CASE REPORT

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Glycine Toxicity and Unexpected Intra-Operative Death

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ABSTRACT: A rare complication of the use of glycine irrigation fluid during prostatic surgery in a 69-year-old man is described. Following cystolithopexy and transurethral resection of the prostate for benign prostatomegaly, abdominal distension developed with increasing ventilatory pressures. Despite retroperitoneal fluid evacuation at subsequent urgent laparotomy, cardiac arrest occurred that was not amenable to resuscitation. At autopsy a traumatic defect in the posterior bladder wall filled with calculus debris was confirmed that did not communicate with the peritoneal cavity. Hyponatremia with markedly elevated levels of blood, urine, and body fluid glycine were demonstrated. Death was, therefore, attributed to glycine toxicity following tracking of glycine through a surgical defect in the posterior bladder wall. Careful dissection of surgical sites is required in such cases to demonstrate any additional trauma that may be associated with the fatal episode. Analysis of body fluids for glycine and electrolytes is also necessary to assist in the determination of possible mechanisms of death.

KEYWORDS: forensic science, forensic toxicology, glycine, hyponatremia, intraoperative death, transurethral resection syndrome

Although the use of glycine as an irrigation solution in surgery is widespread, adverse reactions may occur. The following case is reported to demonstrate an extremely rare case of fatal glycine toxicity occurring following perforation of the posterior bladder wall during surgery.

Case Report

A 68-year-old man was admitted to hospital for elective transurethral prostatic resection and endoscopic bladder stone removal (cystolithopexy). His previous medical history included ischemic heart disease with a previous infarct five years ago, non-insulin dependent diabetes mellitus, hypertension, and hypercholesteremia.

Initially a cystoscopy with endoscopic cystolithopexy was performed, with crushing and fragmentation of the calculus, followed by a transurethral resection of the prostate. Standard 2% glycine (aminoacetic acid) solution was used for irrigation according to established protocols. Towards the end of the procedure oxygen saturations began to fall and ventilatory pressures had to be increased. The abdomen was noted to be tense and a presumptive diagnosis of bladder perforation with subsequent retroperitoneal extension of glycine was made. Laparotomy was immediately performed and retroperitoneal fluid was drained. Cardiac arrest occurred which was unresponsive to 45 min of resuscitation. The blood sodium level taken after resuscitation was 113 mmol/L, compared with a routine preoperative level which was normal (136 mmol/L).

At autopsy a recent laparotomy incision was noted with an abdominal drain attached to a bag containing 1500 mL of clear fluid. There were also 600 mL of free fluid within the abdominal cavity. No defect in the peritoneum was seen. Retroperitoneal tissues posterior to the bladder were markedly edematous and exuded clear fluid. A drainage tube inserted into the right pleural cavity was attached to a bag containing 500 mL of clear fluid. A similar drainage tube and bag in the left chest contained 10 mL of clear fluid.

Examination of the bladder revealed a freshly cauterized bed of the prostate. An oval defect due to surgical trauma was present in the posterior bladder wall with surrounding hemorrhage, adjacent to the right ureteric orifice (Fig. 1). It measured 10 × 5 mm. The ureter was intact. The defect was filled with crushed bladder calculus and extended transmurally into perivesicular adipose tissue. No direct communication with the peritoneal cavity was demonstrated. The surrounding soft tissues were markedly edematous. The bladder contained 20 mL of bloody fluid.

Other autopsy findings included marked coronary artery atherosclerosis with multifocal areas of myocardial fibrosis, mild bilateral nephrosclerosis, and residual benign prostatic hyperplasia.

Postmortem analysis of glycine by ion exchange chromatography with lithium buffers and post-column ninhydrin detection, according to established protocols (1), revealed markedly elevated levels: left pleural fluid, 43 000 μmoles/L; right pleural fluid, 49 000 μmoles/L; peritoneal cavity, 79 000 μmoles/L; urine, 22 000 μmoles/L; and blood, 21 000 μmoles/L. (Normal plasma glycine=150 to 500 μmole/L) (2).

Death was, therefore, attributed to glycine toxicity with hyponatremia following retroperitoneal and intraperitoneal accumulation of glycine irrigation fluid during surgery. It is possible that the presence of significant ischemic heart disease may also have mitigated against successful resuscitation.

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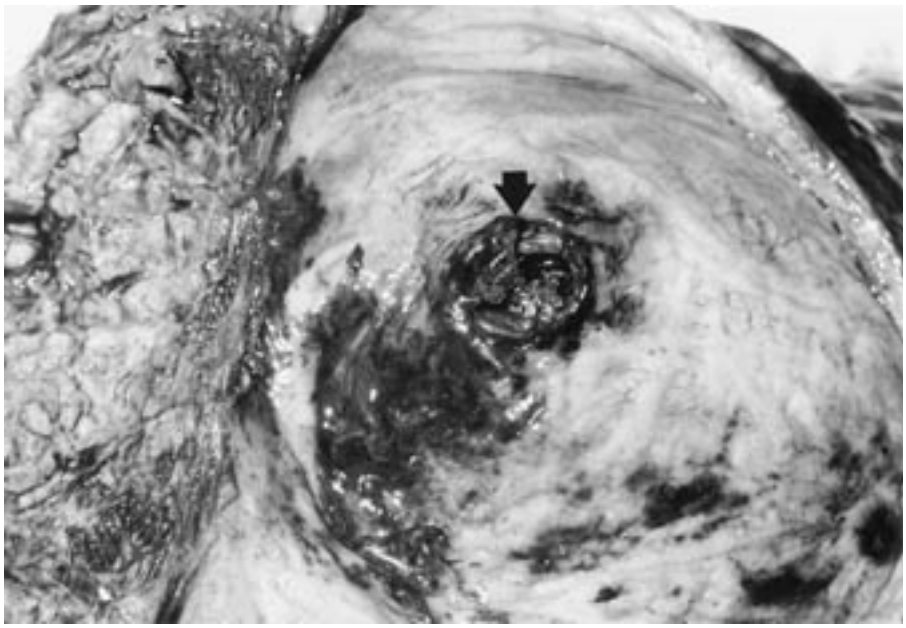

FIG. 1—*Posterior wall of the bladder demonstrating a 10 mm defect filled with crushed bladder calculus (arrow).*

Discussion

Glycine is used as a standard irrigation fluid during prostatic surgery. Although complications are generally rare, a transurethral resection syndrome has been described due to absorption of hypotonic glycine irrigant in which patients manifest cardiovascular and neurological abnormalities, including transient blindness (3,4). The symptoms and signs are believed to be caused by a combination of dilutional hyponatremia and direct glycine toxicity (5) and consist of nausea, vomiting, confusion, bradycardia and hypotension (6). While signs of intoxication have been reported with blood glycine levels of 800 μmole/L (7), others have stated that symptoms will only occur with "tremendously" elevated levels, of greater than 4000 μmole/L (3). The level of blood glycine in the reported case was 21 000 μmole/L.

Glycine may have a variety of effects including direct neurotoxicity as well as having a toxic effect on the kidneys and liver (8). It has been suggested that absorption of glycine occurs via an extravascular route related to bladder pressure during surgery (9,10). Alternatively, cases have occurred where transurethral resection syndrome has resulted following the use of only relatively small amounts of irrigation fluid with normal sodium levels, suggesting that direct absorption of glycine has occurred due to its high lipid solubility (7). While transurethral resection may have contributed to the elevated glycine levels in the reported case, the presence of significant amounts of glycine in the retroperitoneal tissues and peritoneal cavity, with the highest levels of glycine within the abdomen, suggest that infiltration of glycine through the bladder wall defect was a more significant factor. Cases of glycine toxicity following bladder surgery have also been reported due to bladder wall perforation with intraperitoneal accumulation (11).

The reported case illustrates, therefore, an extremely rare complication of bladder and prostate surgery with tracking of glycine through a defect in the posterior bladder wall. Although no direct communication could be demonstrated between the bladder and the peritoneal cavity, sufficient transudation had occurred for abdominal distention to be noted during surgery, associated with marked clinical deterioration. The mechanism of death was complex, most likely involving: i) direct neurotoxic effects of glycine, ii) dilutional hyponatremia, and iii) direct respiratory compromise from reduced lung expansion due to increased intraperitoneal and pleural cavity fluid accumulation.

Careful exploration of the surgical site is required at autopsy in such a case to demonstrate any defects in the bladder wall, or possible communications with the peritoneal cavity. Analysis of urine, blood, and body fluid collections for glycine will assist in determining possible mechanisms of death. Electrolyte analysis is also necessary to demonstrate dilutional hyponatremia, as was also shown in the current case.

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