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Case Report / Приказ болесника

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SUMMARY

Introduction Extragonadal seminomas are rare germ cell tumors that most often occur in the mediastinum and retroperitoneum. Primary localization in the urinary bladder is extremely rare and represents a diagnostic challenge. Acute presentation in the form of intra-abdominal bleeding and hemorrhagic shock has so far been extremely rarely described.

Case report The case of a 36-year-old man who was admitted due to severe abdominal pain, with a clinical picture of acute abdomen and hemorrhagic shock, is presented. Laboratory analyses showed anemia (hemoglobin 58 g/L) and a pronounced inflammatory reaction (CRP 314.8 mg/L). Ultrasound examination of the abdomen revealed a large amount of free intraperitoneal fluid, while native radiography of the abdomen showed several hydroaeric levels without signs of pneumoperitoneum. Due to hemodynamic instability and signs of peritoneal irritation, an urgent exploratory laparotomy was performed. Intraoperatively, a massive hemoperitoneum was verified with the presence of a large tumor with a diameter of about 25 cm, which originated from the wall of the urinary bladder and was actively bleeding. After controlling the bleeding, a complete excision of the tumor mass was performed. Pathohistological and immunohistochemical analysis confirmed the diagnosis of extragonadal seminoma. Clinical examination and evaluation of the testes revealed no abnormalities, thus confirming the primary extragonadal localization.

Conclusion Primary extragonadal seminoma of the bladder wall is an extremely rare condition that can manifest with massive hemoperitoneum and hemorrhagic shock. In hemodynamically unstable patients, urgent surgical exploration plays a key role in controlling bleeding and establishing a definitive diagnosis.

Keywords: extragonadal seminoma; germ cell tumor; urinary bladder; hemoperitoneum; hemorrhagic shock

САЖЕТАК

Увод Екстрагонадални семиноми су ретки тумори герминативних ћелија који се најчешће јављају у медијастинуму и ретроперитонеуму. Примарна локализација у мокраћној бешици је изузетно ретка и представља дијагностички изазов. Акутна презентација у виду интраабдоминалног крварења и хеморагичног шока до сада је изузетно ретко описана.

Приказ болесника: Приказан је случај 36-годишњег мушкарца који је примљен због јаких болова у стомаку, са клиничком сликом акутног абдомена и хеморагичног шока. Лабораторијске анализе су показале анемију (хемоглобин 58 г/Л) и изражену инфламаторну реакцију (CRP 314,8 мг/Л). Ултразвучни преглед абдомена је показао велику количину слободне интраперитонеалне течности, док је нативна радиографија абдомена показала неколико хидроаеричних нивоа без знакова пнеумоперитонеума. Због хемодинамске нестабилности и знакова перитонеалног надражаја, извршена је хитна експлораторна лапаротомија. Интраоперативно је верификован масивни хемоперитонеум са присуством великог тумора пречника око 25 cm, који је потицао из зида мокраћне бешике и активно је крварио. Након контроле крварења, извршена је комплетна ексцизија туморске масе. Патохистолошка и имунохистохемијска анализа потврдиле су дијагнозу екстрагонадалног семинома. Клиничким прегледом и евалуацијом тестиса нису откривене абнормалности, чиме је потврђена примарна екстрагонадална локализација.

Закључак Примарни екстрагонадални семином зида бешике је изузетно ретко стање које се може манифестовати масивним хемоперитонеумом и хеморагичним шоком. Код хемодинамски нестабилних пацијената, хитна хируршка експлорација игра кључну улогу у контроли крварења и постављању дефинитивне дијагнозе.

Кључне речи: екстрагонадални семином; тумор герминативних ћелија; мокраћна бешика; хемоперитонеум; хеморагични шок

INTRODUCTION

Germ cell tumors are the most common malignant tumors in younger men and in most cases arise in the testicles [1]. However, approximately 2–5% of all germ cell tumors occur in extragonadal locations, most often along the midline of the body, including the mediastinum, retroperitoneum, and central nervous system [2]. The mechanism of their origin has not been fully

elucidated, and the most accepted theory implies the lag of primordial germ cells during embryonic migration. Histologically, seminoma represents one of the most common subtypes of extragonadal germinal tumors and is characterized by high sensitivity to therapy based on platinum preparations, which is why timely diagnosis has great prognostic significance [3].

Primary extragonadal seminoma of the urinary bladder is an extremely rare clinical entity. In the available literature, mostly individual case reports. The available literature primarily consists of individual case reports, resulting in a lack of, which is why there are no clearly defined diagnostic or therapeutic guidelines. The clinical picture is usually non-specific and includes hematuria, symptoms of the lower urinary tract, or pain in the small pelvis, while the definitive diagnosis is usually made only after the pathohistological and immunohistochemical analysis of the operative preparation. At the same time, it is necessary to rule out the existence of a primary testicular tumor by clinical examination and ultrasound examination of the scrotum in order to confirm the extragonadal nature of the disease [3, 4].

Even rarer is the presentation of extragonadal seminoma as an acute abdomen due to spontaneous intra-abdominal hemorrhage. In such cases, patients usually present with a clinical picture of hemorrhagic shock, which is why urgent surgical intervention is necessary, while the final diagnosis is made only after histopathological and immunohistochemical analysis. Precisely because of the extreme rarity of this clinical presentation, the presentation of individual cases has a significant contribution to a better understanding of diagnostic and therapeutic challenges [3, 5].

In this paper, we present the case of a 36-year-old man with a primary extragonadal seminoma originating from the bladder wall and presenting with massive hemoperitoneum, hemorrhagic shock, and clinical presentation of an acute abdomen, which required urgent exploratory laparotomy and tumor excision.

CASE REPORT

A 36-year-old male patient was admitted to the Surgical Clinic due to the sudden onset of severe abdominal pain, followed by a progressive worsening of the general condition. On physical examination, the abdomen was diffusely tender, with pronounced muscular defense and signs of generalized peritoneal irritation, while the clinical picture of the patient corresponded to hemorrhagic shock, which required immediate resuscitation and urgent surgical intervention.

Initial laboratory tests showed mild leukocytosis with neutrophilia (WBC $10.32 \times 10^9/L$, neutrophils 83.99%), anemia (RBC $2.8 \times 10^{12}/L$, hemoglobin 58 g/L), hypoalbuminemia (34 g/L), hypoproteinemia (57.7 g/L), elevated inflammatory markers (CRP 314.8 mg/L), elevated creatine kinase (347 U/L) and CK-MB (29.3 U/L), while serum lactate was within normal limits (0.7 mmol/L). Serum tumor markers (received postoperatively) showed normal values of alpha-fetoprotein (AFP, 2.99 ng/mL), carcinoembryonic antigen (CEA, 3.18 ng/mL), carbohydrate antigen 19-9 (CA 19-9, 0.600 U/mL), prostate-specific antigen (PSA, 0.568 ng/mL), and free prostate-specific antigen (Free PSA, 0.286 ng/mL), while neuron-specific enolase (NSE) was significantly elevated (148.7 ng/mL).

Abdominal ultrasound examination showed a large amount of free intraperitoneal fluid, inter-intestinal, intestinal coils dilated and swimming in fluid. (Figure 1) A native radiograph of the abdomen showed several air-liquid levels, without signs of pneumoperitoneum.

Considering the patient's hemodynamic instability, diffuse signs of peritoneal irritation and clinical suspicion of intra-abdominal hemorrhage, an urgent exploratory laparotomy was performed without additional radiological processing. Upon entering the abdominal cavity, a massive hemoperitoneum with a large amount of fresh blood and blood clots was found. After the evacuation of the sanguineous contents, a large hemorrhagic tumor with a diameter of about 25

cm was identified by detailed exploration, which originated from the wall of the urinary bladder. The tumor was actively bleeding and was the source of intra-abdominal bleeding responsible for the onset of hemorrhagic shock. Complete surgical excision of the tumor was performed with careful hemostasis, and the specimen was sent for pathohistological and immunohistochemical analysis. (Figure 2)

Macroscopic pathological findings showed a large solid hemorrhagic tumor with marked zones of fresh and organized bleeding. (Figure 3) Microscopic findings revealed mostly cells with circular, hyperchromatic and partly hypochromatic nuclei with visible nucleoli, basophilic cytoplasm. The entire tumor is permeated with numerous blood vessels, especially subcapsular. Edema of the stroma and microcysts can also be observed in parts. Fields of massive necrosis as well as rare mitoses are present. Immunohistochemical analysis made a definitive diagnosis of extragonadal seminoma. (Figure 4) Immunoprofile of the tumor: CD117+, D2-40+, HCG+, OCT3/4+/-, AFP-, CD30-, GATA3-. Ki67 proliferative index is about 30%. Extensive necrosis is present, as is vascular invasion.

Subsequent clinical and ultrasonographic examination of the testicles revealed no palpable abnormalities, which supported the diagnosis of primary extragonadal seminoma and not metastatic disease originating from an occult testicular primary tumor.

The postoperative course went smoothly, and the patient was referred to the oncology council for further staging and planning of multidisciplinary treatment. The oncology council made a decision on systemic HT according to the PEB protocol.

DISCUSSION

Extragonadal germ cell tumors represent a rare group of malignancies and account for approximately 2–5% of all germ cell tumors. They most often occur in the mediastinum, retroperitoneum and pineal region, while localization in the urinary bladder is extremely unusual [2]. The pathogenesis of these tumors has not been fully elucidated, and the most accepted theory implies a disturbance in the migration of primordial germ cells during embryogenesis, with their retention in ectopic locations [6]. Another theory supports the existence of an occult or regressed ("burned-out") primary testicular tumor. In our case, the absence of clinical testicular abnormalities was in favor of a primary extragonadal origin of the tumor [3, 4].

The special value of the presented case is the extremely rare location of the tumor. In the available literature, only individual cases of seminoma involving the urinary bladder are described, whereby most of the described cases are the result of secondary spread of the tumor originating from the testicles or other extravesical localizations [7]. Primary extragonadal seminoma of the bladder wall is a clinical entity of which there are only sporadic reports. Therefore, there are no clear recommendations on the optimal diagnostic and therapeutic approach, and most conclusions are based on experiences from individual cases. The tumor in our patient was large (about 25 cm), which is probably the result of slow growth and the absence of specific symptoms in the early stages of the disease [3-5].

The clinical presentation of our patient was significantly different from the previously described cases. The most common symptoms of extragonadal seminomas involving the urinary bladder include hematuria, dysuric complaints, lower urinary tract obstructive symptoms, or pelvic pain [3]. In contrast, our patient presented with an acute abdomen, hemorrhagic shock and massive hemoperitoneum. This presentation is extremely rare even in intra-abdominal seminomas. Spo-

radic cases of spontaneous rupture of seminoma in an undescended testis or bleeding of metastatic retroperitoneal masses with the development of hemoperitoneum are described in the literature, but data on primary extragonadal seminoma of the bladder wall leading to intra-abdominal hemorrhage are practically non-existent [8-10].

In the diagnostic sense, this case indicates the importance of timely surgical decision-making in patients with unclear etiology of hemoperitoneum and hemodynamic instability. The ultrasound finding of a large amount of free fluid and the absence of pneumoperitoneum on the native radiograph did not allow establishing an etiological diagnosis, but, together with the clinical picture of peritoneal irritation and hemorrhagic shock, represented a clear indication for urgent exploratory laparotomy. In such situations, postponing operative treatment for the sake of additional diagnostics can worsen the outcome and endanger the patient's life. In our patient, the definitive diagnosis was made only after intraoperative findings and pathohistological analysis of the preparation [3, 8, 9].

Pathohistological and immunohistochemical analysis play a key role in the diagnosis of extragonadal seminoma. Morphologically, the tumor is characterized by uniform large cells with light cytoplasm and pronounced nucleoli, arranged in nests separated by fibrous septa with lymphocytic infiltrate. Immunohistochemical markers such as PLAP, OCT3/4, SALL4 and CD117 represent an important aid in confirming the diagnosis and differentiating seminoma from other malignant bladder tumors, including poorly differentiated urothelial carcinomas, lymphomas and other "small round cell" tumors [3, 4]. In our case, immunohistochemical analysis was of crucial importance for establishing the final diagnosis.

The therapeutic approach to extragonadal seminomas is based on multimodal treatment that includes surgery, systemic chemotherapy and, in some cases, radiotherapy. However, in patients with acute intra-abdominal hemorrhage and hemorrhagic shock, the priority is urgent

surgical control of bleeding and removal of the tumor mass. In our case, the operation had not only therapeutic, but also diagnostic significance, as it enabled a definitive diagnosis and further planning of oncological treatment. Good sensitivity of seminoma to cisplatin-based chemotherapy represents an important prognostic factor and allows a favorable outcome even in advanced forms of the disease [3, 4].

Primary extragonadal seminoma of the urinary bladder is an extremely rare entity that can present atypically, including acute abdomen due to massive intra-abdominal hemorrhage. In hemodynamically unstable patients, urgent surgical exploration can be of crucial importance to control bleeding and establish a definitive diagnosis. Pathohistological and immunohistochemical analysis play a key role in confirming the diagnosis and planning further oncological treatment.

Ethical compliance statement: We confirm that we have read the journal's position on issues involving ethical publication and affirm that work is consistent with those guidelines.

Ethical standards: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest: None declared.

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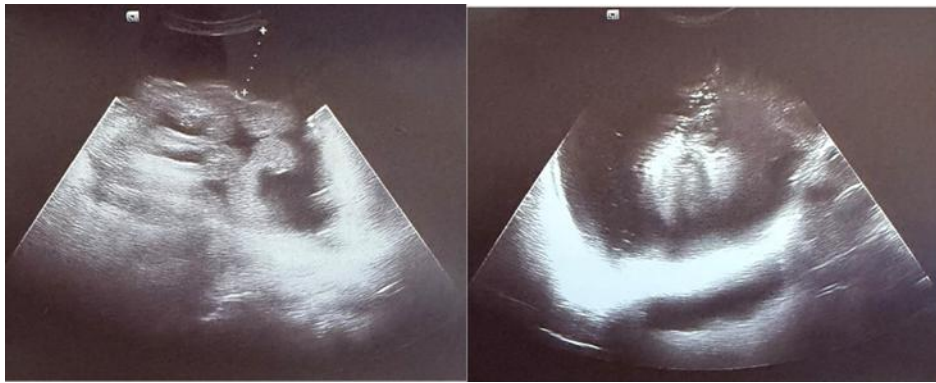


Figure 1. Abdominal ultrasound examination at admission of the patient showing a large amount of free intraperitoneal fluid

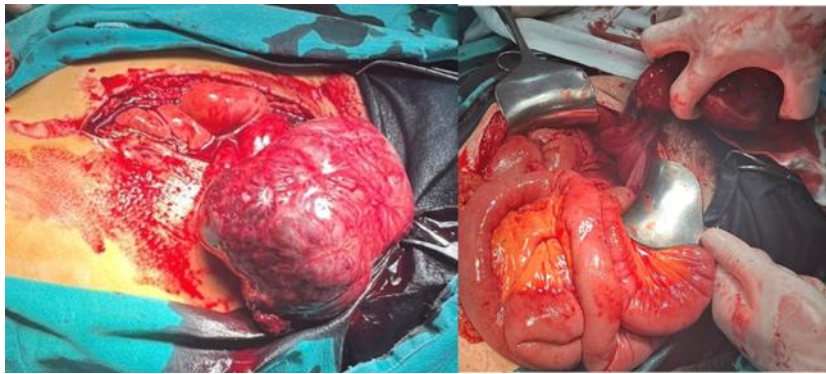


Figure 2. Intraoperative view of a tumor mass originating from the bladder wall with the presence of hemoperitoneum

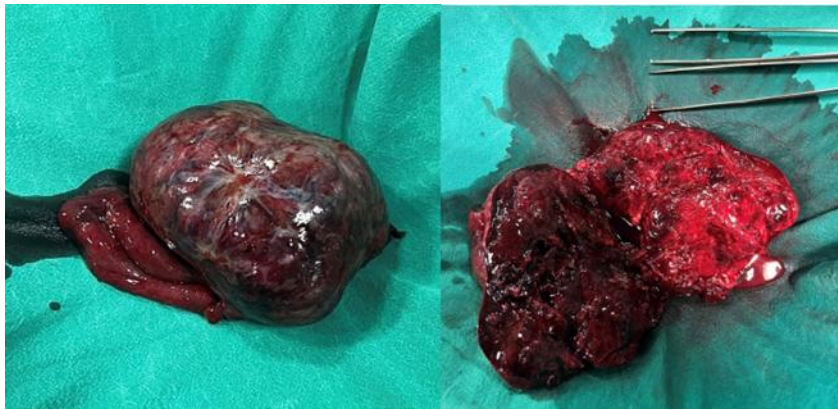


Figure 3. Macroscopic appearance of the tumor after surgical excision: solid tumor mass with hemorrhagic zones and cross-section of the tumor

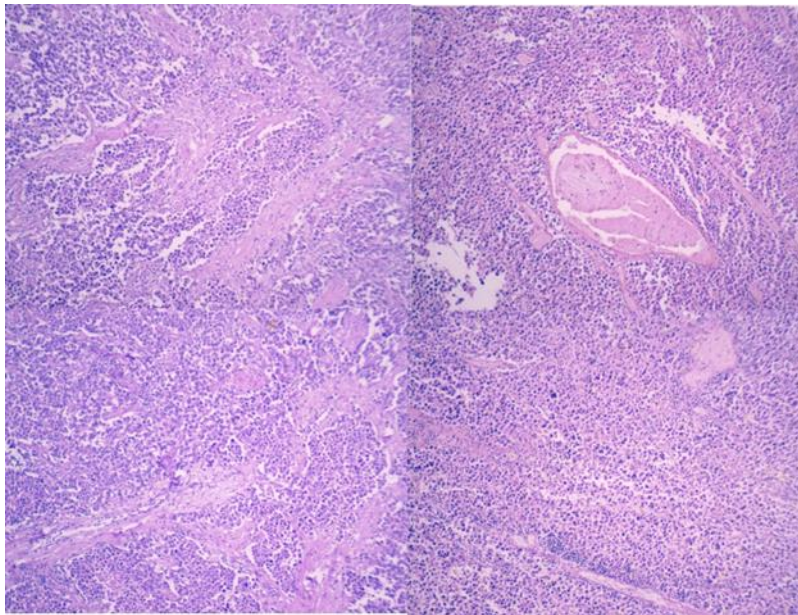


Figure 4. Tumor profile (magnification 10×0.25)