Case Report **Open Access**

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Transurethral resection of the prostate, bladder explosion and hyponatremic encephalopathy: a rare case report of malpractice

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Abstract: We present an original case report of a bladder explosion during a TURP intervention for benign prostatic hypertrophy, that was brought on by the absorption of about 5 liters of glycine 1.5% and then onset of a severe hyponatremia. The quick and inappropriate correction of this electrolyte imbalance led the onset of encephalopathy and the death of the patient. The authors discuss the pathogenesis of these uncommon diseases and, considering the most recent Italian Legislation, they highlight the importance to respect good clinical practice standards and guidelines to ensure the most appropriate treatments for the patient and remove any assumptions of medical liability.

Keywords: TURP; Bladder explosion; Hyponatremia; Encephalopathy; Medical Liability

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1 Introduction

Transurethral prostatic resection (TURP) remains the gold standard method for surgical management of the benign prostatic hypertrophy [1] with good tolerability and safety, despite the use of new techniques [2] or innovative medical devices [3]. The bladder explosion during this endoscopic surgery is extremely rare: these severe events occur in only 0.2% of this procedure [4], with various degrees of bladder injury and the possible electrolyte disorders in the outcome. When this event occurs, the immediate endoscopic exploration, the surgical repair of the bladder and a valid management of the patient's conditions generally provide a good outcome, and the patient can be discharged without complications. Otherwise, we report a rare case of bladder explosion during TURP with bladder's rupture, electrolyte disorders, and death of patient.

2 Case report

A Caucasian male 76 years old, suffering from type II diabetes, hypertension (blood pressure: 165/80 mmHg), chronic obstructive pulmonary disease (COPD), and benign prostatic hypertrophy was subjected to TURP. The procedure was performed in spinal anesthesia, using a 24 French resectoscope (STORZ – GERMANY). The coagulation and the cutting powers were, respectively, 60w and 70w. Glycine 1.5%. was used as irrigant. Upon completion of the surgical procedure, after fifty-five minutes, a violent blow as an explosion was felt while the surgeon proceeded to hemostasis of some blood vessels. The cystoscopy showed a large intraperitoneal lesion of the posterior wall of the bladder. General anesthesia was initiated and a laparotomy was performed. A wide starry rupture of the posterior wall of the bladder about 6.5 cm wide with fringed margins was highlighted. The margins were debrided and the bladder was repaired. During the surgi-

cal intervention packed red blood cells (two pouches) and hydroxyethyl starch volume expanders (Voluven® 500 ml) were administered. Then a urinary catheter and drainages were applied in the peritoneum and in the pelvis. At the end of the anesthesia, the patient showed difficulty waking and looked confused; therefore, the patient was sedated, intubated, connected to the vitascope assisted mediastinoscopy(VAM) and admitted to the intensive care unit. On admission hypothermia (T 35.4 °C) and severe hyponatremia (121 mEq/L) were detected. The preoperative serum sodium level was 138 mEq/L. Hemodynamic values were stable (blood pressure: 150/70 mmHg; heart rate: 80 bpm). A hypertonic saline solution (NaCl 3%, 513 mEq/l) was infused. After about five hours of admission, laboratory tests showed an increase in the serum sodium level (127 mEq/L) and of serum creatinine (1.6 mg/ml). The preoperative creatinine serum level was 1.1 mg/ml. The therapy provided: hypertonic sodium solution (NaCl 3%) + volume expanders (Voluven® 500 + 500 ml) and diuretics (furosemide 20 mg). On the second day, the patient, still sedated, had normal blood pressure levels (145/60 mmHg), but he presented with tachycardia (125 bpm); the body temperature was almost normal (37.4 °C). The blood levels of electrolytes, evaluated every eight hours, tended to improve, but the increase of serum creatinine level continued (2.1 to 2.6 mg/dl). Small amounts of serum blood liquid flowed out through drains; an ultrasound showed blood clots in the bladder. Through the urinary catheter, repeatedly bladder washings were practiced. The diuresis, sodium excretion, and urinary osmolarity were not assessed. On the third day, despite the continued administration of a hypertonic solution of sodium (NaCl 3%) and 500 ml of Voluven, the patient presented with hypotension (110/50 mmHg), tachycardia (124 bpm) and hypovolemia; blood tests showed serum sodium levels between 142 and 148 mEq/L. Additionally, atrial fibrillation had arisen; it was treated by administration of amiodarone. Laboratory tests also showed an increase of transaminases and lactic dehydrogenase. In the fourth day, blood pressure readings were unchanged (blood pressure: 110/50 mmHg), heart rate elevated (100 bpm), serum sodium levels between 147 and 143 mEq/L, and serum creatinine levels were between 3.3 and 2.3 mg/ml. Continuous renal replacement therapy (CRRT) was been initiated and the administration of 3% NaCl was suspended. In the fifth day, the patient was sedated and ventilated presented hemodynamic parameters (blood pressure: 110/60 mmHg, heart rate: 90 bpm), and hypovolemia persisted. In the sixth day, the pharmacological sedation was suspended but the patient, while breathing spontaneously, still appeared confused and disoriented; also, he presented with uncoordinated movements of the facial muscles with a lesion of the right lingual margin. The patient was reconnected to VAM. The blood levels of electrolytes were stable, sodium 132 mEq/L, potassium 3.5 mEq/L. Serum creatinine levels (2.5 mg/ml) and ammonemia (115 mmol/L) were elevated. In the seventh day, the values of the serum electrolytes were acceptable (Na 132-140 mEq/L) and the serum creatinine levels had improved (1.8 mg/ml), but the patient continued to show expired hemodynamics parameters (blood pressure: 110/50 mmHg, heart rate: 88 bpm), and the hypovolemia persisted. The neurological consultation noted a confused, undirected, and aphasic patient, unable to perform simple orders and even small movements of the lower limbs. The electroencephalogram (EEG) showed a marked depression of the cerebral biorhythms and cerebral computed tomography (CT) showed a pericapsular malacica area. In the following days, the clinical picture worsened; the hemodynamic parameters declined further (blood pressure: 100/40 mmHg, heart rate: 100 bpm), the patient had a fever (BT 38.5 °C), inflammatory bronchopulmonary signs arose, and 12 days after surgery the patient died.

The results of laboratory tests are shown in Table 1.

The autopsy showed an increase of brain weight (1350 grams), with smoothing of brain furrows; the histological examination showed an obvious edema. The neurons had suffered regressive phenomena, with eosinophilic cytoplasm and pyknotic nuclei. A slight gliotic reaction was also evident. Cardiac hypertrophic myofibrils and an appreciable increase of the connective tissue were present. The coronary arteries had obvious atherosclerotic plaques, without hemodynamically significant stenosis. The lungs showed diffuse aspects of alveolar emphysema, with numerous cavities occupied by granulocytes, cleaved pneumocytes, macrophages, and fibrin material and a marked congestion of interstitial capillaries. In the peritoneum a serum-blood fluid was present in an appreciable amount (350 ml). The liver showed diffuse aspects of hepatocellular necrosis, but the portal spaces did not present lymphoplasmacytic infiltrates. The kidneys showed sclerotic glomeruli, a noticeable tubulonecrosis, and interstitial inflammatory infiltrate. The bladder mucosa presented a lympho-granulocytic inflammatory infiltration that involved even its muscular structure.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

Informed consent: Informed consent has been obtained from all individuals included in this study.

3 Discussion

This case report of an occurrence of patient mortality is characterized by the bladder explosion during TURP and the onset of a severe hyponatremic encephalopathy; it offers us an opportunity for information about these uncommon diseases. The bladder explosion during TURP is a very rare event. After the first report of Cossuto [5], about 30 cases have been reported in literature [6-24]. It appears to be a negligible entity if it is compared to the particularly high number of TURPs practiced daily. The pathogenesis of this event must be sought in the formation of a mixture of explosive gases that accumulate in the bladder during the prostatic resection; and these gases can catch fire and explode because of sparks produced during the electric resection prostatic or during hemostasis of vessels. Hansen [8] has analyzed the composition of this gaseous mixture in vitro by gas chromatography and has noted that in such a mixture oxygen, hydrocarbons, and hydrogen are present. The presence of hydrogen was related to hydrolysis of intracellular water and to the pyrolysis of the prostatic tissue. However, the presence of this gas is not considered enough on its own to cause an explosion; during the surgical procedure, the presence of the oxygen that can penetrate the air in the bladder is necessary to cause the explosion [19]. Therefore, surgeons should carefully monitor the amount of air, and thus sufficient amount oxygen to generate an explosive mixture that penetrates the bladder during a TURP. Various measures have been reported to limit this possibility and to avoid the risk of bladder explosion during a TURP [20-21]. These measures regard the surgeon activity and the team medical activity (Table 2).

TIPS TO REDUCE THE POSSIBILITY OF BLADDER EXPLOSION DURING TURP
– Limit the operating time
– Use a coagulation current at low voltage
– Use the bladder irrigation adequately
– Limit the times of bladder irrigation
– Use the Ellick evacuator when indicated
– Avoid incongruous openings of the resectoscope

In particular, the attention of the surgeon is necessary to evaluate the presence of small air bubbles that may be formed in the bladder during the TURP, and in such cases, it is suggested that if possible, to not proceed with the prostatic resection, especially in cases of benign prostatic hypertrophy, to limit the time of the surgical procedures, and reduce the production of gas [24]. In many cases, bladder explosion happened at the end of TURP procedures performed for prostate cancers with operative time ranging from 75 to 80 minutes [7,8,14,20]. In the present case, the bladder explosion happened at the end of a TURP procedure performed for benign prostatic hypertrophy, an intervention which was prolonged by about 55 minutes while the surgeon proceeded to coagulate some blood vessels. Many studies [12,17-19,21,22] involve the possibility to eliminate air penetrated in case into the bladder during surgery through suprapubic pressure or the use of a ureteral catheter, also the patient in different positions or angling the beak of the resectoscope while the bladder is emptied. In the present case, these measures were not sufficiently observed, and the bladder explosion occurred at the end of the surgical intervention, resulting to the large laceration of the posterior wall of the bladder while the surgeon proceeded hemostasis of some vessels.

Approximately five liters of 1.5% glycine solution with an osmolarity of 200 mOsm/L, were used for bladder washing and spread into the peritoneum. The implemented surgical intervention was done to repair the bladder injury, but it could not prevent the absorption of glycine solution with consequent alteration of the blood osmotic gradient. At the end of surgery, the patient was hospitalized in the intensive care unit, and he presented with hypothermia (body temperature 35.4 °C) and severe

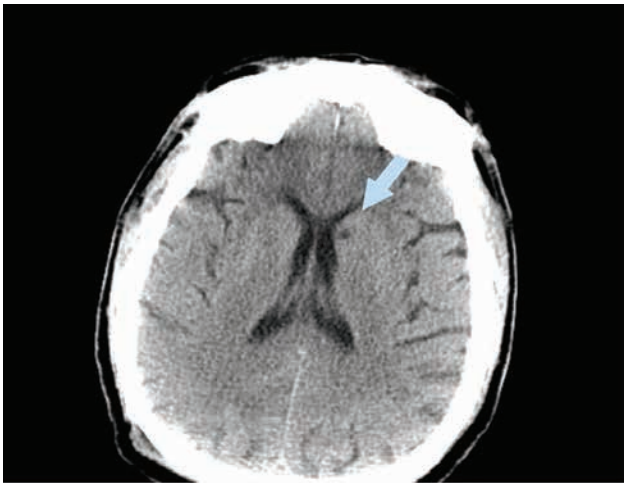

Figure 1: CT scan showing hypodense area at the head of the left caudate nucleus (arrow)

Table 1: Results of laboratory tests

Blood tests	**Postoperative day I**			**II**			**III**			
Time	13.00	18.00	24.00	6.00	15.00	24.00	00.00	7.00	17.00	24.00
Sodium (mEq/l)	121	127	125	132	131	138	133	142	146	148
Potassium (mEq/l)	3.8	3.4	4.0	5.0	5.0	5.0	5.3	4.7	5.0	5.2
Chloride (mEq/l)	88	100	106	103	112	111	111	109	106	107
Magnesium (mEq/l)	1.4			1.6			1.8		1.7	1.7
Glucose (mg/dl)	265	225	120	116	146	121		93	164	127
Urea (mg/dl)	31	37	37	47	56	57	62	68	81	85
Creatinine (mg/dl)	1.1	1.6	1.7	2.1	2.4	2.6		2.9	3.4	3.5
Total protein (g/dl)		4.1		4.4	4.0	3.6		3.4	3.1	2.6
Albumin (g/dl)	2.1	2.8		2.9	2.7	2.1		2.1	2.0	1.6
WBC (ml)	19.000	27.900	23.600	22.900	27.170	25.120		19.760	19.720	13.810
RBC (n/ml)	3.730.000	4.090.000	3.920.000	4.050.000	3.440.000	3.020.000		3.160.000	2.650.000	2.230.000
Hemoglobin (g)	10.8	12.4	11.5	12.5	19.2	8.8		9.0	7.7	6.5
Hematocrin (%)	30.4	34	32.5	33.5	29.5	25.4		26.2	21.7	16.2
Platelet count (n/ml)	201.000	264.000	256.000	288.000	259.000	215.000		207.000	224.000	191.000
PT (sec.)	76	85	91.5	89.2	83	80		65	55	50.2
PTT (sec.)	27	23.9	26.76	30.48	29.9	29.2		35.77	40.6	52.28
INR	1.29	1.14	1.06	1.09		1.21		1.50	1.77	1.94
Fibrinogen (mg/dl)	295	283	278	330	379	415		453	442	406
SGOT/AST (U.I./L)								190		
SGPT/ALT (U.I./L)								175		
LDH (U.I./L)								365		

P.D. =

Blood tests	**IV**			**V**			**VI**		**VII**	
Time	00.00	7.00	15.00	**6.00**	**17.00**	**24.00**	**7.00**	**22.00**	**7.30**	**24.00**
Sodium (mEq/l)	147	148	143	141	135		132		129	137
Potassium (mEq/l)	4.2	4.0	4.2	3.8	4.0		3.5		3.0	3.9
Chloride (mEq/l)	108	108	105	100	103		98		96	104
Magnesium (mEq/l)	2.0	2.3	1.7	1.9	1.7		1.6		1,7	2.0
Glucose (mg/dl)	147	92	109		196		156		280	
Urea (mg/dl)	85	58	54		54		37		40	
Creatinine (mg/dl)	3.3	2.8	2.3		2.9		2.5		2.7	

Blood tests	**IV**			**V**			**VI**		**VII**	
Total protein (g/dl)	3.0	3.5	3.0				2.9			
Albumin (g/dl)	1.9	2.1	1.9				1.5		1.8	
WBC /ml	14.350	14.670	18.940		17.200		19.730	23.04	25.650	26.070
RBC (n/ml)	2.930.000	3.390.000	2.880.000		2.780.000		2.900.000	3.030.000	3.080.000	2.820.000
Hemoglobin (g)	8.5	9.6	8.4		8.4		6.8	8.8	8.9	8.1
Hematocri (%)	19.5%	22.5	24.1		13.6		19.8	26.9	26.9	25.4
Platelet count (n/ml)	192.000	218.000	187.000		186.000			120.000	121.000	99.000
PT (sec.)	54.6	62	56		78.8	75.7	145	97	96.7	93.1
PTT (sec.)	89.29	48.05	51.98		59.2	87.24		103.6	56	50.14
INR	1.78	1.58	1.72		1.23	1.29	90.26	1.00	1.01	1.04
Fibrinogen (mg/dl)	474	531	458		453	369	379	438	474	389
Ammonia (mmol/L)					115					

Blood tests	**VIII**			**IX**			**X**		**XI XII**	
Blood tests	6.00	15.00	23.00	7.00	12.00	22.20	8.00	18.00	7.28	7.40
Time	140	132	131	150			137	136	131	138
Sodium (mEq/l)	4,4	3.7	3.7	3.6			3.2	4.2	4.1	3.6
Potassium (mEq/l)	102	111	106	104				104	1.0	108
Chloride (mEq/l)	1.8	1.9	2.0	1.8				2.6	2.4	
Magnesium (mEq/l)	139	188	299	138			81	145	172	140
Glucose (mg/dl)	36	36	33	29			41	61	58	63
Urea (mg/dl)	1.9	1.8	1.8	1.6			2	2.3	2.1	2.6
Creatinine (mg/dl)	3.7	3.3	3.2	3.6			4	3.6	3.9	4.2
Total protein (g/dl)	2.5	2.1	2.0	2.5			2.3	2.0	2.1	1.9
Albumin (g/dl)	34.300	32.600	36.710	30.500	31.340	26.900	27.170	23.070	26.470	17.840
WBC /ml	3.08	2.59	2.33	2.38	2.57	2.43	2.39	2.26	28.30	2.490
RBC (n/ml)	8.8	7.6	6.7	6.9	7.7	7.2	7	6.6	8.3	7.12
Hemoglobin (g)	28.1	23.1	20.7	21.0	23.0	21.6	21.5	19.8	25.2	22.3
Hematocri (%)	97	99	103	65	85	109	101	116	70	125
Platelet count (n/ml)	94.6	93		89.0	95.7	94.9	87	89.1	88.2	89
PT (sec.)	40.7	35.7		38.36	26.36	29.3	11.1	17.6	25.30	29.85
PTT (sec.)										

hyponatremia (Na 121 mEq/L). It was calculated that the absorption of about 3–4 liters of hypoosmotic fluids, such as glycine, involves a decrease of 20–30 mEq/L of serum sodium, resulting in hyponatremia [25]. In this case, about two hours had elapsed between the bladder explosion, its surgical repair, and the hospitalization of the patient in intensive care—sufficient time to influence the onset of fluid or electrolyte imbalance. Studies indicate the need for rapid time for bladder repair and to establish an effective therapy of fluid or electrolyte imbalance. The excessive retention of liquids within the tissues, caused by hyponatremia, causes cerebral edema; the neurons can offer osmotic phenomena and consequently loss of electrolytes, with possible development of brain damage [26]. In the present case, the correction of hyponatremia was approached in an empirical, intensive, and rapid way, without determining the blood and urinary osmolarity levels, sodium excretion levels, and diuresis. A diuresis greater than 100 ml/hour can be a warning sign of overcorrection of the serum sodium concentration [26]. Three days after surgery, the patient presented a significant hypovolemia, and obvious problems with kidney function and hypernatremia. That suggests an overcorrection of the electrolyte imbalance related to intense diuresis secondary to a reduced secretion of ADH. The CT scan showed a hypodense area at the head of the left caudate nucleus: the expression of a clear neuronal suffering resulting from hypoxic-ischemic phenomena.

To understand the onset of this neuronal hypoxic damage, we assume it arose from the damage caused by cerebral edema and hypotension, leading to reduction of the blood provision of the left lenticulostriate artery. Also because of the presence of the obvious hypovolemia and the renal functional imbalance, the rapid and intense correction of hyponatremia through hypertonic saline solution entailed a further neuronal dysfunction with loss of organic solutes, such as glutamate, thiamine and myoinositol. Also, cerebral dysfunction characterized by movement disorders, catatonia and confusion had arisen in the sixth to seventh day, indicative of osmotic demyelination syndrome as possible extrapontine myelinolysis. Any possible contribution of the neuronal reperfusion injury, with further damages to cellular proteins and nucleic acids, should also be considered in the genesis of myelinolysis. This mechanism could bring about the degradation of unsaturated fatty acids with consequent demyelination, as observed in a case of CO-intoxication [27]. In the present case, an NMR was not performed, though it is the test that would have accurately shown the possible demyelination [28]. Moreover, the glycine absorbed by the body, and subjected to oxidative deamination in the liver, had conditioned the hepatic necrosis with hyperammonemia that competed to depress brain activity. In summary, due to a severe electrolyte imbalance, along with the bladder injury, a severe hyponatremic encephalopathy occurred, and it conditioned a significant deterioration of the clinical picture. The patient died twelve days after surgical intervention. This sequence of events arouses many concerns regarding the care practiced and the therapy chosen. In fact, in correcting severe acute hyponatremia, the operator must be especially careful to consider not only the fluid electrolyte imbalance entity, but also to consider appropriately the timing and method of correction of this condition [29]. The most recent guidelines indicate the need to start administration of hypertonic saline solution 3% to as soon as possible, to the increase the serum sodium concentration by 5 mEq/L because this increase would be enough to make the more severe symptoms disappear [30]. However, the increase of serum sodium levels should not exceed 12 mEq/L in the first 24 hours, or 18 mEq/L in 48 hours [31]. Subsequently, therapeutic indications involve the administration of saline solution (0.9% NaCl) with constant monitoring of electrolytes and water balance, paying close attention to avoid too rapid correction of serum sodium, which can aggravate brain damage and trigger an osmotic demyelinating syndrome. In the present case, an improperly handled correction of the fluid electrolyte imbalance and an inadequate monitoring of electrolyte balance induced a severe encephalopathy in a predisposed patient, because of the probable coexistence of cerebral vascular disease and nephropathy related to diabetes. Indeed, it is often difficult to correct a severe and rapidly arising hyponatremia, because the neurological manifestations are more severe when the hyponatremia is more marked and rises quickly [32,33]. The infusion rate should be adjusted based on serum sodium levels measured every 4 hours; also, diuresis should be closely monitored because excessive diuresis can lead to an overcorrection of hyponatremia. In this case it was not controlled because of the repeated washings of the bladder [34]. There is the possibility of adding desmopressin (1–2 mg, every 6 to 8 hours), and to treat with 3% NaCl to ensure a speed of serum sodium correction equal to 3–7 mEq/L/hour to avoid an overcorrection [35]. A correction of hyponatremia equal to 1.5-–2 mEq/L/hour was obtained by Moritz [36] in marathon runners by administration of 100 ml of 3% saline solution in ten minutes. Indeed, it must not be forgotten that the severe hyponatremia is characterized by a significant increase of mortality and morbidity [37-39], especially in elderly subjects already hospitalized for other causes [40,41]; however, the present case reports the need of care intervention carefully

planned to meet the needs of the case and in accordance with good clinical practice and guidelines. A conduct that will ensure the most appropriate therapeutic resources to the patient will likely remove any possibility of medical liability [42], considering the most recent Italian Legislation [43].

Conflict of interests: No authors report any conflict of interest.

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