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Case Report

Fatal and Forgotten: Acute Hemolytic Anemia and Renal Failure as a Complication of Transurethral resection of the prostate

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Abstract

The Transurethral resection of the prostate (TURP) is the most common and widely used procedure for treatment of symptomatic benign hypertrophy of the prostate (BPH). TURP related hyponatremia is a well-known but infrequently encountered problem caused by scrupulous use of bladder irrigants. Acute intravascular hemolysis is a rare catastrophic complication of TURP with scant representation in the medical literature. We report a case of acute intravascular hemolysis due to hypo-osmolality following TURP that led to acute renal failure to the extent of requiring temporary dialysis. We also aim to conduct a review of the literature and discuss strategies to minimize hematologic complications secondary to TURP.

Keywords: TURP; BPH; Hemolysis; Renal Failure; Prostate; Hyponatremia

Introduction

Transurethral resection of the prostate (TURP) is the most common surgical modality to treat symptomatic benign hypertrophy of the prostate (BPH). The American Urological association (AUA) considers TURP the preferable modality of treatment for symptomatic BPH compared to surgery, as the latter carries a high rate of complications [1]. According to the AUA, in the United States approximately 150,000 people have TURPs performed each year with 88% having immediate improvement in their symptoms. Although TURP represents a declining percentage of primary BPH treatment, annual incidence remains as high as 39% of BPH procedures in 2005 [2]. While TURP is considered minimally invasive and generally has fewer complications than open surgery, widespread use of TURP has revealed some dangerous and even fatal complications. The use of hypotonic bladder irrigants during TURP can lead to acute hypo-osmolar hyponatremia that could be potentially fatal. This complication, also known as TURP syndrome, complicates 0.8-1.2% of TURP [3,4]. A rarely described and potentially fatal complication of TURP is brisk intravascular hemolysis with concomitant secondary acute kidney injury (AKI). To our knowledge, only six cases have reported this finding in the world literature [5-10]. The significant mortality and morbidity associated with this phenomenon merits a more thorough description of TURP syndrome related acute hemolytic anemia.

We report a very rare case of acute intravascular hemolysis leading to renal failure immediately following a TURP procedure.

Case

We report a case of a 63-year-old Caucasian male who underwent elective TURP for benign prostatic hyperplasia (BPH) with preserved kidney function. Seven liters of distilled water were used to irrigate the bladder. At the end of the procedure, he became unresponsive, hypothermic (93.1° F), hypotensive (77/49 mmHg) and severely hypoxemic. Despite aggressive resuscitation attempts, he continued to deteriorate and finally required mechanical ventilation. Further investigation into the etiology of his cardiovascular collapse revealed profound hyponatremia with first measured serum sodium of 118 mEq/L (pre-procedure 140 mEq/L) and hemoglobin of 8.2 g/dL (pre-procedure 15.4 g/dL). Blood was grossly hemolyzed this first, and three subsequent lab draws. Other laboratory data from the initial basic metabolic panel include potassium 3.3 mEq/L, chloride 97 mEq/L, bicarbonate 18 mEq/L, calcium 6.1 mg/dL, BUN 13 mg/dL, and creatinine 1.12 mg/dL. Peripheral smear showed rare schistocytes, slight anisocytosis and poikilocytosis, few target cells, burr cells, and occasional ovalocytosis.

Hypertonic saline and multiple blood transfusions were administered but hemoglobin continued to drop to 5.7 g/dL four hours after initial laboratory data was requested. Peripheral smear obtained at this time showed increasing number of schistocytes, as well as developing thrombocytopenia (as indicated by platelet decrease of 181 $x10^9$/L to 103 $x10^9$/L). Elevated lactate dehydrogenase of 1890 U/L and low haptoglobin of 27 mg/dL were suggestive of intravascular hemolysis. His urine output also declined and serum creatinine began trending up due to acute tubular necrosis as depicted in Figure 1. Serum sodium remained at 118-119 mEq/L during the next several serial measurements over the six hours following initial laboratory investigation. Serum sodium began to rise, due to resuscitation with hypertonic saline, to 122 mEq/L twelve hours after initial measurement, and subsequently as in Figure 1. Unfortunately, serum osmolality was not obtained until about 20 hours after initial hyponatremia was detected, and was low at 275 mOsm/kg. Two urine osmolality measurements obtained the following day were also low at 256 mOsm/kg and 212 mOsm/kg. Comprehensive haematological workup was negative for transfusion reaction or any other etiology for hemolytic anemia. ANA, complement levels, cold agglutinins were checked and were unremarkable. Reticulocyte count (3.07%) was consistent with normal marrow response. Total bilirubin remained within normal range. Urine myoglobin was high at 139 mcg/L. Disseminated intravascular coagulation panel was checked and it was unremarkable: Fibrinogen 247 mg/dL, Prothrombin Time (PT) 11.2 seconds, International Normalized Ratio (INR) 1.1 and Partial Thromboplastin Time (aPTT) 25.6 seconds.

Blood work was consistent with intravascular hemolysis due to absorption of the large amount of distilled water. Aggressive management with hypertonic saline led to normalization of serum sodium levels and serum osmolality with resultant cessation of hemolysis. Correction of anemia was achieved over the next 2-3 days and patient was liberated from the ventilator. However, renal function continued to deteriorate (creatinine 7.7 mg/dL and eGFR 7.1 mL/min) requiring hemodialysis. Renal function recovered after five sessions of hemodialysis. The patient was doing well at one-month follow-up.

Discussion

TURP syndrome is characterized by numerous possible neurologic, cardiopulmonary, hematologic and renal effects that occur due to sudden intravascular volume shifts and plasma solute changes [11]. Continuous irrigation of fluids into the bladder is needed to visualize and distend the operative site as well as to remove tissue, blood and debris. This irrigation fluid can easily enter systemic intravascular space through numerous open venous sinuses in prostatic tissue, causing intravascular fluid shifts as described above leading to TURP syndrome. Effects depend on the type of irrigant used and vary from mild (confusion, restlessness, and dyspnea) to severe (shock, seizures, hypertension, and coma) [11]. Serum sodium levels as low as 120 mEq/L can cause restlessness, confusion and widening of QRS complexes [12]. If serum sodium drops lower than 110 mEq/L; it can precipitate seizures, coma, ventricular tachycardia and fibrillation [12]. These severe effects could be seen at even slightly lower sodium levels depending on acuity of change and underlying comorbidities. Hypo-osmolality rather than hyponatremia per se is the primary etiology of neurological changes and intravascular hemolysis.

Our patient underwent elective TURP for his symptomatic BPH. Immediately post-procedure he deteriorated with shock and altered mental status. Laboratory data showed a sudden drop in his hemoglobin and serum sodium. Serum osmolality was also found to be low though it was obtained at a later time. With such a critical event, resuscitation efforts took precedence and so lowest serum osmolality and lowest serum sodium were not measured at that critical time. It is highly likely that at the time of lowest serum osmolality, the osmotic fragility of RBCs was very high with resultant intravascular hemolysis. This in turn resulted in profound hypotension and tubular precipitation of hemoglobin and cellular debris leading to kidney failure. The laboratory data indicative of hemolysis support this conclusion. Following correction of serum sodium (and osmolality), intravascular hemolysis ceased and within several days renal function also recovered (Figure 1).

Water intoxication was first described by Wier et al in 1922 [13]. Severe hemolytic anemia and AKI can occur due to acute hypo-osmolar hyponatremia secondary to systemic absorption of distilled water used for bladder irrigation during TURP. Acute absorption of huge quantities of distilled water with very low solute load leads to acute drop in serum osmolality. Hence, TURP syndrome could be potentially fatal by causing renal failure, CNS demyelination, and myocardial infarction. No other cause could explain severe hemolytic anemia and acute renal failure in this case besides acute hyponatremia due to distilled water (7 liters) that was used as an irrigant for the TURP. Limited earlier data supports this fact [5,6]. These symptoms belong to the spectrum of water intoxication related complications as described previously [14].

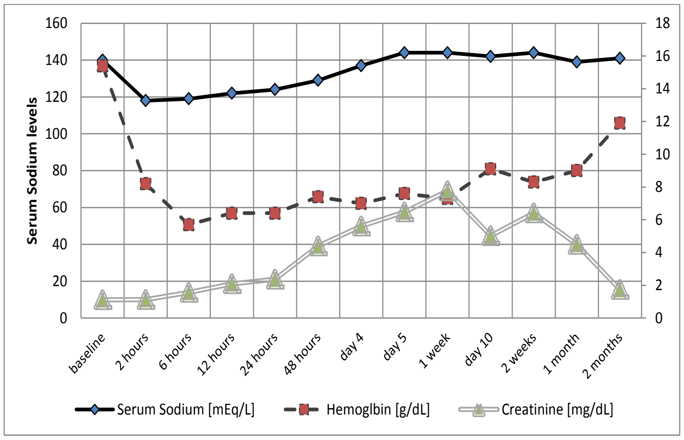

Figure 1. Graphical representation of serum sodium levels [mEq/L] [Primary vertical-Axis, on left] to hemoglobin [g/dL] and serum creatinine [mg/dL] on [secondary vertical-axis, on right] over the course of time since hospitalization post-procedure. Horizontal-axis represents time.

TURP has been the gold standard for years and is still considered the procedure of choice by American Urological Association, Canadian Urology Association, and European Urological Association [1,15,16]. TURP is efficient, cost-effective and durable in terms of sustained efficacy with low rate of long-term complications and re-treatment rates [3,4]. Newer modalities are being explored and developed in hope of finding better alternatives. Until then, we must recognize that TURP is not free of side effects or complications even in the hands of experienced surgeons. Awareness of TURP syndrome, associated hemolytic anemia, and its management is limited. Early recognition could prevent end organ damage in patients with TURP syndrome. We strongly recommend minimizing the use of hypotonic irrigants and the duration of the procedure reduce the complications.

Currently no standard guidelines are available for management. Treatment of this potentially fatal complication starts with extreme vigilance. There should be no delay in starting initial resuscitation and obtaining blood tests for electrolytes, blood gas analysis, hemoglobin and hematocrit, coagulation profile, glucose and ammonia level (depending on the type of irrigant utilized). Intubation and mechanical ventilation should be considered if the patient is having signs of altered mentation, hemodynamic instability, and pulmonary edema. Every patient undergoing TURP should be monitored for hyponatremia and treatment should be stared if there are clinical signs of hyponatremia. Further management should take place in the ICU setting. Recognizing complications such as seizures or arrhythmias while correcting their causes (hyponatremia, hyperkalemia, hypokalemia, hypoxia, and hypothermia) should be prioritized.

We recommend minimizing use of hypotonic solutions, in particular, distilled water. Duration of surgery should be minimized. Irrigation bags should be kept no more than 60 cm above the surgical field to minimize hydrostatic pressure of the fluid [17]. Extent of bladder distension should be minimized by frequent drainage of the bladder in order to avoid increased absorption through open venous sinuses. During the whole procedure, adequate blood pressure should be maintained (and therefore normal per prostatic venous pressure) to avoid increased absorption through open venous sinuses. Expertise and need for alternative irrigation solutions are necessary steps to prevent overall incidence of this complication.

Conclusion

In summary, hemolysis due to distilled water irrigant increases the likelihood for acute renal failure and recovery of hemolytic anemia correlates with resolution of hyponatremia. This subject merits discussion due to the large number of patients undergoing TURP yearly. Awareness about the etiology and management is limited. Close scrutiny can save renal function in patients with TURP syndrome. We recommend minimizing the amount of hypotonic irrigant fluid usage and the duration of the TURP procedure, and also suggest using alternative solutions for TURP to limit its associated morbidity and mortality.

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