CASE REPORT

# Recurrent Haematuria in a Toddler: A Journey from Suspected UTI to Precocious Puberty.

**Nurul Husna Azmi, Najihah Abdul Razak, Mohammad Che Man.**

*Department Family Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, Indera Mahkota Campus, Kuantan, Malaysia.*

**Corresponding Author**
Nurul Husna Binti Azmi
Department of Family Medicine, Kulliyyah of Medicine
International Islamic University Malaysia, Kuantan, Malaysia.
Email: husnaabdullah@iium.edu.my

Submitted: 28/08/2024. Revised edition: 15/10/2024. Accepted: 21/10/2024. Published online: 01/11/2024.

**Abstract**

Numerous factors can contribute to the presence of blood in the urine. While the causes of gross haematuria often suggest a urological origin, it may also result from gynaecological pathology contaminating the urine. We present a case of a 2-year-2-month-old girl who presented with recurrent haematuria, her third episode in five months. Her previous two episodes were treated as urinary tract infections (UTI). One week before this most recent presentation, she had an upper respiratory tract infection, which resolved with a course of antibiotics. Although she was normotensive, she was referred to a tertiary centre for suspected post-streptococcal glomerulonephritis, based on urinalysis findings of erythrocytes 3+, trace proteinuria and presence of leukocytes. At the hospital, she was initially treated with antibiotics for probable UTI. However, persistent fresh blood staining her diaper prompted a second genital evaluation, which revealed blood seeping from the vagina. Further assessment showed signs of puberty suggesting that menstruation was contaminating the urine sample. This case report highlights the need for clinicians to consider a broad differential diagnosis when evaluating haematuria in paediatric patients and the importance of thoroughly assessing secondary sexual characteristics in young girls with haematuria to facilitate early recognition of precocious puberty.

**Keywords**: *Gross haematuria; post-streptococcal glomerulonephritis; precocious puberty.*

## Introduction

Haematuria, a common occurrence in children, can be seen either macroscopically or microscopically. Gross haematuria may manifest as red, pink, brown or dark urine. While the causes of macroscopic and microscopic haematuria may overlap, gross haematuria often points towards a urological origin, whereas microscopic haematuria is more commonly associated with glomerular issues [1]. While most cases of gross haematuria in the paediatric age group are typically linked to urinary tract sources, in a girl, the blood may originate from the genital tract. Therefore, a thorough evaluation of the genitourinary system is crucial in cases of haematuria to avoid overlooking external injuries to the urethra or vagina, such as those resulting from physical or sexual abuse, or, in rare instances, to prevent overlooking menstruation as the cause.

Precocious puberty (PP) in females occurs when pubertal signs appear before the age of eight, with breast development being the earliest manifestation [2]. Other than advanced thelarche and pubarche, menarche is one of the most common presentations of PP [3,4]. A study in Korea reported that the overall incidence of central precocious puberty in girls was 15.3 per 100,000 [5]. Despite its rarity, it is crucial to promptly identify precocious puberty, as it can signal underlying conditions like brain or gonadal tumours. Furthermore, early puberty can lead to complications, including impaired growth due to premature epiphyseal closure, early onset of cardiovascular diseases, and psychosocial challenges.

## Case report

A 2-year-2-month-old Malay girl was brought in by her mother, who reported that her daughter had blood in her urine. The mother noticed fresh blood staining her daughter's diapers, along with urine every time she changed them over the past two days. She did not observe any blood clots. The mother also reported that her daughter showed no signs of irritability, fever, or foul-smelling urine. She denied any signs of injury or abuse to her daughter's genital area. Apart from a history of fever, cough, and runny nose that resolved with antibiotic treatment a week earlier, her daughter had been otherwise healthy. There were no known episodes of bleeding disorders, and her child's prenatal and developmental histories were unremarkable. The girl had no documented medical conditions, no history of hospitalisation, and was not taking any prescribed, over-the-counter, or traditional medications at the time of the visit.

An initial assessment at the health clinic revealed a non-syndromic child with normal vital signs. There were no signs of periorbital or limb oedema, abuse or neglect, or palpable abdominal masses. Examination of the genitalia showed no signs of trauma. Urinalysis at the clinic revealed erythrocytes 3+ with trace proteinuria and presence of leukocytes. Based on these findings, she was referred to a tertiary centre to evaluate for probable post-streptococcal glomerulonephritis (PSGN). Upon further questioning, it was revealed that the child had experienced two similar episodes before the current one within the past five months, and had been treated for urinary tract infection (UTI) with antibiotics on both occasions.

On the first occasion, the mother took her daughter to see a healthcare practitioner after noticing blood staining her daughter's urine-soaked diapers over the past two days. The blood was minimal and appeared only once or twice daily during diaper changes. The child appeared well during the visit, with no history of upper respiratory tract symptoms or skin lesions. Although her blood pressure was not measured, there was no documented fever. The healthcare practitioner provided a urine specimen bag and instructed the mother to return later that day with a sample collected using it. Urinalysis revealed traces of erythrocytes and leukocytes, with negative results for protein and nitrite. The child was diagnosed with a UTI and was prescribed a course of antibiotics, though no urine culture was taken beforehand A follow-up appointment was

scheduled for one week later. By the time of the follow-up, her symptoms had resolved, and repeated urine tests showed no evidence of UTI and a negative erythrocyte count.

During the second episode, two months after the initial one, the family was on vacation when similar symptoms recurred. The mother sought treatment at a different healthcare provider and informed them of her daughter's previous UTI episode. Her daughter was also well during the visit. There was no documented fever, and she was normotensive. Urinalysis revealed the presence of erythrocytes and leukocytes. She was prescribed another course of antibiotics and advised to visit the nearest hospital or clinic for further evaluation if the symptoms persisted or recurred. Since the symptoms resolved and her daughter remained well, she did not seek further evaluation until her current episode.

Upon assessment at the tertiary centre, the paediatric team admitted her to the paediatric ward for further observation and investigations. The initial examination findings were similar to those at the health clinic, with normal vital signs and unremarkable systemic examinations. Examination of her genitalia showed no signs of external injury; the hymen was intact, with no features suggestive of abuse or foreign bodies. While in the ward, she was initially started on oral Cefuroxime to cover for a potential UTI. Her urine and blood samples were taken to investigate for both UTI and PSGN. Her repeated urinalysis, obtained using a specimen bag before antibiotic commencement, showed pale yellow urine with no evidence of UTI and negative for erythrocytes. Baseline blood investigations, including renal profile, were unremarkable, and anti-streptolysin O titre was negative. Despite daily inspections showing pale yellow urine, she continued to experience intermittent episodes of blood staining her urine-soaked diapers. A repeat urine sample obtained via catheterisation showed a similar finding to the initial one. An abdominal X-ray and ultrasound were also performed to assess for urinary tract abnormalities, stones, or renal masses. Both imaging studies revealed a normal urinary tract system with no masses, hydronephrosis, or stones. After three days in the hospital, with a negative urine culture and ongoing episodes of blood staining her nappies, her genital area was re-examined. During this examination, minimal blood was observed coming from her vagina.

Further assessment revealed the development of sexual characteristics consistent with Tanner stage II, including both breast and pubic hair development. A significant growth spurt was observed in the child between the ages of 1 year and 2 years 3 months, during which her height increased sufficiently to cross two centile lines on the growth chart, as in Figure 1. Given these findings, her antibiotics were discontinued, and blood samples were taken for hormone studies (follicular stimulating hormone, luteinizing hormone, oestradiol, beta-human chorionic gonadotrophin, morning cortisol, thyroid function test, prolactin, insulin-like growth factor, alfa fetoprotein, and dehydroepiandrosterone sulfate (DHEA-S). A left wrist X-ray was also carried out to assess her bone age, revealing findings consistent with that of a 3-year-old child (Figure 2). An ultrasound of the pelvis and a brain MRI were requested to investigate the underlying cause of her precocious puberty. She was referred to the paediatric endocrinologist for further evaluation and management. After one year of follow-up, and extensive investigations, she was diagnosed with central precocious puberty secondary to pituitary microadenoma. She was started on monthly GnRH analogue therapy in December 2020, a course of treatment that persists to the present day.

## Discussion

Recurrent episodes of blood mixed with urine in a diaper were evaluated as potential haematuria. Since UTI is one of the significant causes of haematuria in the paediatric population, with easily accessible urinalysis for interpretation, it is one of the most common causes of referral to the emergency department [6].

In 2000, the Paediatric Nephrology Journal published a practical primary care approach for haematuria cases in children. Based on this guideline, several steps must be taken during an investigation of possible haematuria cases. The first and most crucial step is determining whether the haematuria is gross or microscopic, as each type suggests different underlying pathologies. While the aetiology may overlap, gross haematuria often points towards a urological origin such as UTI, urethral trauma or stone; meanwhile, microscopic haematuria is commonly associated with glomerular diseases such as PSGN or IgA Nephropathy. The second step involves confirming that blood is the cause of the discoloured urine, as substances like certain foods, myoglobin, and bilirubin can also alter urine colour. Once the presence of blood in the urine is confirmed, the next step is to identify its origin—whether it is from the kidneys, upper or lower urinary tract, or a gynaecological source in girls. Determining the source of the blood is essential for guiding appropriate referrals to nephrology, urology, gynaecology, or general paediatrics for further evaluation. The final step is to determine the underlying cause of the haematuria, typically achieved after referral to a tertiary centre, as they are equipped with the necessary tools and expertise for further evaluation [7].

Urine inspection is a mandatory first step in the evaluation of haematuria. Bright red urine typically indicates lower urinary tract pathology, while tea-coloured urine suggests upper urinary tract involvement due to the oxidation of blood. A diagnosis dilemma occurred when the mother complained that bright red blood had stained her daughter's urine-soaked diaper and urinalysis showed significant erythrocytes that warrant classification into gross haematuria. However, urine inspection revealed pale yellow urine, while the other parameters showed trace leukocytes and protein. Despite being normotensive, with a prior history of URTI, it initially favours PSGN as a likely diagnosis.

However, subsequent urinalysis during hospital admission, one from a urine bag specimen and another via catheterisation, consistently showed no signs of a UTI or presence of erythrocytes. Urine catheterisation, with 95% sensitivity and 99% specificity, is a highly reliable method for diagnosing UTIs, making it a dependable approach to rule out infection in this case [8]. Studies have also shown that contamination rates with bag urine specimens can reach up to 70% [9]. Therefore, the negative urine culture from the urine bag specimen was another reliable way to exclude UTIs.

Despite the awareness that gynaecological causes can contaminate urine samples, precocious puberty is a rare encounter. In cases like this, with an inexperienced eye coupled with an initial focus on identifying genital trauma, signs of sexual abuse and foreign bodies, it is easy to miss the secondary sexual characteristics that are right before the eyes. Failure to consider menarche when evaluating a child with gross haematuria may lead healthcare providers to undervalue identifying other critical indicators of early pubertal development during assessments, such as thelarche and growth spurt. Eventually, this can result in a missed or delayed diagnosis and management of precocious puberty.

Therefore, a thorough evaluation of the genitourinary system is crucial in cases of girls presenting with haematuria to avoid overlooking external injuries to the urethra or vagina, such as those resulting from physical or sexual abuse, or, in rare instances, to avoid missing menstruation. Early detection aids in reducing potential complications linked to PP, including the premature closure of growth plates that can result in a diminished final adult height and psychological and social difficulties arising from early physical maturation.

## Conclusion

This case highlights the importance of a systematic approach in evaluating children with gross haematuria. It underscores the necessity of assessing the genitourinary system to avoid

overlooking significant causes of haematuria, such as precocious puberty.

**Acknowledgement**
We would like to thank Dr Selamah (Paediatrician) and Dr Daud (FMS KK Beserah) for their advice and input in this case report.

**Authors' contributions**
All authors contributed equally to the concept, data collection and writing of the manuscript.

**Conflict of interest**
The authors declare that they have no conflict of interest.

**Funding**
This case report is supported by the International Islamic University Malaysia research management committee grant scheme (RMCG20-024-0024).

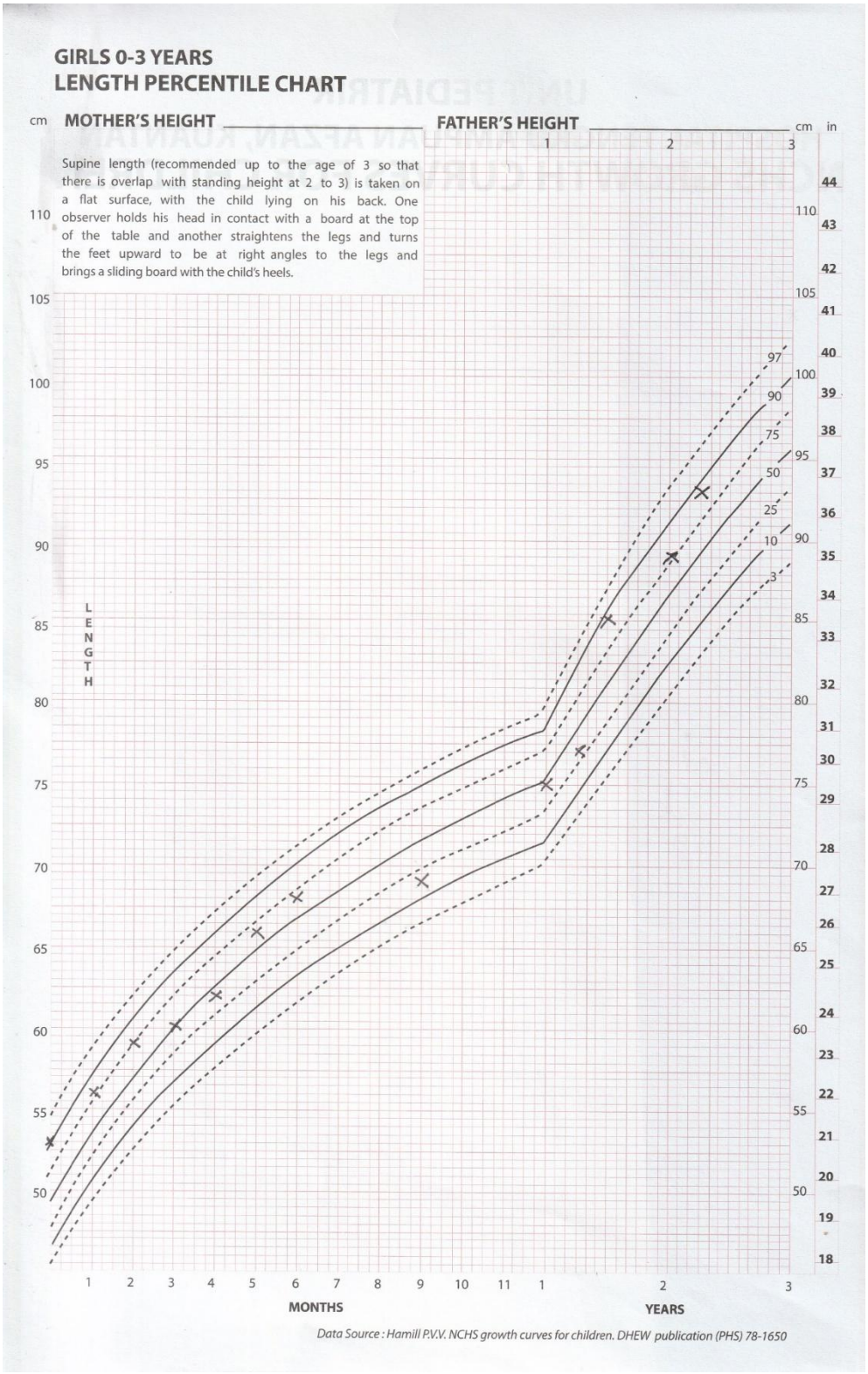


Figure 1. A significant growth spurt was observed in the child between the ages of 1-year-old and 2-year-3month-old, during which her height increased enough to cross two centile lines on the growth chart [10].

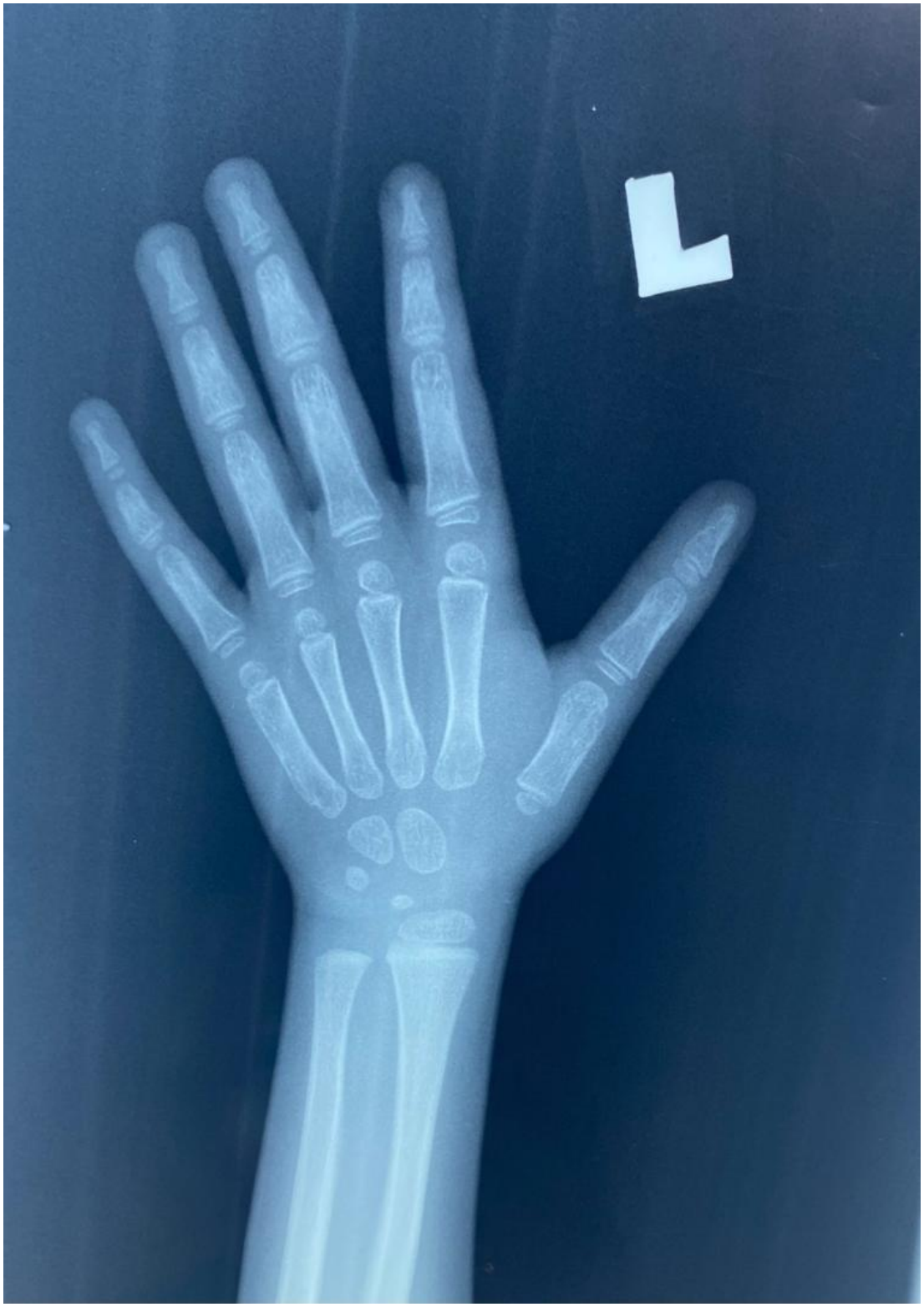

Figure 2. X-ray of the left hand and wrist showing bone age that is consistent with the skeletal age of a 3-year-old based on the Radiographic Atlas of Skeletal Development of the Hand and Wrist (Greulich and Pyle) [11]

## References


[1]. Meyers KE. Evaluation of hematuria in children. Urologic Clinics. 2004 Aug 1;31(3):559-73.

[2]. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Archives of disease in childhood. 1969 Jun;44(235):291.

[3]. Adze J, Bature S, Durosinlorun AM, Mohammed C, Taingson M, Baduku S. Precocious Puberty: Case Report of a 3-year Old Girl. Journal of Research in Basic and Clinical Sciences. 2021 Jun 30;2(1):63-6. .

[4]. Akhtar H, Guha K, Nahar Z. Precocious puberty: a case report. TAJ: Journal of Teachers Association. 2008;21(2):177-9.

[5]. Kang S, Park MJ, Kim JM, Yuk JS, Kim SH. Ongoing increasing trends in central precocious puberty incidence among Korean boys and girls from 2008 to 2020. PLoS One. 2023 Mar 22;18(3):e0283510.

[6]. Shaw KN, Gorelick M, McGowan KL, Yakscoe NM, Schwartz JS. Prevalence of urinary tract infection in febrile young children in the emergency department. Pediatrics. 1998 Aug 1;102(2):e16-.

[7]. Diven SC, Travis LB. A practical primary care approach to hematuria in children. Pediatric nephrology. 2000 Jan;14:65-72.

[8]. McGillivray D, Mok E, Mulrooney E, Kramer MS. A head-to-head comparison:“clean-void” bag versus catheter urinalysis in the diagnosis of urinary tract infection in young children. The Journal of pediatrics. 2005 Oct 1;147(4):451-6.

[9]. Al-Orifi F, McGillivray D, Tange S, Kramer MS. Urine culture from bag specimens in young children: are the risks too high?. The Journal of pediatrics. 2000 Aug 1;137(2):221-6.

[10]. Hamill PV, Drizd TA, Johnson CL, Reed RB, Roche AF. Growth curves for children. Birth-18 years, United States. Vital and Health Statistics, Ser. 1977;11

[11]. Greulich WW. Radiographic atlas of skeletal development of the hand and wrist.