently interpreted as reassuring.

First, the absence of a palpable mass does not exclude a renal tumour, particularly when the lesion involves the collecting system or arises in the renal pelvis.⁶⁻⁸ Second, painless haematuria is not reassuring; in bladder neoplasia it is the rule rather than the exception.⁹ Third, an initial urinalysis compatible with infection does not confirm infection. Leucocyturia accompanies a wide range of urinary tract pathology and empirical antibiotic therapy in this setting creates a well-recognised anchoring effect, in which the presumed diagnosis is retained after the evidence supporting it has disappeared. A sterile urine culture in a child treated empirically for presumed UTI invalidates the

Table 1. Age at presentation and relative frequency of paediatric renal tumours

Tumour	Typical age	Relative frequency	Notes relevant to haematuria
Congenital mesoblastic nephroma	Neonatal period	Most frequent neonatal renal tumour	Usually presents as abdominal mass; benign.
Malignant rhabdoid tumour	Mean around 11 months	Under 2% of renal tumours	Abdominal distension, mass, gross haematuria, fever; synchronous intracranial tumours.
Clear cell sarcoma of the kidney	Peak 2 to 4 years	Around 3 to 4%	Male predominance; bone metastases; haematuria among reported symptoms.
Wilms tumour	Peak 3 to 4 years	80 to 85%	Mass (80%); gross haematuria (around 18%); haematuria predominates with collecting system involvement.
Ossifying renal tumour of infancy	Infancy	Exceptionally rare	Gross haematuria is the most common presenting symptom, often without palpable mass.
Renal cell carcinoma	Adolescence	Over half of renal malignancies at 10 to 15 years	Haematuria; flank pain and mass; often symptomatic at diagnosis.
Angiomyolipoma	Variable	Benign	Associated with tuberous sclerosis; contains macroscopic fat; may bleed.

Table 2. Features in a child with gross haematuria that warrant renal and bladder ultrasonography

Category	Feature
Examination	Palpable abdominal or suprapubic mass; hypertension; abdominal distension.
Symptom pattern	Painless haematuria; persistent or recurrent haematuria; haematuria with no identified cause.
Laboratory	Sterile urine culture after empirical treatment for presumed urinary tract infection.
Background	Known tumour predisposition syndrome; constitutional symptoms; unexplained anaemia.

diagnosis of urinary tract infection and requires it to be reconsidered, particularly when haematuria persists or recurs.^{3,11} Frequently, a patient assessed in the ED is not contacted once the urine culture result becomes available, does not attend follow-up appointments, or simply has no designated paediatrician, all of which are important barriers to the continuity of investigation.¹²⁻¹⁴

In practice, the failure is rarely one of clinical reasoning at first contact; it is one of pathway, in that a pending laboratory result may have no clinician explicitly responsible for acting upon it.

Diagnostic approach

Evaluation begins with history, physical examination including blood pressure measurement and urinalysis with microscopy, complemented by urine culture.^{11,15} Renal and bladder US is the appropriate first-line imaging modality: it is widely accessible, non-invasive and able to identify a renal or bladder mass and characterise its solid or cystic nature within minutes. Contemporary guidance recommends kidney and bladder ultrasonography in children with asymptomatic gross haematuria.¹⁶ Computed tomography (CT) is reserved for lesion characterisation, staging and surgical planning once a mass has been identified, or

for specific scenarios such as suspected urolithiasis or trauma.^{5,17}

We do not advocate imaging every child with gross haematuria. Given a probability of malignancy close to 1%, universal imaging would be disproportionate and would generate incidental findings of uncertain significance. Renal incidentalomas are relatively frequent in the paediatric population undergoing abdominal ultrasonography, renal cysts being among the best studied findings, with a prevalence of 2.2% in a large paediatric cohort of 70,500 ultrasound examinations.¹⁸ We propose instead a narrower criterion, compatible with routine practice: when gross haematuria has been treated empirically as UTI, a sterile urine culture, or recurrence of haematuria after completion of treatment, should trigger renal and bladder ultrasonography before resolution is assumed. This criterion is deliberately conservative. It targets a small, clearly defined group in which the working diagnosis has already been contradicted by laboratory evidence and it requires an investigation without radiation exposure and of low cost.

Implementation depends less on clinical knowledge than on the organisation of results handling. Ensuring

that a negative urine culture reaches a clinician able to act on it and that the child is actively recalled, is a low-cost intervention with the potential to shorten the diagnostic interval.

Limitations

This is a narrative and not a systematic review. The search was restricted to English-language publications indexed in PubMed and no formal appraisal of study quality was undertaken. Several of the entities discussed are sufficiently rare that the available evidence consists of case reports and small institutional series, which are subject to publication bias towards atypical presentations and may overstate the frequency of haematuria as a presenting feature. The proposed imaging criterion is derived from the reviewed literature and clinical reasoning and has not been prospectively validated; its diagnostic yield and cost-effectiveness remain to be established.

Conclusion

Gross haematuria in children is benign in the great majority of cases and neoplasia accounts for approximately 1% of presentations. That low probability is precisely what makes malignancy easy to overlook. The tumours that present with haematuria vary predictably with age and haematuria becomes the dominant sign when the lesion involves the collecting system or arises in the lower urinary tract. Neither the absence of a palpable mass nor the absence of pain excludes a tumour and an initial urinalysis suggesting infection does not confirm it. Gross haematuria should not be considered resolved until the urine culture supports the presumed diagnosis. When the culture is sterile, or when haematuria recurs, renal and bladder ultrasonography is a proportionate and low-risk next step.

Compliance with Ethical Standards

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