



# Case report on rhabdomyolysis after minimally invasive surgery for squamous cell carcinoma of the uterine cervix and adhesions due to deep infiltrating endometriosis☆

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## ABSTRACT

Rhabdomyolysis is a rare clinical condition resulting from severe muscle damage that can cause potentially life-threatening complications. Amongst other causes, muscle compression due to patient positioning during prolonged surgery may result in extensive skeletal muscle breakdown. We report on a 39-year-old nulligravida who developed rhabdomyolysis after prolonged laparoscopic surgery for cervical cancer and adhesions due to deep infiltrating endometriosis. Minimally invasive surgical procedures offer major advantages in gynecologic cancer surgery, and preventive methods provide effective pressure reduction and play a crucial role in avoiding physical harm after surgical positioning. Nevertheless, a combination of surgical and patient-related risk factors may increase the risk of postsurgical onset of rhabdomyolysis. Immediate referral to a specialist center is necessary to ensure prevention of serious complications.

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## 1. Introduction

Rhabdomyolysis is a rare condition resulting from acute necrosis and lysis of muscle fibers with subsequent distribution of intracellular muscle components to the blood. The condition is characterized by more than tenfold increases in serum creatine kinase (CK) levels [1]. Clinical symptoms are often unspecific, or even absent, and include muscle pain, tenderness, swelling, or impaired sensation in the muscle regions affected. Furthermore, dark-colored urine (pigmenturia) from myoglobinuria may occur [2]. In severe cases, rhabdomyolysis may cause electrolyte imbalances or compartment syndrome, and renal failure may occur as a potentially life-threatening subsequent complication in up to 46% of reported cases [2]. Risk factors for rhabdomyolysis include male gender, obesity, and prolonged operative times [3].

Furthermore, rhabdomyolysis may result from muscle membrane destruction caused by extensive exercise, drug/alcohol abuse as a direct toxin to myocytes, or physiological effects such as hyperthermia or arterial vasoconstriction. Connective tissue disease or inherited myopathies with congenital errors in glycogenolysis or other metabolic pathways can also lead to muscle destruction [4]. Moreover, compression of muscles during prolonged surgery can cause rhabdomyolysis due to surgical

positioning (especially flank or lithotomy positions) [5]. Hence, rhabdomyolysis has been described as a post-surgical complication, mainly after laparoscopic urological surgery and bariatric procedures [3]. Generous volume replacement with 0.9% saline solution under careful monitoring is indicated to prevent major harm, including heart failure or lung edema [2].

Here we report a case of rhabdomyolysis occurring after laparoscopic surgery in a patient with cervical cancer and deep infiltrating endometriosis (DIE).

## 2. Case

A 39-year-old nulligravida was referred to our department for further treatment of squamous cell carcinoma of the uterine cervix, grade (G) 2. Her surgical history was significant for three laparotomies for leiomyoma enucleation and resection of DIE. Furthermore, she underwent fertility treatment and several in-vitro fertilization cycles due to primary sterility. Her medical history was unremarkable aside from occasional smoking and an elevated body mass index of 27.7 kg/m<sup>2</sup>.

Clinical examination, including cystoscopy and rectoscopy to exclude parametrial, bladder, and rectal tumor involvement, revealed no infiltration of the two adjacent organs. Additionally, the patient underwent staging by magnetic resonance imaging of the thorax, abdomen, and pelvis in combination with positron emission tomography (PET). No pelvic lymph node enlargement, parametrial involvement, or metastatic disease was detected. PET revealed a hypermetabolic

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focus of 15 × 18 × 19 mm (standardized uptake value average 3.2) in the cervix, matching the cervical cancer. Thus, the diagnosis as established by clinical staging was consistent with Stage IB1 squamous cell carcinoma of the uterine cervix according to the International Federation of Gynecology and Obstetrics (FIGO) system.

Still wishing to preserve fertility, the patient primarily underwent large conization. However, histopathological work-up revealed microscopic positive margins (R1) and lymphangitis carcinomatosa (L1). Thus, hysterectomy and pelvic lymphadenectomy were discussed with the patient within a randomized study comparing total hysterectomy with radical hysterectomy for early-stage cervical cancer. The patient was randomized to the arm for total hysterectomy and pelvic lymph node dissection. Preoperative laboratory results were all within the normal range. For surgery, the patient was placed in a dorsal lithotomy, steep Trendelenburg position. Intraoperative inspection of the surgical site revealed a frozen pelvis with severe endometriosis due to DIE (revised American Society of Reproductive Medicine classification (rASRM), stage 4). As a consequence, extensive adhesiolysis and resection of endometriosis were necessary to enable hysterectomy and pelvic lymphadenectomy to be performed. Total surgery time was 5.5 h, due to the need for extended adhesiolysis, and total blood loss was 150 ml. No perioperative surgical and anesthetic complications occurred. Final pathology confirmed a G2 squamous cell carcinoma of the uterine cervix, TNM stage pT1b1 pN0 (0/5 sentinel lymph nodes; 0/42 lymph nodes) L1 V0 Pn1 R0.

After surgery, the patient was transported to the recovery room. Here she complained of nausea, severe pain, and cramps in the right calf and both shoulders. Magnesium was administered, and her symptoms gradually eased. However, postoperative laboratory evaluation revealed elevated levels of creatine kinase (CK; 7480 U/L, upper reference limit (URL) 170 U/L) and CK-MB (133 U/L, URL 24 U/L), with all other parameters being within the normal range. There were no irregularities in urinary volume. Postoperative pain was well controlled by oral tilidine and nonsteroidal anti-inflammatory drugs (NSAIDs).

Rhabdomyolysis was suspected and the patient was immediately transferred to the Department of Internal Medicine. Electrocardiography revealed no signs of cardiac ischemia, nor were there any increases in troponin T levels over time. The patient was instructed to maintain a daily fluid intake of at least 3 l and was returned to the gynecology ward the following day.

On postoperative day 2, creatinine levels increased to 9413 U/L (URL 170 U/L). The patient reported no persisting symptoms, and no impairment of kidney function was noted. On postoperative day 3, CK levels gradually began to decrease, and the patient was discharged without any symptoms on postoperative day 6.

### 3. Discussion

To the best of our knowledge, this is the first case of postoperative rhabdomyolysis described in a patient who underwent laparoscopic surgery for cervical cancer and DIE. Postoperative rhabdomyolysis has been previously reported predominantly in bariatric surgery cohorts and patients undergoing urologic surgery, and has been found to be associated with morbid obesity, patient positioning in a lateral position, and extended operating times [6, 7]. Thus, a combination of surgery- and patient-related risk factors may increase the risk of postsurgical development of rhabdomyolysis.

Rhabdomyolysis has been reported to develop following urologic procedures of at least 4.5 h' duration in the lithotomy position, highlighting the association between onset of rhabdomyolysis and prolonged operating time [7]. Furthermore, reduced perfusion pressure through elevation of the lower extremities may also contribute to muscle damage [6].

At our department, we have established guidelines for the prevention of intraoperative injuries and complications caused by patient positioning during prolonged minimally invasive surgical interventions. Our

precautionary measures include ensuring correct patient positioning every 2 h, using intermittent pneumatic compression pumps for the lower extremities, providing shoulder padding, and normalizing the patient's posture for about 10 min every 3 h. Such preventive methods have previously been demonstrated to effectively reduce pressure on sensitive parts of the body by spreading forces over larger areas and, thus, to play a crucial role in avoiding physical harm after gynecologic surgery [8].

In minimally invasive gynecologic surgery, the steep Trendelenburg position is usually preferred as it ensures pelvic visualization, thus enabling the surgery to be performed effectively. However, during prolonged surgery, the steep Trendelenburg may cause the patient to slip in the cranial direction, which can cause stretch injury of the brachial plexus, neck strain, and leg extension. This physical strain mostly results in postoperative pain and muscle weakness, but rarely leads to permanent sensory or motor deficits [8]. In addition to patient positioning, intra-abdominal pressures of 12–15 mmHg due to intraperitoneal CO<sub>2</sub> insufflation for laparoscopic surgery can contribute to reduced perfusion pressure and may increase the risk for rhabdomyolysis, especially in obese patients. Permissive hypertension could potentially improve tissue perfusion, thereby preventing the development of rhabdomyolysis. In the event of rhabdomyolysis, it can be important to maintain stable hemodynamic status in order to prevent hypotension and acidosis as potential contributing factors [2].

In the present case, even though prevention measures were applied properly and there were no apparent patient-related risk factors, it remains unclear why postoperative rhabdomyolysis developed. However, when asked about symptoms after previous surgery, the patient reported having experienced similar, though much weaker, symptoms after large conization. Here, the operating time of 40 min in lithotomy position differed significantly from the duration of, and positioning during, laparoscopic surgery. The symptoms reported after conization gradually resolved without any specific treatment. This suggests that apart from environmental factors, genetic factors may also contribute to the development of postoperative rhabdomyolysis.

A wide variety of rare genetic defects leading to metabolic or neuromuscular disorders are known to cause rhabdomyolysis [9]. A positive family history, exercise-induced muscle pain, and recurrent rhabdomyolysis can be predictors of a genetic condition [9]. Our patient's family history was negative for rhabdomyolysis. However, rhabdomyolysis may also result from a combination of environmental circumstances and genetic factors. Therefore, testing for rhabdomyolysis using a multi-step approach should be considered in questionable cases [9].

In conclusion, when rhabdomyolysis is suspected, immediate referral to a specialist center and close monitoring of CK levels and kidney function should be ensured in order to prevent serious complications. The present case may warrant further investigation in the setting of gynecologically complex, radical, and therefore prolonged surgical procedures. Correct patient positioning is critical in avoiding physical harm after gynecological surgery and thus, patients at a higher risk of developing postoperative rhabdomyolysis need to be monitored closely during perioperative management, as further complications may be prevented if muscle destruction is detected early.

### Contributor

All authors have contributed to conception and design of the study, drafting the article, revising it critically for important intellectual content.

All authors have approved the final article.

### Conflict of Interest Statement

The authors declare that they have no conflicts of interest and nothing to disclose.

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