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Review Article

Renal papillary necrosis in patients with sickle cell disease: How to recognize this 'forgotten' diagnosis

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Summary

Introduction
Renal papillary necrosis is not commonly seen in daily practice, but can have severe consequences when it is not diagnosed in time. It is known to be associated with sickle cell hemoglobinopathies; however a wide range of etiologies are possible, and it is therefore not the first diagnosis clinicians consider in patients with sickle cell disease who present with hematuria.

Methods
A literature search was performed to summarize the current knowledge about renal papillary necrosis associated with sickle cell disease. These findings are illustrated with a case of a 9-year old girl with sickle cell disease who was referred with painless gross hematuria.

Results
Typical radiologic signs for renal papillary necrosis are necrotic cavities that fill with contrast, small collections of contrast peripheral to the calyces in the papillary region (ball-on-tee sign), calcification of the papillary defect, filling defects, hydronephrosis, blunted papillary tip, clefts in the renal medulla filled with contrast, hyperattenuated medullary calcifications, non-enhanced lesions surrounded by rings of excreted contrast, and clubbed calyces.

Discussion
This study focuses on the pathophysiology of renal papillary necrosis associated with sickle cell disease, the possible symptoms, as well as the diagnostic steps, with a special interest in particular presentation on old (retrograde pyelography) and new (computed tomography) gold standard in radiologic imaging, and the management for this pathology.

Conclusion
This study aims to remind clinicians of this "forgotten" diagnosis and what signs to look for in pediatric patients with sickle cell disease who present with hematuria. In pediatric cases radiation protection is important, therefore knowing what radiologic signs can be found on retrograde pyelography can lead to early identification of this pathology without having to proceed to computed tomography.

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Introduction

Renal papillary necrosis (RPN) has a wide range of possible etiologies and is therefore not the first diagnosis clinicians consider when a patient with sickle cell disease (SCD) presents with hematuria. However, it is important to consider the possibility of an underlying RPN in these patients. A wide range of renal abnormalities, such as proteinuria in adults which may progress to a nephrotic syndrome and supranormal renal hemodynamics with elevations in both effective renal plasma flow and glomerular filtration rate in young patients, are described in patients with sickle cell hemoglobinopathies [1—5]. One of these abnormalities is RPN. It is believed that this is the result of intravascular stasis and thrombosis as a result of the sickling of the red blood cells. The hyperosmolarity and low oxygen are unique traits of the renal medulla. These conditions help the sickling process, which will lead to considerable stasis [6]. The aggregation of sickle shaped red blood cells in patients with SCD can cause the micro-circulation to become obstructed, which then again results in ischemic necrosis. These vaso-occlusive crises are very painful. Most often bones with high bone marrow-activity, such as the spine, are affected. However, the renal medulla and papillae have a specific arrangement of their hypertonic environment and blood supply, which makes them particularly susceptible to this ischemic necrosis [7,8]. This study aims to give an overview of this often overlooked diagnosis, so that clinicians are reminded what signs to look for in specific cases and illustrates this with a case of a 9-year old girl with SCD and hematuria.

Methods

Literature search

A literature search was performed to summarize the current knowledge on RPN associated with SCD. This search focused on the pathophysiology of RPN associated with SCD, the possible symptoms, and other etiologies of RPN as well as the diagnostic steps, with a special interest for the radiologic signs on retrograde pyelography (RPG) and computed tomography (CT), and finally the management.

Case report

A 9-year-old girl with SCD was referred because of diffuse abdominal pain and decreased intake, with regular sickle cell crises and a splenectomy in her personal medical history. Despite analgesics the pain increased progressively, and the patient indicated elevated scores on the visual analogue pain scale. There were no urinary symptoms at presentation. Physical examination showed no irregularities. Further technical investigation showed some pyuria and some calcium oxalate crystals on urine dipstick and microscopic examination; however, urine culture showed no bacterial growth. Laboratory tests came back normal. An ultrasound of the kidneys showed no signs of hydronephrosis or nephrolithiasis. Therefore, the differential diagnosis was that of a sickle cell crisis, a urinary tract stone or gastritis caused by use of an NSAID, ibuprofen in this case. Adequate pain therapy was started in combination with a proton pump inhibitor and the girl was discharged.

A couple of days later the girl was readmitted with excessive painless macroscopic hematuria. Again, no infection of the urinary tract could be demonstrated on urine culture. A urine sample was checked for protein and the result was negative. New ultrasound was once again normal. Therefore it was decided to perform a cystoscopy under full anesthesia. At this point the differential diagnosis contained the following: AV-malformation, tumor, schistosomiasis (because the patient used to live in Angola), or a hemorrhagic cystitis. Bladder lesions could not be found during cystoscopy; however, a continuous flow of blood was visible from the right orifice. Therefore a RPG was performed, which showed the absence of renal papillae (Fig. 1). From this image RPN was suspected, which was confirmed on a subsequent CT scan (Figs. 2—4). Intravenous fluids, analgesics, alkalization, and bed rest were initiated. Under this therapy the hematuria cleared up after a few days and the girl was discharged.

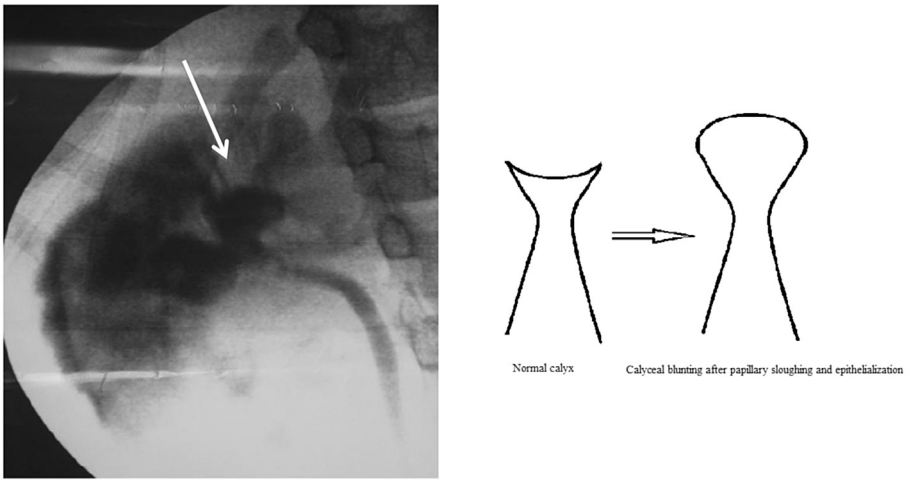

Figure 1 Clubbed calyces and diffuse parenchymal enhancement of the kidney.