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| RESEARCH ARTICLE

The Unlikely Duo: Gross Hematuria and Clubbing Revealing Hidden Malignancy

Abdelrahman Idris Mohamed Idris[1], Basimathul Ain Mohamed Saleem[2], Areej Ahmed Abdalla Hassan[3], Abeer Ebrahim Mohamed[4], Fatema Abbas Jahromi[5], Zainab Yusuf Yaqoob[5], Rehma Yousuf[6], Fatema Hani Abdulla Hasan[7], Sayed Fadhel Hashem Neama[7], Saffaa Ahmed Hersi[8], Zainab Habib ALQallaf[7], and Shatha Adel Sarhan[9]

1- First Author, Kassala Teaching Hospital
2- Second Author, KAP Viswanatham Government Medical College
3- Third Author, Hamad Medical Corporation
4- Salmaniya Medical Complex
5- Sultan Qaboos University Hospital
6- Jilin University
7- Mansoura University, Faculty of Medicine
8- Ain Shams University, Faculty of Medicine
9- Royal College of Surgeons in Irland, Bahrain

Corresponding Author: Abdelrahman Idris Mohamed Idris, **Email:** abdoidris23@gmail.com

| ABSTRACT

A previously healthy 47-year-old Saudi male presented with a two-month history of painless gross hematuria and notable digital clubbing. The hematuria was intermittent, dark red, and unassociated with dysuria, flank pain, or systemic symptoms. Physical examination confirmed clubbing of the fingers, while vital signs and general assessment were unremarkable. Laboratory evaluation revealed mild polycythemia and borderline hypercalcemia, with otherwise normal renal and liver function. Urinalysis excluded infection or glomerular disease, and urinary cytology was negative for urothelial malignancy. Given the combination of persistent hematuria and paraneoplastic signs, imaging studies were prioritized. Renal ultrasonography identified a heterogeneous right upper pole mass, subsequently characterized by contrast-enhanced CT as a 6-cm right renal mass with heterogeneous enhancement and areas of necrosis, consistent with renal cell carcinoma (RCC), without evidence of metastasis. Multidisciplinary discussion favored radical nephrectomy, which was performed successfully with en bloc excision of the kidney, perinephric fat, and regional lymph nodes. Histopathology confirmed clear cell RCC, Fuhrman grade II, with negative margins and no lymphovascular invasion (pT1bN0M0). Postoperatively, hematuria resolved, and early regression of clubbing was observed. This case highlights the diagnostic significance of gross hematuria combined with paraneoplastic manifestations such as clubbing, emphasizing the importance of early imaging and prompt surgical intervention for localized RCC to optimize outcomes.

| KEYWORDS

Malignancy, Renal Cell Carcinoma, Clubbing, Gross Hematuria, Painless Hematuria, Paraneoplastic Syndrome.

| ARTICLE INFORMATION

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Introduction

Renal cell carcinoma (RCC) is the most common primary malignancy of the kidney in adults, accounting for approximately 2–3% of all adult cancers worldwide [1]. Its clinical presentation is highly variable, ranging from incidental findings on imaging to overt symptoms such as hematuria, flank pain, or palpable mass. Historically, the classical triad of hematuria, flank pain, and abdominal mass was considered pathognomonic for RCC; however, contemporary series demonstrate that fewer than 10–15% of patients present with all three features [2]. Modern detection has increasingly relied on incidental imaging studies, yet symptomatic presentations remain clinically significant because they often reflect more aggressive disease and a higher tumor burden [3]. Among symptomatic cases, gross hematuria is the most frequent initial complaint, occurring in approximately 40–50% of patients, and can result from tumor invasion into the renal pelvis or calyces [4]. Hematuria in RCC is often painless, persistent, and intermittent, distinguishing it from the acute, painful hematuria seen in nephrolithiasis or urinary tract infection [1,5]. Early recognition of hematuria, even in the absence of other classical features, is critical for timely diagnosis and improved outcomes [6]. Clubbing of the fingers and toes is a less common but noteworthy manifestation of RCC and is considered a paraneoplastic phenomenon. Clubbing may develop due to the secretion of circulating factors by the tumor, including vascular endothelial growth factor, platelet-derived growth factor, and other mediators that promote vascular proliferation and connective tissue changes at the distal phalanges [7,8]. While often associated with pulmonary disease, digital clubbing can also occur in the context of abdominal malignancies such as RCC, hepatocellular carcinoma, and gastrointestinal cancers [9]. In patients presenting with clubbing alongside hematuria, the combination should raise suspicion for underlying neoplasia, prompting expedited evaluation rather than attributing the findings to benign causes [10]. Paraneoplastic syndromes are observed in approximately 20–40% of RCC patients and may include erythrocytosis, hypercalcemia, hypertension, fever, and cachexia, further complicating the clinical picture [11,12]. Recognition of these syndromes can provide early clues to the presence of malignancy, particularly when the primary tumor remains clinically occult. Epidemiologically, RCC predominantly affects males in the sixth to seventh decades of life, but younger patients are not exempt, and presentation in the fourth or fifth decade is well-documented [1]. Risk factors include smoking, obesity, hypertension, and certain hereditary syndromes, although many cases occur sporadically without identifiable predisposing factors [1,3]. In the Saudi population, recent studies have highlighted the increasing incidence of RCC, particularly in urban centers where imaging studies are more frequently utilized, and symptomatic presentations often drive clinical encounters [4,5]. Gross hematuria remains the most actionable clinical sign in this population, as it often prompts urologic referral and imaging, potentially leading to earlier diagnosis compared with incidental detection. Imaging is the cornerstone of RCC diagnosis and staging. Ultrasound is typically used as an initial screening modality for patients presenting with hematuria, allowing rapid detection of renal masses. Computed tomography (CT) with contrast remains the gold standard for characterizing the lesion, assessing local invasion, and detecting regional or distant metastases [1,2]. Magnetic resonance imaging can provide additional information in patients with contraindications to contrast CT or when evaluating venous involvement. Imaging findings often correlate with histopathology, with clear cell carcinoma being the most common subtype, followed by papillary and chromophobe variants [2,3]. The size, location, and vascular involvement of the tumor are critical in determining the surgical approach, whether radical nephrectomy, partial nephrectomy, or minimally invasive options are employed. The clinical significance of early recognition of both hematuria and clubbing cannot be overstated. While hematuria is directly linked to the local presence of tumor, clubbing serves as an indicator of systemic effects and possible paraneoplastic activity, suggesting that the disease may already be exerting effects beyond the kidney [7,8]. For clinicians, the combination of these findings should trigger a comprehensive diagnostic approach, including imaging, laboratory evaluation, and early involvement of urology and oncology services. Timely identification of RCC in patients with gross hematuria and clubbing significantly influences prognosis, as localized disease is associated with 5-year survival rates exceeding 90% following surgical resection, whereas advanced or metastatic disease carries a substantially worse prognosis [1,4,6]. Early surgical intervention not only addresses the primary tumor but can also ameliorate paraneoplastic manifestations, including clubbing and systemic symptoms such as fever or weight loss. This case report describes a previously healthy adult male from Saudi Arabia who presented with painless gross hematuria and noticeable digital clubbing, ultimately revealing a previously undiagnosed RCC. The case underscores the critical importance of recognizing subtle paraneoplastic signs, correlating them with urinary findings, and initiating prompt imaging and specialist referral. Through a detailed account of presentation, investigation, management, and discussion, this report aims to provide clinicians with practical lessons for early recognition of RCC, particularly when atypical or systemic manifestations such as clubbing are present. The discussion emphasizes epidemiological data, clinical patterns, diagnostic reasoning, and evidence-based management, drawing from recent reviews, systematic analyses, and guideline-based recommendations [1–13]. By highlighting both classical and subtle cues, this report reinforces the need for vigilance in patients with gross hematuria and systemic signs, demonstrating that early identification and timely intervention can substantially alter clinical outcomes.

Case Presentation

Patient's history and Physical Examination

A previously healthy 47-year-old Saudi male presented to the outpatient clinic with a two-month history of painless hematuria. The hematuria was gross, intermittent, and dark red in color, without associated clot passage or dysuria. The patient first noticed the discoloration while urinating in the morning, which persisted sporadically throughout the day. He denied flank pain, urinary frequency, urgency, or nocturia. There was no history of trauma, recent strenuous exercise, or previous urinary tract infections. He also denied systemic symptoms such as fever, chills, night sweats, or significant weight loss at initial presentation. The patient reported increased fatigue over the preceding several weeks but attributed it to work-related stress. His past medical history was unremarkable. He had never been hospitalized and had no chronic illnesses. He took no medications regularly and denied use of over-the-counter drugs, herbal remedies, or supplements. He was a nonsmoker, consumed alcohol rarely, and had no history of illicit drug use. Family history was notable for a father with hypertension and a mother with type 2 diabetes, but no history of kidney disease, malignancy, or congenital anomalies was reported. Occupationally, he worked in an administrative office, with no known chemical or radiation exposure. He had not traveled recently and had no significant environmental exposures. On general examination, the patient appeared well, with normal body habitus. Vital signs were within normal limits. He was alert, oriented, and in no apparent distress. Notably, inspection of the fingers revealed clubbing, characterized by increased distal finger pad convexity and loss of the normal nail bed angle, with nail curvature evident (Image 1). The remainder of the integumentary system showed no rashes, cyanosis, or edema. Cardiovascular examination revealed regular heart rate and rhythm, normal heart sounds, and no murmurs or peripheral edema. Pulmonary examination was unremarkable, with clear lung fields on auscultation and normal respiratory effort. Abdominal examination demonstrated no palpable masses, tenderness, organomegaly, or bruits. Examination of the flanks revealed no tenderness or costovertebral angle discomfort. Genitourinary inspection was unremarkable aside from evidence of blood in the urine sample provided (Image 1). Neurological and musculoskeletal examinations were normal, with intact strength, reflexes, and coordination. The patient's presentation was notable for the combination of painless gross hematuria and digital clubbing. He had no prior history of urinary tract pathology, nephrolithiasis, or systemic disease. There was no evidence of infection, trauma, or coagulopathy. The chronicity of symptoms, absence of pain, and physical findings suggested a potentially underlying neoplastic or paraneoplastic process. The outpatient setting provided the opportunity for early recognition and referral to imaging studies to identify a possible renal or urinary tract mass.

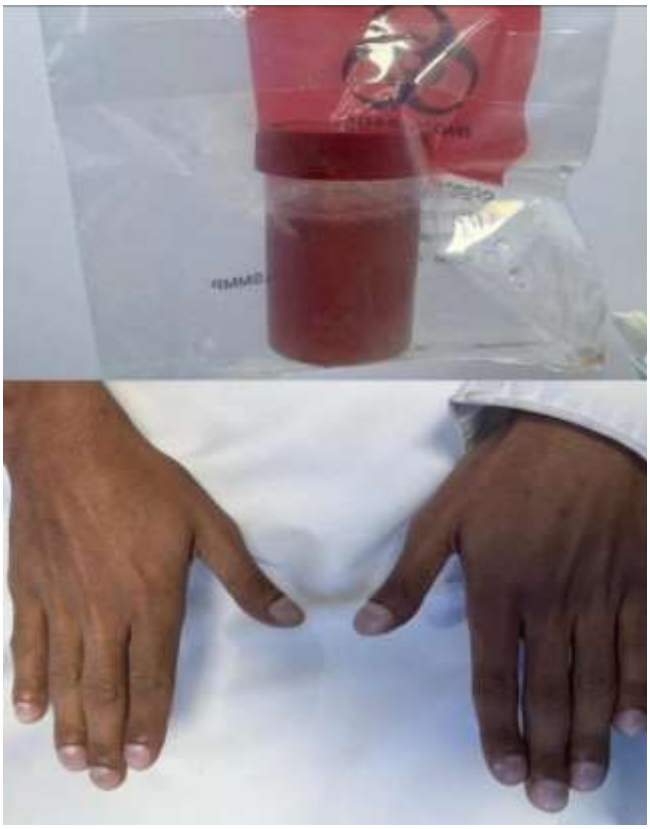

Image 1: showing unexplained finger clubbing and urine sample consistent with gross hematuria.

Investigations and diagnostic reasoning:

The initial evaluation focused on determining the source of hematuria and assessing for potential systemic implications suggested by clubbing. Urinalysis confirmed the presence of gross hematuria without significant proteinuria or pyuria. A urine sample demonstrated uniformly dark red coloration with numerous red blood cells on microscopy (Image 1). No casts, crystals, or bacteria were observed, suggesting a noninfectious origin. Given the combination of painless hematuria and clubbing, the differential diagnosis included renal malignancy, urothelial carcinoma, and, less likely, vascular or glomerular disorders. Imaging was prioritized due to the persistent gross hematuria and paraneoplastic clue of clubbing. A renal ultrasound revealed a heterogeneous mass within the upper pole of the right kidney, measuring approximately 6 cm, with areas of increased echogenicity and internal vascularity. The mass was well-circumscribed but demonstrated some irregular margins, prompting further characterization. No hydronephrosis or calculi were noted. Based on these findings, contrast-enhanced CT of the abdomen and pelvis was performed, demonstrating a right renal mass with heterogeneous enhancement, areas of necrosis, and early contrast washout, consistent with renal cell carcinoma. There was no evidence of local lymphadenopathy or venous invasion. Chest imaging was obtained to evaluate for metastases and was negative. The clinical reasoning centered on explaining the patient's painless hematuria in conjunction with clubbing. RCC is known to invade the renal collecting system, causing intermittent bleeding, which corresponds with the patient's intermittent gross hematuria. Clubbing served as a systemic marker, raising suspicion for paraneoplastic activity, consistent with known mechanisms in RCC involving vascular endothelial growth factor and other circulating mediators. The absence of infection, nephrolithiasis, or trauma supported a neoplastic cause. Additionally, no family history or hereditary risk factors were identified, suggesting a sporadic form of RCC. Additional laboratory evaluation aimed to assess for paraneoplastic effects. Complete blood count was within normal limits aside from mild polycythemia, consistent with erythropoietin production by the tumor. Serum calcium was mildly elevated. Liver function tests and kidney function were normal. Coagulation profile and urinalysis excluded underlying bleeding diathesis or glomerular disease. Urinary cytology was negative for malignant urothelial cells, supporting a renal origin rather than bladder or ureteral malignancy. The combination of imaging findings, laboratory results, and clinical features pointed to a localized right renal mass as the source of hematuria and clubbing. The case highlighted the importance of recognizing systemic clues, such as clubbing, as indicators of potential underlying malignancy, prompting expedited diagnostic imaging. The images included in Image 1 visually illustrate both the gross hematuria and the characteristic finger clubbing, reinforcing the clinical correlation between systemic paraneoplastic manifestations and local tumor effects. Subsequent management planning focused on confirming histology via percutaneous biopsy or proceeding directly to surgical intervention based on imaging features, tumor size, and absence of metastasis.

Management course

Management aimed to address the underlying malignancy while mitigating paraneoplastic effects and preserving renal function. After multidisciplinary discussion including urology and oncology, the patient was counseled regarding options of partial versus radical nephrectomy. Given the tumor's size, location in the upper pole, and absence of metastatic disease, a right radical nephrectomy was planned to achieve complete resection while minimizing local recurrence. Preoperative preparation included assessment of renal function, cardiovascular evaluation, and anesthetic risk stratification. Blood pressure, hemoglobin, and coagulation were optimized. The patient received counseling regarding perioperative expectations, postoperative care, and potential complications such as bleeding, infection, and altered renal function. Imaging studies were reviewed intraoperatively to guide surgical approach, with particular attention to vascular anatomy. Surgery was performed under general anesthesia, with careful mobilization of the kidney and ligation of the renal artery and vein. The tumor was excised en bloc with perinephric fat and regional lymph nodes for staging. Intraoperative findings confirmed a well-circumscribed mass without evidence of gross invasion into surrounding structures. Postoperatively, the patient was monitored in a high-dependency unit, with serial vital signs, fluid balance, and renal function evaluation. Pain control, early mobilization, and respiratory physiotherapy were implemented to reduce postoperative complications. Histopathology confirmed clear cell RCC, Fuhrman grade II, with negative surgical margins and no lymphovascular invasion. Pathological staging was pT1bN0M0. Postoperative recovery was uneventful. Gross hematuria resolved within days, and finger clubbing showed early signs of regression over subsequent weeks, consistent with the removal of the paraneoplastic stimulus. The patient was counseled on long-term surveillance, including periodic imaging, renal function assessment, and monitoring for recurrence. Lifestyle modifications, including maintenance of healthy weight, blood pressure control, and smoking avoidance, were discussed to reduce long-term risk.

Discussion

Renal cell carcinoma (RCC) remains a clinically challenging malignancy due to its variable presentation, diverse histologic subtypes, and potential for paraneoplastic manifestations. Globally, RCC accounts for approximately 2–3% of adult malignancies, with a higher prevalence in males and peak incidence in the sixth to seventh decades of life [1]. However, sporadic cases in younger adults are increasingly reported, highlighting the need for clinician vigilance across age groups. Symptomatic

presentation often correlates with larger tumor size and more aggressive histology, whereas incidental detection generally identifies smaller, localized tumors with a more favorable prognosis [2,5]. This case exemplifies a symptomatic scenario in a previously healthy Saudi male presenting with painless gross hematuria and digital clubbing, both of which serve as important diagnostic cues. Gross hematuria is the most frequent presenting symptom in symptomatic RCC, reported in up to 50% of patients [4,6]. Its intermittent and painless nature, as seen in this patient, reflects tumor bleeding into the renal pelvis or calyces rather than acute injury or infection. Hematuria associated with infection or nephrolithiasis is often accompanied by dysuria, pain, or fever, whereas neoplastic bleeding typically lacks these features [1,4]. In this context, persistent hematuria, even in the absence of pain or systemic symptoms, should prompt imaging of the renal tract. The detection of hematuria in outpatient settings is a critical opportunity for early identification of RCC, as delayed recognition is associated with more advanced stage at diagnosis and poorer outcomes [6,13].

Digital clubbing in this patient represents a noteworthy paraneoplastic phenomenon. Although clubbing is most commonly associated with pulmonary disease, its occurrence in RCC is well documented, albeit rare [7–10]. Pathophysiologically, clubbing arises due to tumor-derived circulating mediators such as vascular endothelial growth factor (VEGF), platelet-derived growth factor (PDGF), and other cytokines that promote angiogenesis and connective tissue proliferation at the distal phalanges [8]. The resolution of clubbing following nephrectomy in multiple reports, including this case, supports a direct paraneoplastic mechanism. Recognizing clubbing in conjunction with urinary symptoms can accelerate diagnostic evaluation, highlighting the importance of careful physical examination and systemic assessment, even in patients without classic pulmonary or gastrointestinal disease. Paraneoplastic syndromes are identified in approximately 20–40% of RCC patients, encompassing endocrine, hematologic, and metabolic effects [11,12]. These include erythrocytosis secondary to erythropoietin production, hypercalcemia from parathyroid hormone–related protein, hypertension, fever, and weight loss. In this patient, mild polycythemia was noted, aligning with the known frequency of erythropoietin-driven hematologic effects in RCC. Clinicians should maintain a high index of suspicion for underlying malignancy when unexplained systemic signs accompany local findings such as hematuria, as early recognition may influence prognosis and therapeutic planning [1,11,12]. Epidemiologically, male predominance is well established, with male-to-female ratios ranging from 1.5:1 to 2:1, and risk factors including smoking, obesity, and hypertension [1,3]. The absence of identifiable risk factors in this patient underscores the sporadic nature of many RCC cases. Regional data, including recent studies from Saudi Arabia and southern India, suggest increasing detection rates, often symptomatic, in urban populations [4,5]. Symptomatic tumors generally demonstrate more aggressive histology, higher Fuhrman grade, and larger tumor size compared with incidentally detected lesions [5,6,10]. These observations highlight the critical role of clinical recognition and timely investigation to optimize outcomes.

Diagnostic reasoning in this case illustrates the integration of local and systemic cues. Gross hematuria indicated a renal or urinary tract source, while clubbing suggested a systemic or paraneoplastic process. Imaging was guided by this combination of features. Ultrasound detected the mass, whereas contrast-enhanced CT confirmed tumor characteristics, including size, location, enhancement patterns, and absence of metastases. These findings aligned with typical radiologic features of clear cell carcinoma, the most common RCC subtype [2,3]. The CT findings of heterogeneous enhancement with areas of necrosis correspond to literature demonstrating that symptomatic tumors often exhibit more aggressive imaging characteristics, which have prognostic implications [10]. Surgical management remains the cornerstone of treatment for localized RCC. Radical nephrectomy was appropriate given the tumor's size, location, and absence of metastasis. The procedure achieved complete excision, resolution of hematuria, and regression of paraneoplastic clubbing, highlighting the dual benefit of oncologic control and alleviation of systemic manifestations. Histopathology confirmed clear cell carcinoma, Fuhrman grade II, with negative margins and no lymphovascular invasion, translating into a favorable prognosis. Literature supports excellent 5-year survival for stage I tumors following complete resection, reinforcing the value of early detection and prompt surgical intervention [1,4,6]. The lessons from this case extend beyond individual patient care. Clinicians should maintain vigilance for subtle systemic signs such as clubbing when evaluating urinary complaints, as they may provide early indication of malignancy. Hematuria should never be dismissed as benign, especially when gross, persistent, or associated with paraneoplastic phenomena. Multimodal imaging, including ultrasound and contrast-enhanced CT, is essential for accurate staging and surgical planning. Furthermore, multidisciplinary collaboration, encompassing urology, oncology, radiology, and pathology, ensures comprehensive care and optimal long-term outcomes. This case also illustrates the importance of contextual epidemiology. Symptomatic RCC presentation remains common in regions with limited incidental imaging, such as parts of the Middle East. Recognition of regional trends can inform public health strategies, screening, and early referral protocols. Finally, documenting rare paraneoplastic features like clubbing adds to the clinical literature, emphasizing that systemic manifestations can precede or accompany local tumor effects, aiding earlier diagnosis and intervention [7–12]. In conclusion, the combination of painless gross hematuria and digital clubbing serves as a strong clinical signal for underlying RCC. Early recognition, thorough evaluation, and timely surgical intervention are key to favorable outcomes. This case reinforces several teaching points: the significance of paraneoplastic signs, the diagnostic value of integrating local and systemic features, and the critical role of imaging and pathology in guiding management. By understanding these principles, clinicians can enhance early detection, improve prognosis, and contribute to the growing body of knowledge regarding RCC presentations and paraneoplastic manifestations.

Conclusion

Painless gross hematuria accompanied by digital clubbing should alert clinicians to the possibility of underlying renal malignancy. Early recognition, prompt imaging, and timely surgical intervention can not only achieve oncologic control but also reverse paraneoplastic manifestations. Systemic signs such as clubbing provide valuable diagnostic clues, and their presence alongside urinary abnormalities should never be overlooked. Multidisciplinary care and structured follow-up are essential to optimize long-term outcomes. This case underscores the importance of integrating local and systemic clinical cues to facilitate early detection and effective management of RCC.

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