

Case – Hematuria with clot retention after clonidine/arginine growth hormone stimulation testSami Mostafa¹, Hailey H. Frye², Brent Cleveland¹, Duong Tu¹, Martin Koyle¹¹Department of Urology, University of Minnesota, Minneapolis, MN, United States; ²University of Minnesota Medical School, Minneapolis, MN, United States**Cite as:** Mostafa S, Frye HH, Cleveland B, et al. Case – Hematuria with clot retention after clonidine/arginine growth hormone stimulation test. *Can Urol Assoc J* 2025 May 16; Epub ahead of print. <http://dx.doi.org/10.5489/cuaj.9162>

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ABSTRACT

Arginine and clonidine Time Testing has been utilized to stimulate growth hormone (GH) in the pediatric population. This challenge test has been associated with transitory, self-limited, gross painless hematuria. We report a pre-pubertal child who underwent a GH stimulation test that led to painful hematuria with clot retention. The patient was managed expectantly as an outpatient, with subsequent resolution of all clots in the bladder on repeat US. GH

stimulation test with arginine and clonidine has the potential to cause significant hematuria with clot retention that might entail intervention and has not previously been reported in the literature.

KEY MESSAGES

- Arginine and clonidine stimulation testing has the potential to cause significant gross hematuria with clot retention in pediatric patients.
- This can manifest as increasing abdominal pain, urinary frequency with small volumes, blood clots, and burning with urination after GH stimulation test
- Treatment can include Foley catheter, suprapubic tube, or expectant management depending on patient anatomy, preference, and extent of clotting.

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. 90 micrograms of oral clonidine was given. During administration, his blood pressure decreased to 60s/30s which improved with a 183 milliliter bolus of normal saline. He was subsequently given 9 grams of 10% L-arginine solution intravenously.

Two days after the 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 ER for further evaluation which confirmed these findings. A bladder and kidney ultrasound was obtained in the ER that demonstrated a distended, clot filled bladder without hydronephrosis of either kidney. 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, Timeline of events). He was seen via virtual appointment 6 weeks after his initial visit and at that time had no gross hematuria.

DISCUSSION

The literature describes self-limiting gross, painless hematuria following growth hormone provocation Arginine and Clonidine 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 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 8 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.*² 34 patients were prospectively enrolled to track their degree of hematuria following GH stimulation testing. Of the 34 subjects enrolled, 3 (8.8%) subsequently developed hematuria, and in all patients spontaneously resolved by 7 days after testing without the need for intervention. Another study by Marinkovic *et al.*³ similarly concluded that hematuria following GH provocation testing is self-limiting with observation, and in their cohort all patients that developed hematuria spontaneously resolved within 3-4 days. 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 indeed did 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.

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FIGURES AND TABLES

Figure 1. (A) Demonstrates his bladder full of blood clots upon his 1st ER 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.

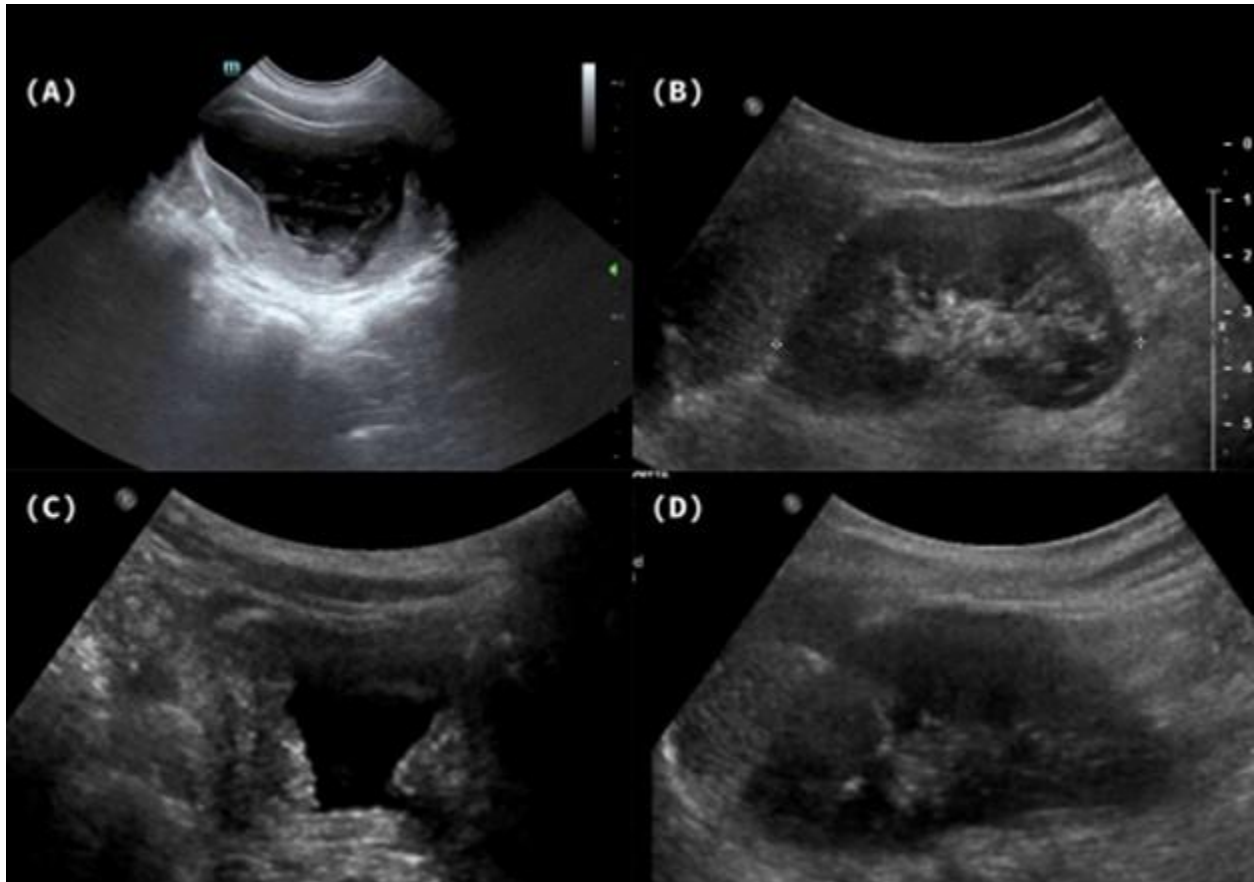
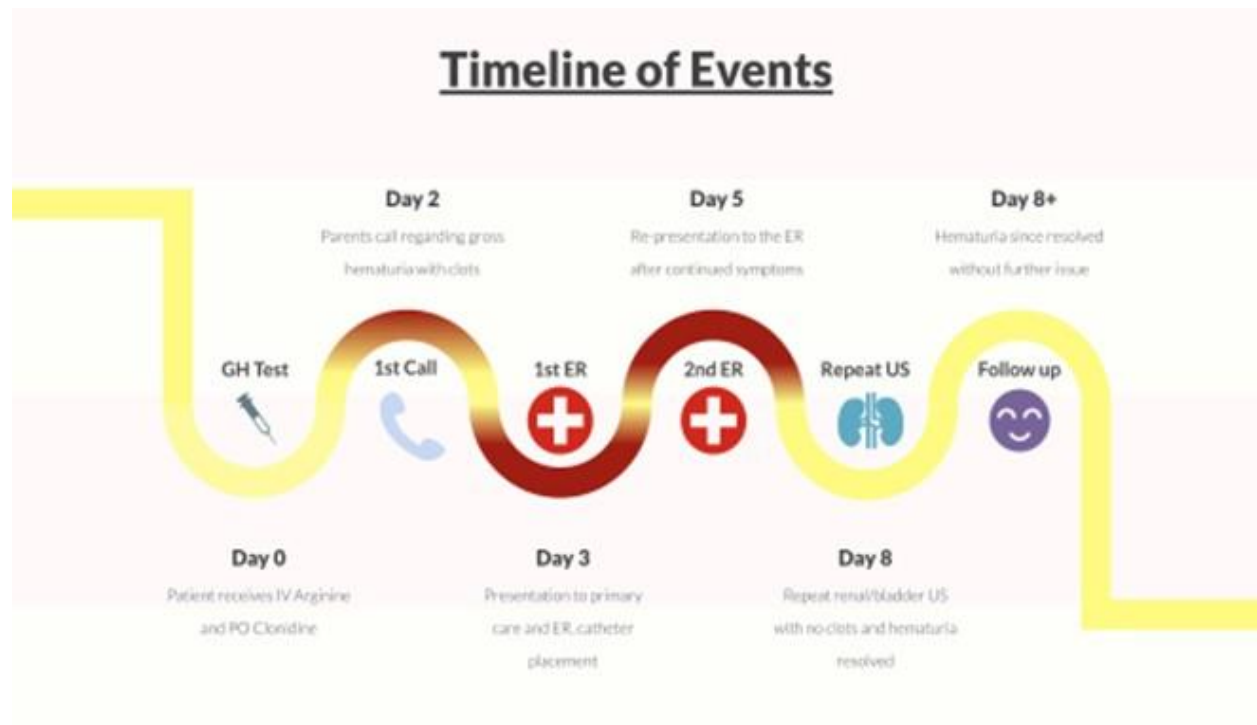


Figure 2. Timeline of events.



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