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

Hui Yi Shan

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. The reported 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
months (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. Micro-
scopic 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. Conserva-
tive 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).

<table>
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<th>Urinalysis color</th>
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<th>Urinalysis RBC</th>
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</table>

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 hematu-
ria during the week following the DDAVP treatment and subse-
quently 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 pa-
tients with hemophilia and von Willebrand factor deficiency. It is
also commonly used by nephrologists to manage bleeding complica-
tions 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 vWF supports platelet adhe-
sion to vascular subendothelium more actively than multimers of
normal size. Increased hemostasis 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 substan-
tial 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 maxi-
mal 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.

References
