# Case - Hematuria with clot retention after clonidine/arginine growth hormone stimulation test

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## INTRODUCTION

In the adult population, gross hematuria with clot retention is not an uncommon management issue. In the pediatric population, however, it is a rare entity, most commonly associated with chemotherapy-induced hematuria in bone marrow transplant recipients. It can often present challenges to invasive intervention secondary to the anatomic limitations of the pre-pubertal male urethra in particular.[1] Arginine and clonidine administration have been used to stimulate growth hormone production and have been associated with self-limited, gross, painless hematuria.[2,3] Herein, we present the first case of significant gross, painful hematuria with clot retention, an unexpected complication as a result of an intravenous arginine infusion and oral clonidine administration.

## CASE REPORT

A 10-year-old pre-pubertal boy of Southeast Asian descent with no known medical issues presented in consultation to endocrinology for concern of growth delay. As part of his workup, he underwent a Clonidine Arginine Time Test. He was given 90 micrograms of oral clonidine. During administration, his blood pressure decreased to 60s/30s, which improved with a 183 ml bolus of normal saline. He was subsequently given 9 g of 10% L-arginine solution intravenously.

Two days after the growth hormone (GH) stimulation, his mother reported blood in the urine associated with severe abdominal pain, which led to his presentation to an urgent care center. They were contacted later that day by endocrinology, and parents reiterated that he was having increasing abdominal pain, urinary frequency with small volumes, blood clots, and burning with urination. There was no improvement while being managed with observation and by the third day after the Time Test, he presented to his primary care office in retention, blood at the meatus, and a palpable, distended, and tender bladder.

They were sent to our emergency department (ED) for further evaluation, which confirmed these findings. A bladder and kidney ultrasound was obtained in the ED that demonstrated a distended, clot-filled bladder without hydronephrosis of either kidney (Figure 1). Under ketamine sedation, a 6 French catheter was placed with successful decompression of the bladder and lightly irrigated, although without success in removing discrete clots, but with moderate improvement in urine color. The patient was managed and discharged expectantly.

He re-presented on day 5 after the stimulation test with similar symptoms. Repeat bladder ultrasound showed persistent clots, and the parents and child were offered continued observation with close follow-up or surgical management, which likely would have included suprapubic tube placement due to his small urethra. They elected expectant management and by day 8, a renal and bladder ultrasound demonstrated healthy, normal kidneys without hydronephrosis and resolution of all bladder clots. Figure 2 shows a timeline of events. He was seen via virtual appointment six weeks after his initial visit, and at that time, had no gross hematuria.

## DISCUSSION

The literature describes self-limiting gross, painless hematuria following GH provocation Clonidine Arginine Time Test not requiring intervention.[2,3] Our case is the first that demonstrates that hematuria resulting from Clonidine Arginine Time Test may result in clot retention and both pediatric urologists and endocrinologists should be aware of this potential complication.

Due to his small urethra, catheterization and irrigation were able to decompress the bladder but were unsuccessful in clot evacuation. The catheter was then removed. A conservative approach was taken in this

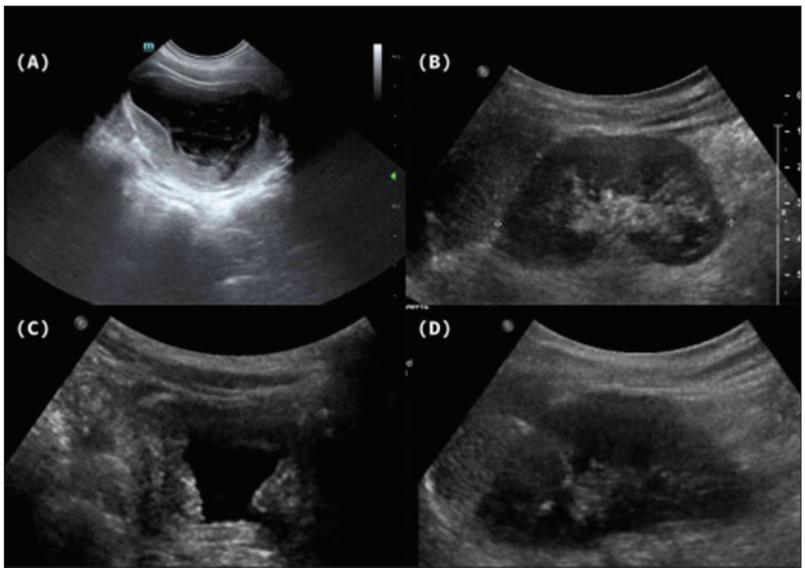


**Figure 1.** (A) Demonstrates his bladder full of blood clots upon his 1st ED presentation. (B) A sagittal view of his left kidney at the same time point demonstrates no hydronephrosis. (C) Demonstrates subsequent resolution of clots with renal ultrasound (D) on day 8 after GH test.

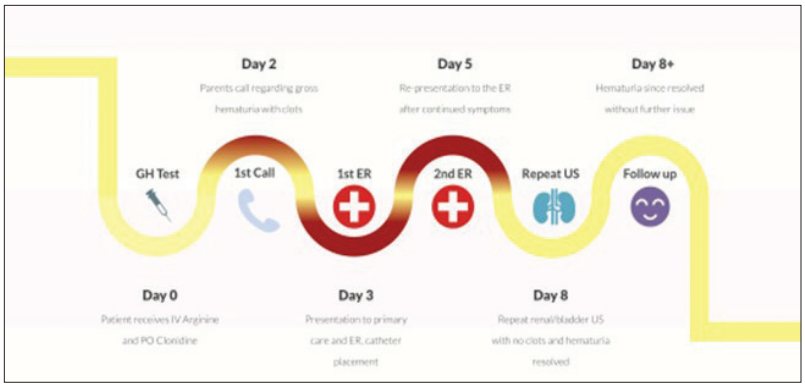


**Figure 2.** Timeline of events.

case, given that previous reports of bleeding associated with the Time Test have been self-limiting, he had no hydronephrosis on ultrasound, and pain was controlled after catheterization. Clots spontaneously resolved over eight days, thus avoiding a visit to the operating room.

The small-caliber, pre-pubertal male urethra makes hematuria with clot evacuation a much more challenging procedure than in adults, and suprapubic tract creation to facilitate the removal of clots might have been necessary in our patient had the clots not resolved themselves. Most cases with severe hemorrhagic cystitis in the pediatric population have been in patients who have undergone bone marrow transplantation or have received toxic cytolytic therapy with cyclophosphamide and/or radiation therapy.[1]

In the literature, there are several studies citing hematuria as a potential side effect of arginine and clonidine stimulation. In the study by Thirunagari et al, 34 patients were prospectively enrolled to track their degree of hematuria following GH stimulation testing.[2] Of the 34 subjects enrolled, three (8.8%) subsequently developed hematuria, and in all patients spontaneously resolved by seven days after testing without the need for intervention. Another study by Marinkovic et al similarly concluded that hematuria following GH provocation testing is self-limiting with observation, and in their cohort all patients who developed hematuria spontaneously resolved within 3–4 days.[3] Our patient's clots resolved spontaneously by day 8, which is similar to these experiences, and suggests that initial observation is still in order, despite the discomfort that our patient was experiencing.

Although the mechanism of hematuria is uncertain, it has been speculated that the transient hypotension experienced by patients may lead to nephritic changes responsible for the hematuria.[3] Our patient did indeed experience a period of hypotension, which responded to crystalloid volume replacement.

## CONCLUSIONS

Arginine and clonidine stimulation testing has the potential to cause significant gross hematuria with clot retention requiring intervention, and pediatric urologists and endocrinologists should be aware of this potential.

COMPETING INTERESTS: The authors do not report any competing personal or financial interests related to this work.

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