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Case Report

Refractory hematuria post actinic cystitis. Role of potassium alumen as treatment – Case Report

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Abstract

Actinic cystitis hematuria is a frequent complication after pelvic radiotherapy, present in approximately 5% of patients exposed to this therapy. The management of these cases seems to be a challenge for today's urologists. In this article, we present the case of a 73-year-old man diagnosed with actinic cystitis after pelvic radiotherapy and admitted to our service with a clinical picture of refractory macroscopic hematuria. During admission, the patient underwent multiple procedures and blood transfusions, without success in controlling hematuria. After a review of the literature, we chose to use Potassium Alum in the patient's treatment. Under general anesthesia, we performed a cystoscopy with the evacuation of clots and subsequently infused a 1% solution of potassium alum into the bladder at a rate of 200 ml/h for 25 hours. Less than 24 hours after Alum infusion, there were no more clinical signs of hematuria, which remained until hospital discharge. After 6 months of treatment, the patient did not present another episode of hematuria.

Introduction

Hemorrhagic Cystitis is a condition of hemorrhage and diffuse inflammation of the vesical mucosa [1] and is one of the biggest challenges faced by urologists and/or oncologists. Its presentation can vary from a mild clinical condition to more severe conditions that can pose a risk to the patient's life. It can be the result of infectious conditions, exposure to chemotherapy, and pelvic radiotherapy.

In this article, we describe the success of treatment with intravesical alum installation in a severe case of refractory hematuria due to actinic cystitis.

Clinical case

A 73-year-old male patient, who underwent exclusive pelvic radiotherapy 3 years ago for treatment of prostate cancer, was admitted to the urological emergency room of our hospital, with a decline in his general condition due to macroscopic hematuria associated with acute anemia. After initial stabilization, the

patient underwent cystoscopy under general anesthesia with the evacuation of clots. During the procedure, we observed that the bladder mucosa was diffusely erythematous with areas of hemorrhage without any tumor evidence, compatible with hemorrhagic actinic cystitis. To control the hemorrhage, coagulation of bleeding foci was performed using the resection loop of a monopolar resectoscope. During surgery, 2 packed red blood cells were transfused. In the immediate postoperative period, the patient was kept under urinary irrigation for 5 days and was discharged after 10 days of hospitalization without the use of a urinary catheter.

A new episode of macroscopic hematuria associated with acute anemia occurred 10 days after hospital discharge. As the patient was hemodynamically stable, he was again submitted to cystoscopy with the evacuation of clots and electrocoagulation with a monopolar loop of intravesical bleeding foci. After 15 days of hospitalization, the patient was discharged without signs of hematuria and was referred to a hyperbaric oxygen therapy session. Initially, 5 weekly sessions of 90 minutes were scheduled, however, after 12 sessions the treatment was

interrupted by the patient due to panic during hyperbaric therapy.

40 days after the first episode, the patient returns to the unit with a new condition of hematuria associated with anemia, this time accompanied by acute kidney injury, due to repeated bladder tamponade by clots, not dependent on dialysis. As there was no hemodynamic instability, a cystoscopy was performed with the evacuation of clots and cauterization of bleeding points. Postoperatively, the patient continued to present hematuria and urinary retention by clots when continuous urinary irrigation with saline solution was suspended, preventing the removal of the urinary catheter.

In managing the third episode, the following tests were performed: urinalysis, urine culture, and urinary cytology. The results did not show significant changes, such as bacterial growth or cell atypia.

Due to the failures in the previous treatments, we chose to perform a new cystoscopy to evacuate the clots, followed by bladder irrigation of 5000 ml of 1% Potassium Alum solution in an infusion pump at 200 ml/h. The patient was monitored during treatment for possible symptoms of aluminum poisoning. After the installation period, the patient presented clear urine and bladder irrigation was discontinued. Twenty-four hours after the end of irrigation, a new episode of hematuria occurred, which made us return to continuous bladder irrigation with 0.9% saline solution for a period of 48 h after which there were no signs of hematuria. During this period, there was an improvement in renal function, in addition to stabilization of the blood count. After 5 days from Alum infusion, the patient had no recurrence and was discharged from the hospital without a urinary catheter.

Currently, 6 months after treatment with Alum, the patient remains under outpatient follow-up, with no recurrence of hematuria, improvement in general status, anemia, and no renal dysfunction.

Discussion

Hemorrhagic Cystitis is a condition of hemorrhage and diffuse inflammation of the vesical mucosa [1] and is one of the greatest challenges faced by urologists. It can present as mild conditions that respond to conservative measures, or even as severe conditions that impair the quality of life, with chronic anemia, and recurrent bladder obstructions, which can be a threat to the patient's life.

The presence of urinary tract infection, of bacterial or viral origin, can be the trigger for hematuria. In these cases, hematuria tends to improve after treating the infection. The treatment of viral clinical conditions is supportive, with hydration, stimulation of diuresis, vesical irrigation, and even the use of antivirals.

The use of chemotherapy drugs such as cyclophosphamide and ifosfamide are also known causes of hemorrhagic cystitis. Between 2 to 40% of patients exposed to cyclophosphamide develop hemorrhagic cystitis, starting within 48 hours after

the onset of exposure [1]. The acrolein metabolite excreted in urine causes bladder irritation leading to hemorrhagic cystitis.

Another important risk factor for hemorrhagic cystitis is actinic cystitis caused by pelvic radiotherapy. Approximately 5% of patients undergoing the procedure develop hemorrhagic cystitis. Its onset can vary between 6 months to 10 years after radiotherapy treatment [2]. Factors such as radiation dose, area of the exposed bladder, and how it is administered are associated with higher risks. Radiation causes changes in the bladder mucosa that, over time, can lead to progressive endarteritis, leading to vascular obstruction and mucosal and submucosal ischemia, culminating in the development of fragile telangiectasias that tend to bleed.

It is important to remember that the use of cyclophosphamide and pelvic irradiation are risk factors for bladder cancer. Therefore, this must be excluded before assuming that it is hemorrhagic cystitis [3].

In addition to a specific treatment, as in infectious conditions, general supportive measures are the basis of the approach: intravenous hydration, urinary catheterization with bladder irrigation, evacuation of clots, and blood transfusion, if necessary, usually initially resolve moderate cases [3].

In our environment, hyperbaric oxygen therapy is one of the main forms of treatment for actinic cystitis. It presents a resolution rate of 80 to 90%, usually with the maintenance of results for about 2 years [4,5]. Increased oxygen pressure reduces hypoxia caused by endarteritis and facilitates tissue recovery. Unfortunately, its use has limitations in the treatment of acute bleeding, especially in those patients who need hospitalization for bladder irrigation.

Cases refractory to less invasive measures may require more aggressive treatments. Intravesical 1-4% formalin causes coagulation of urothelium proteins and consequent vascular occlusion. Despite having a 90% success rate in the control of hemorrhagic cystitis, it is not free from complications and may lead to bladder retraction and even bladder wall necrosis and, consequently, bladder perforation in more severe cases [6]. Internal iliac artery embolization is reserved for severe cases of hemodynamic instability. Despite immediate control of bleeding in 90% of cases, the duration of this control is still not well documented. Cystectomy is the most extreme measure and can be performed in those patients who are refractory to all other previous treatments. However, it is important to bear in mind that the procedure has high rates of complications and morbidity, as patients, in general, are elderly and already heavily consumed by chronic bleeding.

Cases of hemorrhagic cystitis refractory to initial measures can be treated with bladder irrigation with aluminum potassium sulfate (Alum). Alum irrigation was first reported in 1982 in the treatment of six patients with hemorrhagic cystitis of different etiologies. Unlike the installation of formalin, which requires the procedure to be performed in the operating room under general anesthesia, Alum can be instilled in the ward and in the patient's bed. It acts by causing coagulation and precipitation



of urothelial proteins, stimulates vasoconstriction, and reduces vascular capillarity, controlling bleeding and reducing edema and urothelial inflammation. Small case series have demonstrated a success rate above 60% in controlling acute bleeding, good tolerance, and low risk for patients. In those responsive to therapy, the response was durable in 54%, not requiring further hospitalizations for hemorrhagic cystitis in a mean follow-up of 16 months [7]. It is important to pay attention to signs of aluminum intoxication, especially in chronic renal patients, whose clearance is reduced, and in those with large bladder areas. Signs of intoxication include lethargy, mental confusion, vomiting and even seizures. Even so, despite its safety, availability, low cost and recommendation in the main literatures, the use of Intravesical Alum is still not widespread and the experience of urologists with the use of this substance are still limited.

Conclusion

Our case report suggests that alum irrigation is a safe, inexpensive, and effective management strategy for macroscopic hematuria secondary to hemorrhagic actinic cystitis after pelvic radiotherapy. Considering the surveys carried out in the literature and in the reference centers of urology in the State of Rio de Janeiro, it may be an underutilized practice. We believe that patients with normal renal function and chronic hematuria due to actinic cystitis, requiring recurrent and prolonged hospitalizations for bladder irrigation

and clot evacuation, can benefit greatly from its use, especially in the current context of the COVID-19 pandemic. and the increased risks of virus infection in the hospital environment.

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