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Case Report

Successful Management of Intractable Gross Hematuria with Vasopressin in Polycystic Kidney Disease

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Abstract

Gross hematuria is a well-known complication in patients with autosomal dominant polycystic kidney disease (ADPKD). While most of the hematuria episodes in patients with ADPKD are self-limited, severe and unremitting gross hematuria can occur. Successful non-invasive medical managements for severe episodes of gross hematuria in patients with ADPKD are rarely reported and are associated with significant adverse effects. In this article, the author reports a patient with ADPKD who had a preserved renal function and developed intractable gross hematuria for 10 months. He was treated successfully with infusions of 1-desamino-8-D-arginine vasopressin (DDAVP) without adverse effects. The success observed in this patient suggests that DDAVP infusion provides a relatively safe and noninvasive treatment method to successfully control severe renal bleeding in patients with ADPKD. Its use may be considered before subjecting these patients to invasive procedures such as embolization or nephrectomy that will further compromise their renal functions.

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) affects approximately 1 in 800 individuals worldwide and this disease accounts for 7 to 10 percent of patients on hemodialysis [1]. Episodes of gross hematuria are seen in at least 40 % of patients with ADPKD [2]. Repeated episodes of gross hematuria are a risk factor for progression of renal impairment. While most of the hematuria episodes are self-limited, severe and unremitting gross hematuria can occur. Successful non-invasive medical management for severe episodes of gross hematuria in patients with ADPKD is rarely reported. To the best of the author's knowledge, there are only 2 reported cases documenting the use of hemostatic agents to treat severe renal bleeding in ADPKD patients but the reported treatment options are associated with significant risks. Raoreported the use of epsilon aminocaproic acid (EACA) to treat protracted hematuria in a patient [3]. However, due to the high urinary concentration of EACA, the danger of obstructive clot formation in the urine is increased [4]. Aprotinin was used to successfully treat a patient with severe gross hematuria [5]. Aprotinin is no longer available in the United States due to the findings of a study on cardiac surgery patients showing an increased risk of death with aprotinin compared with aminocaproic acid and tranexamic acid [6]. In this article, the author reports a patient with ADPKD who had normal renal function and experienced intractable gross hematuria for 10 months. His severe gross hematuria was treated successfully with infusions of 1-desamino-8-D-arginine vasopressin (DDAVP) without adverse effects.

Case Report

A 46 year-old African-American man with no significant past medical history presented to clinic with his first episode of gross hematuria. There was no history of kidney stones. His blood urea nitrogen was 9 mg/dL (3.2 mmol/L), creatinine 1.0 mg/dL (76.2 µmol/L). Urine culture showed no bacterial growth. Kidney ultrasound followed by abdominal CT revealed his kidneys are enlarged (left kidney measures 8.0 x 9.4 x 14.7 cm, right kidney measures 5.8 x 8.4 x 12.1cm) with innumerable bilateral cysts, consistent with a diagnosis of polycystic kidney disease. His gross hematuria resolved spontaneously in one day. Nine months later the patient returned with new onset gross hematuria and flank pain. There was no use of ASA, NSAIDs or anti-coagulant/anti-platelet agents. Besides occasional jogging, there was no other strenuous physical activity or recent physical trauma. Laboratory tests revealed hemoglobin 13.1 g/dL (131 g/L), hematocrit 41.7%, platelet count 284 x 103/µL (284 x 109/L), prothrombin time (PT) 11.5 seconds (normal range 8.7-11.5 seconds), partial thromboplastin time 26

seconds (normal range 24-33 seconds). Factor VIII activity was 226% (normal range 50-150%) and von Willebrand Factor (vWF) activity was 204% (normal range 50-170%). Urine color was dark red, with specific gravity of 1.015, pH 7.0, 3+ blood, 3+ protein, negative nitrite and leukocyte esterase, negative glucose. Microscopic examination of the urine sediment showed packed fields of nondysmorphic red blood cells. There were no casts. Culture of the urine showed no bacterial growth. Repeat abdominal CT scan showed multiple hyperdense, hemorrhagic cysts (Figure 1).

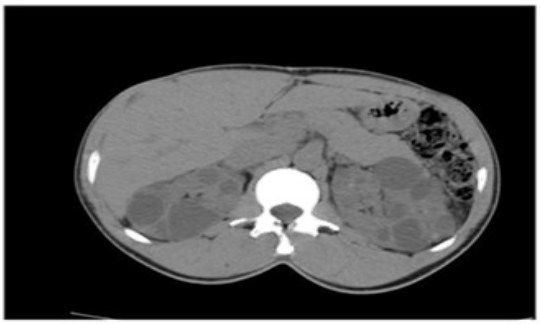

Figure 1: Multiple cysts are present in both kidneys, some contain high density material suggesting hyperdense, hemorrhagic cysts.

Patient was advised to stop all strenuous exercise. Conservative therapy consisted of bed rest and increased fluid intake did not abate the gross hematuria. His hematuria persisted for 10 months and became progressively worse with passage of multiple blood clots. In spite of worsening hematuria, patient did not follow up as instructed. His hemoglobin dropped from 13.1 g/dL (131 g/L) to 6.9 g/dL (69 g/L) as a result of the bleeding and patient began to report occasional dizziness (Table 1).

	Date	Hemoglobin (g/dL)	Urinalysis color	Urinalysis blood	Urinalysis RBC
	6/2009	13.3	Yellow	Negative	None
	7/2009	13.1	Red	2+	Moderate
	10/2009	11.3	Red	3+	Many
DDAVP →	5/2010	6.9	Red	3+	Many
	7/2010	9.8	Yellow	Negative	None
	9/2010	12.5	Yellow	Negative	None
	12/2010	13.7	Yellow	Negative	None

Table 1. Laboratory values.

Cystoscopy demonstrated prostatic enlargement without bladder tumors or stones. CT angiogram was performed and showed the intrarenal branches were stretched around the multiple cysts within the kidneys. There was no pseudoaneurysm and no evidence of an enhancing mass or arterial blush. The total kidney volume was 970 ml (right kidney 415 ml, left kidney 555 ml), which is more than twice the normal size for men. Normal averages about 404 ml [7]. Because conservative therapy was unsuccessful with stopping the bleeding and he developed symptomatic anemia over time, intravenous DDAVP was given at 0.3 mcg per kilogram for 3 consecutive daily doses at 24 hour intervals. Patient tolerated the treatments well. The patient reported a steady decrease in hematuria during the week following the DDAVP treatment and subsequent complete resolution of gross hematuria. Patient returned to clinic for follow up at two, four and seven months after the DDAVP treatment. There have been no further episodes of gross hematuria. Urinalyses remained negative for blood.

Discussion

Desmopressin (1-deamino-8-D-arginine vasopressin, DDAVP) is a synthetic analogue of the antidiuretic hormone L-arginine vasopressin. Plasma concentrations of factor VIII and von Willebrand factor (vWF) are approximately doubled or quadrupled by the administration of desmopressin, reaching a peak 30 to 60 minutes after intravenous infusion. This is thought to be due to the release of vWF from vascular endothelial cells. This is observed in both patients with hemophilia and von Willebrand's disease as well as in healthy volunteers [8,9]. Because of this effect, DDAVP has been used to effectively treat bleeding complications in patients with hemophilia and von Willebrand factor deficiency. It is also commonly used by nephrologists to manage bleeding complications in uremic patients. The exact mechanism of how DDAVP stopped the bleeding in this patient with preserved renal function remains unknown, but the effect of DDAVP may be mediated by the attainment of supranormal plasma concentrations of vWF. The formation of ultra-large multimers of vWFsupports platelet adhesion to vascular subendothelium more actively than multimers of normal size. Increased hemostatsis may also be mediated by high plasma concentrations of factor VIII, a rate accelerating factor in the process of fibrin formation [8,10,11].

Hematuria can generate patient anxiety and in severe case of bleeding, it becomes a difficult management issue for the clinician. When the bleeding is massive and intractable, procedures such as transarterial embolization (TAE) or nephrectomy are considered. However, these invasive procedures are associated with substantial risks, including substantial loss of renal function. Given that the Type I PKD patient generally develops end stage renal disease by the early to mid 50's and the Type II patient about 20 years later, preservation of renal function is crucial and noninvasive medical therapies should be emphasized.

Conclusion

Gross hematuria has high rate of recurrence in patients with ADPKD. Repeated episodes of gross hematuria are associated with progression of renal impairment. The overall management of gross hematuria in this patient population should focus on maximal preservation of renal function by controlling the hematuria episodes. Medical therapy utilizing hemostatic agents should be

considered and explored in treating severe gross hematuria before subjecting these patients to invasive procedures that could further compromise their renal functions. Thus far, the 2 reported methods of hemostasis using EACA and aprotinin have been associated with significant side effects, the success observed in this patient suggests that DDAVP infusions may offer a relatively safe and effective approach to the treatment of intractable hematuria associated with ADPKD.

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