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Case Report

An unusual ultrasound appearance of renal hemosiderosis in acute sickle cell nephropathy

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ABSTRACT

Sickle cell disease is the most common inherited blood disorder in the United States. The primary driver of pathology is microvascular occlusion which affects multiple organ systems including the kidney. The renal pathology usually manifests as hematuria, proteinuria, or microalbuminuria, and up to 10% of individuals with homozygous sickle cell disease (HbSS) develop renal failure over their lifetime. At ultrasound, the most common finding is increased size with mild variation in echogenicity of the renal parenchyma. We report the ultrasound appearance of a case of acute sickle cell nephropathy with markedly abnormal, enlarged, and echogenic kidneys due to intravascular hemolysis and hemosiderosis, confirmed by biopsy. Knowledge of this potential presentation of sickle cell nephropathy may help aid in earlier diagnosis of renal complications and avoidance of unnecessary renal biopsies.

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Introduction

Sickle cell disease is the most common inherited blood disorder and is characterized by the sickling of red blood cells

in low oxygen environments. This hemoglobinopathy affects numerous organ systems including the renal system. Increased sickling within the vasa recta of the kidney can lead to ischemic damage and eventually microalbuminuria, hematuria, and chronic renal disease [1,2]. Patients with sickle cell

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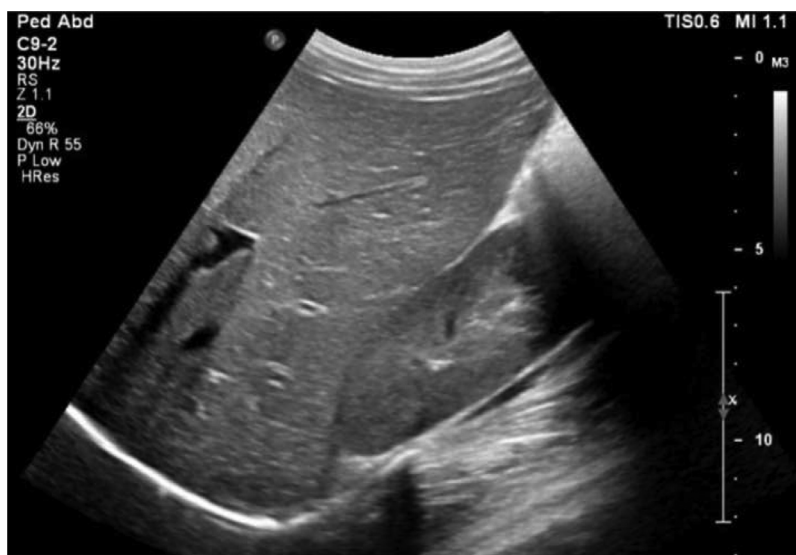


Fig. 2 – Comparison imaging from 5 months prior – sagittal sonographic image of the liver and right kidney 5 months prior demonstrating a normal appearing kidney with similar echogenicity to the liver. There were mildly dilated intrahepatic ducts and a mildly dilated common hepatic duct.

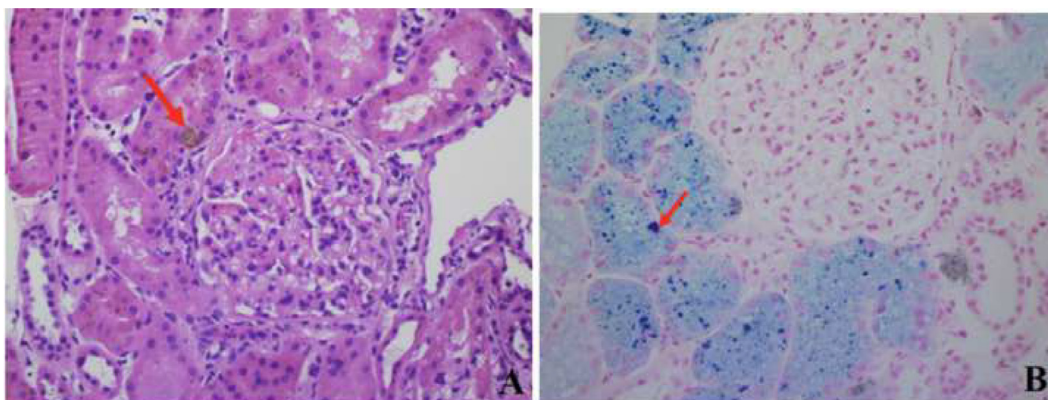


Fig. 3 – (a) and (b) Pathologic evaluation of renal biopsy at the time of patient presentation. (a) H&E stained section shows brown granules within the cytoplasm of tubular epithelial cells, compatible with hemosiderin pigment deposition. 20X Objective. (b) Gomori stain for iron shows abundant hemosiderin appearing as blue material within the tubular epithelial cells. 20x Objective.

Ultrasound imaging (Fig. 1a-d) demonstrated bilaterally large-for-age kidneys measuring 13.0 cm and 12.1 cm for the right and left kidneys, respectively (average size of kidney for age is approximately 11.0 cm). There was markedly echogenic renal parenchyma, more so in the medulla than the cortex, although the central cortex was echogenic as well. There was no hydronephrosis. Color Doppler was also performed, which demonstrated normal blood flow. A right upper quadrant ultrasound performed in evaluation of the biliary tract 5 months prior demonstrated loss of corticomedullary differentiation but otherwise normal appearing right kidney (Fig. 2).

Because of the persistent high nephrotic range proteinuria and the hematuria, in addition to the markedly abnormal ultrasound, the decision was made to proceed to a renal biopsy for definitive diagnosis.

Two 16-gauge core biopsies measuring up to 1.7 cm in length were obtained from the lower pole of the native left kidney at biopsy and submitted for light, immunofluorescence, and electron microscopy. The patient tolerated the procedure well with only a small perinephric hematoma identified after the second biopsy, controlled by 10 minutes of manual compression.

At pathologic evaluation, there were normal glomeruli at light microscopy with mild patchy interstitial inflammation. Hemosiderin pigment was diffusely present throughout the tubules and a Gomori stain for iron (Prussian Blue) showed extensive hemosiderin within the tubular epithelial cells (Fig. 3a and b). The ultimate diagnosis of extensive hemosiderin within the tubules was concluded.

Follow-up ultrasound performed 6 months after initial presentation demonstrated decreased size of the bilateral

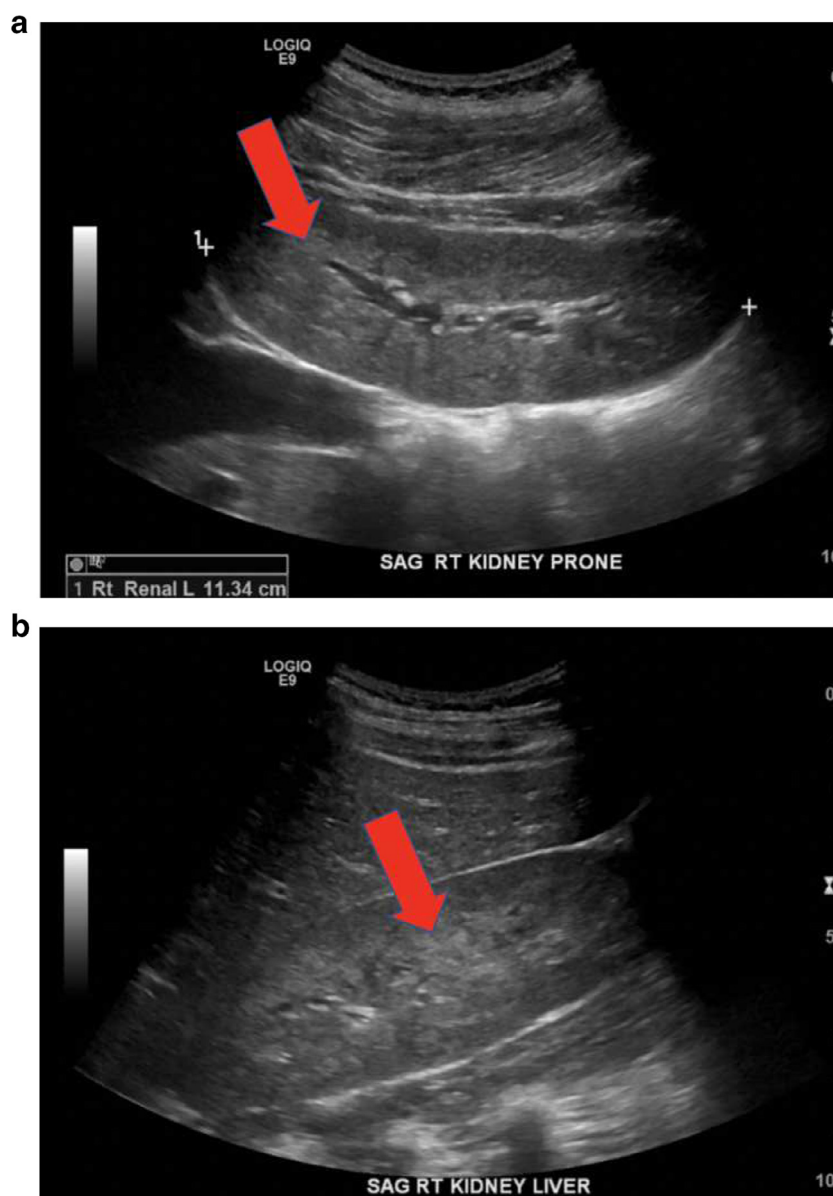


Fig. 4 – (a) and (b): 6-month follow up renal ultrasound – sagittal sonographic image of the liver and right kidney at 6-month follow up demonstrating slightly large-for-age right kidney with persistent abnormal, yet decreased overall degree of echogenicity of the medullary pyramids.

kidneys (11.3 cm right kidney and 11.1 cm left kidney) although they remained large for the patient's age. There was persistent abnormal echogenicity of the kidneys with the medullary pyramids appearing more echogenic than the cortex, however, the overall degree of parenchymal echogenicity was decreased compared to prior (Fig. 4a and b).

Discussion

The sickling of biconcave red blood cells into rigid and irregular cells predisposes to intravascular hemolysis which is increased in low oxygen tension, hyperosmolar intersti-

tial environment of the medulla, and small renal capillary beds [1]. After repeated cycles of oxygenation and deoxygenation, irreversible damage to the erythrocyte membrane forms deformed, sickled-shaped cells [4]. Sickling within the vasa recta of the kidney leads to ischemic damage and thrombosis, which is further compounded by an increased glomerular filtration rate and hyperfiltration leading to microalbuminuria or hematuria [1,2]. Chronic ischemia may ultimately result in chronic kidney disease.

About one half of sickle cell disease patients will have large kidneys at ultrasound primarily because of engorgement due to hypoxia and compensatory increase in renal blood volume [3–5]. This can eventually lead to atrophy in the later stages of sickle cell disease [3]. Other common renal abnormalities

on imaging include papillary necrosis and hemosiderosis of the renal cortex causing varying degrees of echogenicity changes [3].

A majority of patients have normal renal echotexture at ultrasound, however, approximately 3%-5% of patients may have a slight generalized increase in echogenicity or increase in medullary echogenicity, primarily due to iron deposition or nephrocalcinosis [3,4]. Free hemoglobin as a result of the red blood cell degradation can be reabsorbed and stored in the renal cortex as hemosiderin, which may contribute to the diffuse increase in the echogenicity of the kidney [3]. According to a previous study, 89% of patients have normal renal echogenicity, 5% may be mildly, diffusely echogenic, and 3% may exhibit increased medullary echogenicity with normal cortical echogenicity [6].

While our patient did have increased-for-age kidneys bilaterally, the echogenicity was markedly abnormal and did not fall into any of the previously mentioned categories. While the kidneys were diffusely echogenic, the medullary pyramids were markedly hyperechoic with a cortex that was slightly less hyperechoic, but with an increased echogenicity nonetheless, and sparing of thin band of the peripheral outer cortex. Observation of a similar appearance was described in sickle cell anemia by Zinn et al., however, there was no pathologic explanation for the imaging abnormality [7]. In a review by Daneman et al., a spectrum of echogenic patterns was observed ranging from a homogeneous, diffuse increase in echogenicity to concentrated regions of increased echogenicity in the center or peripheral aspects of the renal pyramids [8]. Although the increased echogenicity can be explained by a combination of vascular congestion and papillary necrosis, it is still unclear as to the etiology of the different sonographic patterns and their relation to the different histologic changes within the renal parenchyma.

During intravascular hemolysis in sickle cell disease free hemoglobin is freely filtered through the glomerulus and is reabsorbed by the tubular epithelium, which will manifest on

a kidney biopsy as hemosiderin-laden tubules and increased iron deposition at pathology. Our pathology-confirmed biopsy demonstrated diffuse hemosiderin appearing as blue material within the tubular epithelial cells at pathology, leading us to the conclusion of renal hemosiderosis secondary to acute intravascular hemolysis in a patient with sickle cell disease. Awareness about this unusual and rare ultrasound presentation of renal hemosiderosis may facilitate faster diagnosis without implementation of invasive biopsies.

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