# CASE REPORT

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# Sudden Death Due to Intravascular Hemolysis After Bladder Irrigation with Distilled Water

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**ABSTRACT:** A 45-year-old white man was hospitalized with gross hematuria, one month after cystoscopy and biopsy for the same complaint. The biopsy revealed cystitis glandularis. One day after admission, he developed seizures and died within hours. Autopsy, laboratory tests, and further questioning of the hospital staff showed that he died of acute hyponatremia and massive intravascular hemolysis after irrigating the bladder with sterile water. Two deep bladder ulcers with exposed veins served as the portals of entry. Until now, this fatal complication had been described only during transurethral surgery. Both a careful autopsy and hospital investigation is necessary to differentiate in-hospital natural death from iatrogenic fatality.

**KEYWORDS:** pathology and biology, iatrogenic death, accidental death, hyponatremia, intravascular hemolysis, complications of bladder trauma, sterile-water irrigation, hypotonic solution

Sudden death occurs often in hospitalized patients. While the manner of death is usually natural, an unknown percentage are accidental. These can be the result of a diagnostic procedure or therapeutic mistake. A thorough medicolegal investigation is required to separate iatrogenic from sudden natural deaths as this case serves to illustrate.

## Case Report

A 45-year-old white man was admitted with gross hematuria. Four weeks prior to admission, this divorced teacher was seen in the emergency room for low back pain and "blood" in his semen after heterosexual intercourse. An intravenous pyelogram revealed left kidney "malrotation." Cystoscopy showed a single raised bladder lesion medial to the left ureteral orifice. The biopsy showed cystitis glandularis and he was treated with ciprofloxacin (Cipro®). He had no other medical problems.

On this admission, he complained of sudden gross hematuria. His blood pressure was 140/80 mm Hg, pulse 84/min, respiratory rate 16/min, and temperature 98.5 F. His physical

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exam was normal. His weight was 128 lbs. A foley catheter was introduced into his urethra and his bladder was irrigated. He continued to pass blood clots. His admission laboratory tests included a hematocrit of 41.1%, white blood cell count of 10.1 K, serum sodium of 139 mEq/L, potassium of 4.7 mEq/L, blood urea nitrogen (BUN) of 16 mg/dL, prothrombin time of 11.6 seconds, partial thromboplastin time of 29.2 seconds, and bleeding time of 10 min (with aspirin). He was started on intravenous cefazolin (Ancef®).

At 10 A.M. the next morning, he had a grand mal seizure after the nurse irrigated his bladder. After the initial postictal period, his blood pressure was 138/100 mm Hg, pulse 124/min, and respiratory rate 24/min. He was still afebrile. He had several more seizures over the next 3 h until his death at 2:20 P.M. He remained hypertensive, tachycardic, and tachypneic throughout this time. A computed axial tomography (CAT) scan of his brain was normal. The first two blood samples after his seizures began were reported as "hemolyzed." The third sample, just prior to his death, revealed a serum sodium of 122 mEq/L, potassium of 4.8 mEq/L, BUN of 26 mg/dL, lactate dehydrogenase (LDH) of 2600 IU/L (normal is 313 to 618 IU/L), and haptoglobin of 8 mg/dL (normal is 13 to 163 mg/dL).

At autopsy, the decedent weighed 149 lbs (increase of 21 lbs in one day). The foley catheter contained abundant clear, red urine. One liter of red, slightly cloudy ascitic fluid was present. The heart and epicardial vessels were normal. The aortic intima was orange rather than the usual yellow. The heavy lungs (1780 gm combined) showed pulmonary edema. The dark brown kidneys with their smooth capsules expressed abundant cloudy, brown fluid. The bladder wall was extremely friable, perforating easily upon handling. The bladder mucosa contained two 0.5 cm (in diameter) ulcers. One was located on the trigone, the other on the anterior wall (Fig. 1). The ulcers had sharp, flat "punched-out" borders with a deep red-tan roughened base. Dilated thrombosed veins were present. The surrounding mucosa was dark red-black and friable. Multiple areas of hemorrhage without ulceration were present on the superior wall. The 1500 g brain was normal except for a subjective increase in white matter. Heart blood revealed no ethyl alcohol by gas

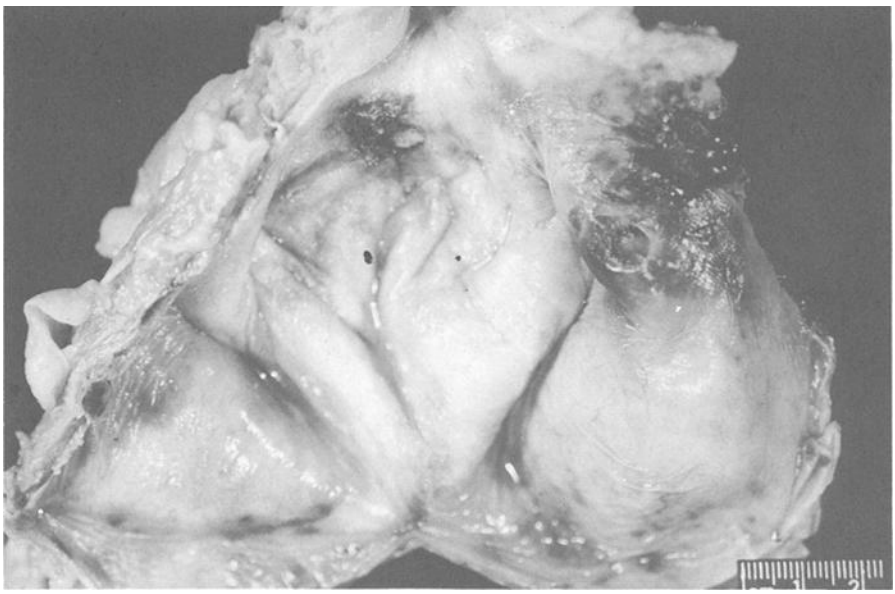

FIG. 1—*Gross photograph of the opened bladder revealing two round ulcers with surrounding gangrenous inflammation.*

chromatography. The urine did not contain any of the usual drugs of abuse by enzyme multiplied immunoassay technique (EMIT) and thin layer chromatography (TLC).

Microscopically, the bladder mucosa and wall showed transmural acute inflammation with ulceration, disruption, and necrosis (Fig. 2). No infectious organisms were seen. One area of mucosa contained granulation tissue. There were many extravasated red blood cells which were pale or colorless lying in a sea of red-brown material (Fig. 3). This was shown to be hemoglobin by the Dunn-Thompson hemoglobin stain [*1*]. The vessels in other organs showed many abnormal red blood cells varying from enlarged round to colorless to fragmented shapes. The vessels were all uniformly dilated. The renal tubules contained many red, granular casts (Fig. 4) which were positive by the Dunn-Thompson hemoglobin stain. No other pathology was seen. The postmortem urine showed many red blood cells and was strongly positive for protein and hemoglobin.

A careful review of the hospital record and interview with the nurses showed that the decedent was initially irrigated with normal saline. From 8 A.M. until noon on the day of his seizures and death, however, he was irrigated with sterile water instead. The doctor's order did not specify the frequency, quantity, or type of solution to be used for irrigation.

## Discussion

Accidental injury and death due to diagnostic and therapeutic procedures in hospitals have been reviewed and reported by other authors [*2–4*]. Deaths often occur during anesthesia and surgery. Many times the medical examiner is never informed of these cases. Sudden death due to natural causes is also common in the hospital and the differentiation between natural and accidental iatrogenic death can be difficult.

In this case, the decedent presented with hematuria 4 weeks after cystoscopy. He was initially irrigated with normal saline, but this was changed to sterile water. This hypotonic solution would not have entered the intravascular space had the deep ulcers with their exposed veins not been present. This is analogous to transurethral surgery, which involves

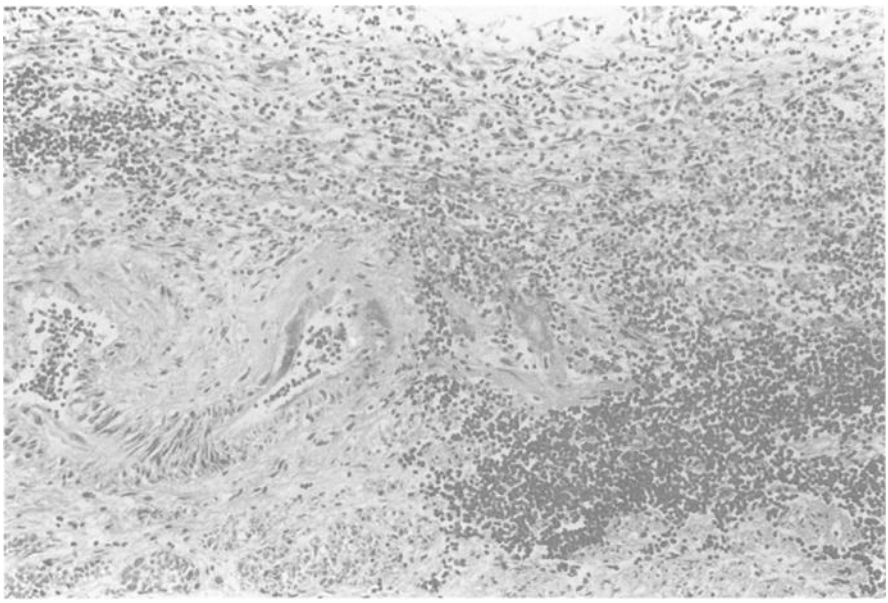

FIG. 2—*The bladder wall shows acute inflammation with edema, hemorrhage, and fibrinoid necrosis of small arterial walls (125x, H+E).*

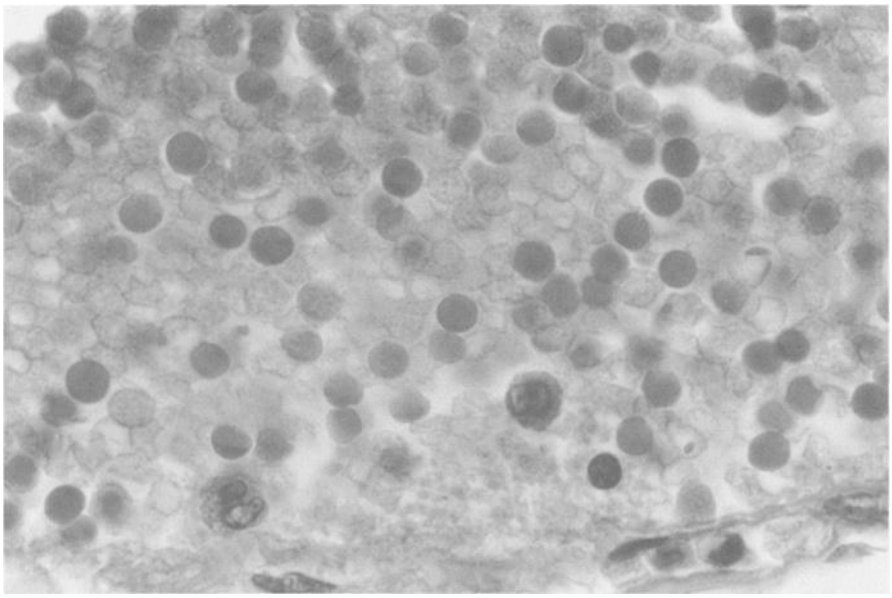

FIG. 3—*Within the bladder wall, these erythrocytes vary from enlarged spherical cells to colorless "ghost" cells (500x, H + E).*

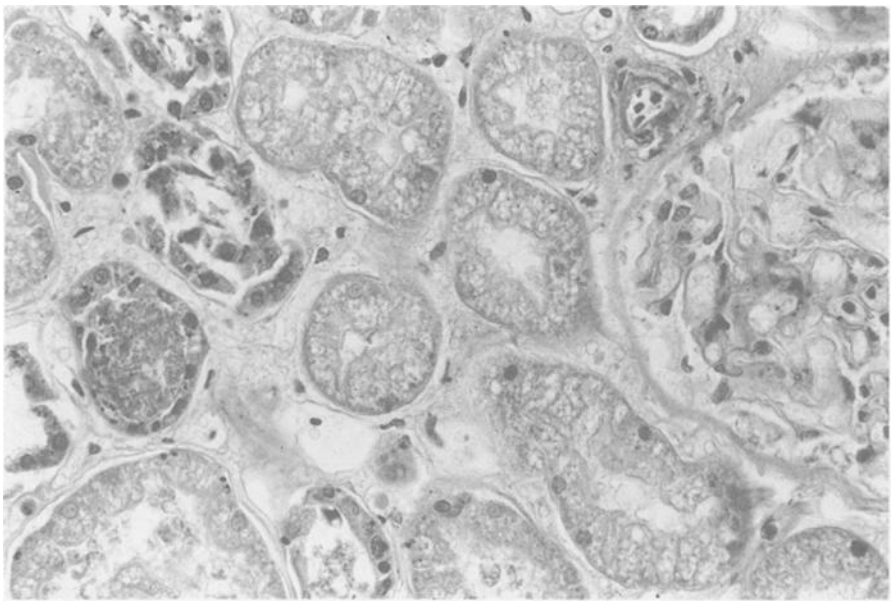

FIG. 4—*Within the kidney, the renal tubules display both hydropic change and acute tubular necrosis with hemoglobin casts (312x, H + E).*

surgically opening venous sinuses that lead to the absorption of irrigating fluid when the pressure of the solution is higher than the venous pressure [5]. The sterile water produced increased intravascular volume, intravascular hemolysis, and a dilutional hyponatremia. The rapidity of these physiologic imbalances produced seizures and death. The intravascular hemolysis produced the repeatedly "hemolyzed" blood samples, low serum haptoglobin, high serum lactate dehydrogenase, orange staining of the aortic intima, and the hemoglobin casts found in the renal tubules. The serum potassium level was not elevated because of the dilutional effect as well as the kidneys ability to increase potassium excretion and maintain homeostasis. Both solutions gained access to the intravascular space and markedly increased intravascular volume. This produced hypertension and tachycardia. These solutions diluted blood proteins thus lowering the osmotic pressure. This produced ascites, pulmonary edema, cerebral edema, and the apparent weight gain. Septic shock, which the clinician believed was the cause of death, would have produced fever and hypotension, both of which were absent. Although hypotonic hemolysis is known to urologists in the setting of transurethral resection, this was not considered in the differential diagnosis until after the hyponatremia was discovered. Thus, the true mechanism of death is understood.

The etiology of the bladder ulcers is less clear. There was obviously ulceration with acute exudative cystitis. One area within the trigone showed granulation tissue. The bladder has a limited ability to react to injury and dissimilar causes may produce the same host response [6]. Enterococcus grew in postmortem cultures of the bladder ulcer. Bacterial cystitis, however, never produces ulcers and this extensive transmural inflammation in the absence of indwelling catheters or surgical intervention. The decedent had no antibodies to human immunodeficiency virus (HIV) by ELISA technique. No obvious causative agent was seen microscopically including bacteria, actinomyces, tuberculosis, syphilis, candida, cytomegalovirus, schistosoma, or entameba histolytica. Both the history and pathology are incompatible with interstitial cystitis. The discrete nature and circumscription of the lesions as well as the identical location of the biopsy site 4 weeks previously suggests that these were caused by the cystoscopy and biopsy. Finally, these lesions could be caused by autoerotic stimulation. This practice has caused death, although by dissimilar mechanisms [7,8].

This case report emphasizes the importance of a thorough medicolegal investigation in unexpected sudden hospital deaths. It also demonstrates that even the most seemingly innocuous procedures can prove fatal.

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