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TESTICULAR MIXED GERM CELL TUMOR PRESENTING WITH UPPER GASTROINTESTINAL BLEEDING: A CASE REPORT

Emilija Nikolovska Trpchevska[1], Beti Todorovska[1], Magdalena Bogdanovska Todorovska[2], Meri Trajkovska[1], Dafina Nikolova[1], Darko Dzambaz[3], Gjorgji Deriban[1], Fana Licoska-Josifovikj[1]

[1] University Clinic of Gastroenterohepatology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, RN Macedonia

[2] University of Ss. Cyril and Methodius, Faculty of Medicine, Institute of Pathology, Skopje, RN Macedonia

[3] University Clinic of Digestive Surgery, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, RN Macedonia

Corresponding author: Emilija Nikolovska Trpchevska, University Clinic of Gastroenterohepatology, Faculty of Medicine, Ss. Cyril and Methodius University, Skopje, RN Macedonia; email: emilijanikolovskageh@gmail.com

ABSTRACT

Testicular mixed germ cell tumors (TMGCTs) are aggressive neoplasms that often have metastases at the time of diagnosis, primarily in the lungs, bones, and brain. Gastrointestinal metastases are rare, occurring in less than 5% of cases, while duodenal involvement is extremely rare, with only few reported cases. Furthermore, gastrointestinal bleeding is an atypical initial presentation of metastatic TMGCTs. Herein, we present a very rare case of upper gastrointestinal bleeding caused by a duodenal metastasis of a TMGCT in a 24-year-old man. The patient was admitted to our hospital due to abdominal pain and melena with a hemoglobin level of 52 g/L. He had no history of testicular swelling, or any other symptoms or signs of a testicular tumor. Upper gastrointestinal endoscopy revealed a duodenal tumor mass with irregular bleeding, and abdominal ultrasound and computed tomography showed a duodenal mass that infiltrate retroperitoneum. Emergency surgery was performed, and the histopathological findings of the resected specimen were consistent with TMGCT metastasis. Subsequently, a testicular tumor was confirmed and surgically removed; however, multiple metastatic deposits were observed in the lungs. Due to the patient's poor general condition, chemotherapy was not performed. The patient died 3 months after the initial diagnosis. This case suggests that, although duodenal metastatic TMGCTs are rare, they should be considered in the differential diagnosis of gastrointestinal bleeding in young male patients.

Keywords: upper gastrointestinal bleeding, duodenal metastasis, testicular mixed germ cell tumor

INTRODUCTION

Testicular germ cell tumors are divided into seminomas and non-seminomas. Mixed germ cell tumors, which belong to the latter group, account for approximately 32−60% of all germ cell tumors and occur in younger patients 15−35 years of age [1]. They usually contain more than two components; choriocarcinoma cells are often seen with other types of non-seminoma cells [2,3]. Testicular mixed germ cell tumors have a malignant potential similar to that of pure testicular choriocarcinomas [4], which represent less than 1% of all testicular [5,6], and are likely to spread quickly to other parts of the body, including the lungs, bones, and brain. Gastrointestinal metastases are rare, with an incidence of less than 5%, and duodenal involvement has been reported

in only 1.4% of cases [7,8]. Herein, we report a rare case of a testicular mixed germ cell tumor initially presenting with gastrointestinal bleeding from a duodenal metastasis.

CASE REPORT

A 24-year-old male patient was admitted to our hospital due to upper gastrointestinal bleeding. Emergency endoscopic gastroduodenoscopy revealed a submucosal tumor mass in the third duodenal portion, with a large surface ulceration with a clot in the bottom surrounded by elevated, irregular edges (Figure 1). Several biopsy samples were collected, and histopathological analysis revealed a malignant neoplasm with morphological characteristics of a mixed germ cell tumor.

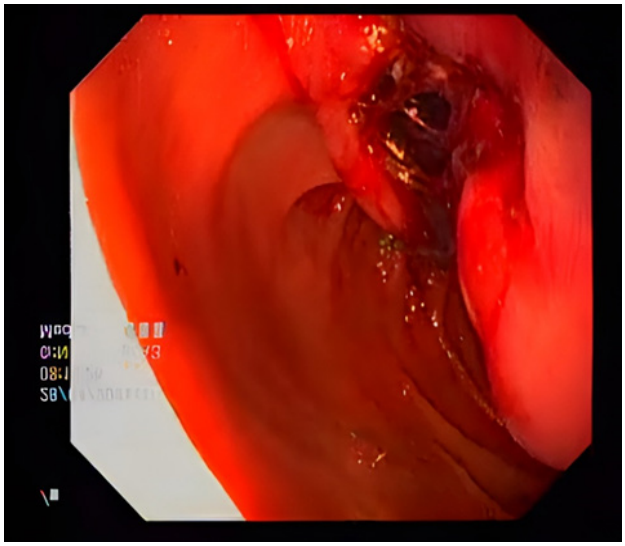


Figure 1. *Endoscopic findings on admission.*

Additionally, abdominal ultrasound showed a large tumor mass with a diameter of 10 cm located in the retroperitoneum. Computed tomography (CT) revealed active bleeding duodenal mass that infiltrate into retroperitoneum (Figure 2). Therefore, emergency surgical treatment was indicated.



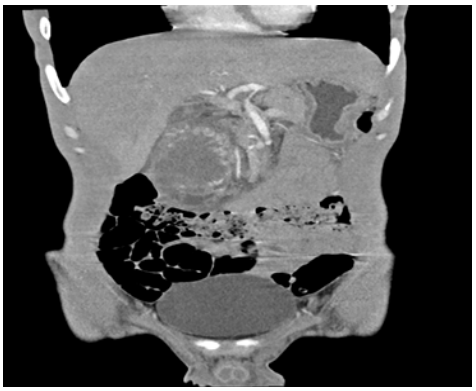


Figure 2. *Axial (A) and coronal (B) computed tomography images showing bleeding duodenal mass that infiltrate into retroperitoneum*

Resection of duodenum and extirpation of retroperitoneal tumor were performed and the bleeding was stopped (Figure 3). Postoperatively, the patient received pantoprazole therapy and a transfusion of two blood units. However, several days after the surgery, he developed acute abdomen due to kinking of the gastrojejunal anastomosis. Revision surgery was performed and a new gastrojejunal anastomosis was made.

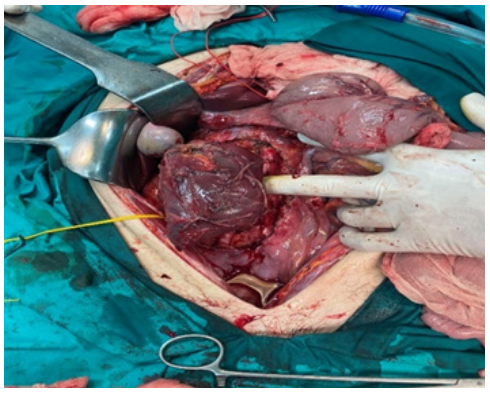


Figure 3. *Intraoperative image of the retroperitoneal tumor mass.*

Histopathological examination of the surgical specimen revealed the following. Macroscopically, the tumor consisted of a large, tan-to-gray-colored, soft tissue mass measuring 10×6×5 cm, with extensive hemorrhagic and necrotic zones on the surface and a cystic component at the periphery (Figure 4A). Microscopically, the tumor was composed of a mixture of mononuclear cytotrophoblast cells, multinucleated syncytiotrophoblast cells, and intermediate trophoblast with extensive hemorrhage and necrosis (Figure 4B). Mitotic figures were frequent, and vascular invasion was also present. In addition to the choriocarcinomatous component, the tumor contained a teratomatous

component, comprising epidermoid, columnar, and mucinous cells, and small foci of mature lymphoid and smooth muscle tissue. Immunohistochemical staining revealed diffuse strong positivity for CKAE1/AE3. Many of the syncytiotrophoblast cells were positive for beta human chorionic gonadotropin (β-hCG; Figure 4C). Both cytotrophoblast and syncytiotrophoblast cells were positive for CK7, CK18, and CK19, and negative for MUC2, MUC5AC, CK20, CK5/6, CDX2, vimentin, CD30, PLAP, and OCT3/4. The final histopathological diagnosis was mixed germ cell tumor with choriocarcinoma (70%) and teratoma components (30%).

Following the receipt of the histopathological findings, additional testing was performed. Laboratory analysis showed an elevated β-hCG level (3,000 IU/L), and chest CT showed multiple metastatic deposits in the lungs. The urological physical examination revealed a tumor mass in the right testicle, which was subsequently surgically removed. The postoperative histopathological findings were consistent with a germ cell tumor with a mixed choriocarcinoma (6070%) and teratoma morphology (30−40%). Therefore, primary testicular mixed germ cell tumor was diagnosed. Postoperatively, the patient's condition was poor; thus, salvage chemotherapy was postponed. However, the patient died 3 months after last surgery.

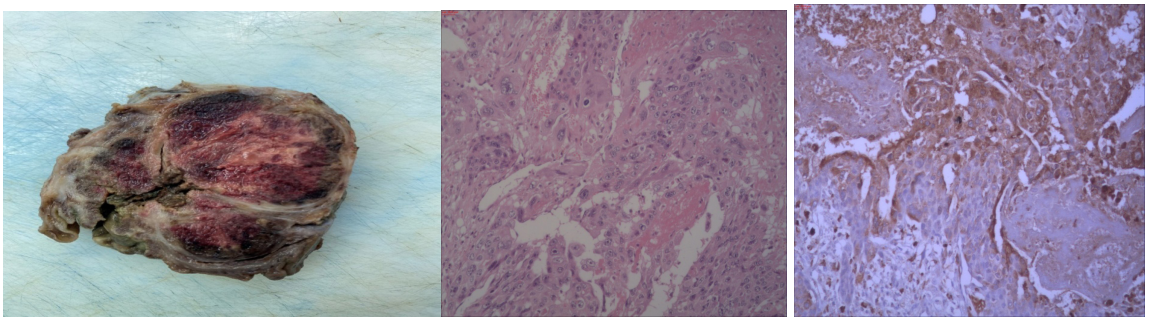


Figure 4. *Histopathological findings. A) Macroscopic image showing a soft tissue tumor mass with necrotic, hemorrhagic, and cystic components; B) Photomicrograph showing mononuclear polygonal cytotrophoblast cells and multinucleated syncytiotrophoblast cells with eosinophilic cytoplasm and large hyperchromatic nuclei (hematoxylin and eosin staining, magnification ×100); C) Photomicrograph showing positive immunohistochemical staining for beta human chorionic gonadotropin (anti-β-hCG staining, magnification ×100).*

DISCUSSION

Testicular germ cell tumors are the most common tumors in young men, accounting for 95% of all solid tumors in this population. They usually present with a painless testicular swelling; however, in rare cases, there may be wide-spread metastases without a palpable or visible on imaging testicular mass [9]. These are called burned-out tumors, and in such cases, clinical diagnosis can be difficult [10]. In addition, germ cell tumors are commonly associated with increased plasma levels of β-hCG and alpha-fetoprotein. In our patient, although the diagnosis was confirmed histopathologically, laboratory testing showed high β-hCG levels, but the level of alpha-fetoprotein was within the normal range.

Testicular ultrasound is an imaging technique with a 100% sensitivity for detecting a testicular mass, while CT and magnetic resonance imaging can provide a better estimation of the extent of the disease [11]. Fast-growing tumors are usually associated with early metastases. Our patient had an active bleeding duodenal tumor deposit that infiltrate into retroperitoneum, and multiple metastasis in the lungs were detected.

Gastrointestinal metastases of solid malignant tumors are rare, occurring in less than 5% of cases, with deposits most commonly found in the stomach. The most common tumors that give rise to the gastric metastases are breast, lung, and esophageal cancer, and malignant melanoma, while gastrointestinal metastases of germ cell tumors are rare. Prior studies have demonstrated that gastrointestinal involvement is more likely with non-seminoma than with seminoma germ cell tumors [12,13]. Metastatic deposits in the stomach more often present as solitary than as multiple lesions [14,15], and their endoscopic features may resemble those of peptic ulcers, submucosal lesions, polyps, or black spots characteristic of malignant melanoma. For these reasons, it is sometimes difficult to distinguish between a pri-

mary tumor and metastatic deposit endoscopically [16,17] and it is even more difficult to distinguish if the tumor mass is primary metastasis in the duodenum or it is infiltrating metastasis from retroperitoneum. Duodenal metastatic lesions are extremely rare, reported in only 1.4% of cases. Altamar et al. reported a case of testicular seminoma with a small component of embryonal carcinoma in a 20-year-old man with a metastatic deposit in the duodenum [18]. In the present case, the metastatic lesion was solitary, located in the duodenum, and endoscopically closely resembled a submucosal tumor with active bleeding.

Upper gastrointestinal bleeding is an extremely rare initial manifestation of metastatic testicular germ cell tumors, particularly with duodenal involvement [19,20]. The most frequently reported gastrointestinal manifestations include abdominal pain (46%) and melena (44%), followed by hematemesis and hematochezia in approximately 24% of cases, while non-bloody vomiting, abdominal mass, and distension are less common [21]. Duodenal metastases usually present with melena and/or hematemesis, along with anemia. Our patient was admitted with abdominal pain and melena, and severe anemia.

Seminomas have a better prognosis than non-seminoma germ cell tumors; they are less aggressive, usually diagnosed at an early stage, and more sensitive to radiation therapy and platinum-based chemotherapy [22]. The treatment of mixed germ cell tumors is similar to that of pure choriocarcinomas because of the similar aggressiveness and high metastatic potential of these two tumor types. Approximately 8% of testicular germ cell tumors contain a choriocarcinoma component. In our case, the tumor was composed of cells with choriocarcinoma (60−70%) and teratoma (30−40%) morphology [23,24]. Current guidelines recommend cisplatin-based combination chemotherapy with bleomycin, etoposide, and cisplatin as first-line therapy for advanced non-seminoma germ cell tumors [25,26]. In our patient, salvage chemotherapy was not started due to his poor general condition following the surgical treatment.

CONCLUSION

Upper gastrointestinal bleeding is an atypical initial clinical manifestation of a duodenal metastasis of a testicular mixed germ cell tumor. Nonetheless, this case suggests that this aggressive and highly metastatic malignant disease should be considered in the differential diagnosis of gastrointestinal bleeding in young male patients.

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Резиме

МЕШАН ГЕРМИНАТИВЕН ТЕСТИКУЛАРЕН ТУМОР МАНИФЕСТИРАН СО ГОРНОДИГЕСТИВНО КРВАВЕЊЕ – ПРИКАЗ НА СЛУЧАЈ

Емилија Николовска Трпчевска[1], Бети Тодоровска[1], Магдалена Богдановска Тодоровска[2], Мери Трајковска[1], Дафина Николова[1], Дарко Џамбаз[3], Ѓорѓи Дерибан[1], Фана Лицоска-Јосифовиќ[1]

[1] Универзитетска клиника за гастроентерохепатологија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[2] Институт за патологија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

[3] Универзитетска клиника за дигестивна хирургија, Медицински факултет, Универзитет „Св. Кирил и Методиј“ во Скопје, РС Македонија

Мешаните герминативни тумори на тестисите (TMGCTs) се агресивни неоплазми што најчесто при поставување на дијагнозата имаат далечни метастази, првенствено во белите дробови, во коските и во мозокот. Гастроинтестиналните метастази се ретки, се јавуваат во помалку од 5% од случаите, додека метастатски депозит во дуоденумот се среќава исклучително ретко, со мал број објавени случаи во литературата. Гастроинтестиналното крвавење е атипична презентација на метастатски TMGCTs.

Се опишува многу редок случај на горно гастроинтестинално крвавење предизвикано од дуоденална метастаза на TMGCT кај 24-годишен маж. Пациентот беше примен поради болки во стомакот и мелена со ниво на хемоглобин од 52 g/L, без историја и клинички знаци за тумор на тестисите.

Горнодисгестивната ендоскопија покажа дуоденална туморска маса со неправилни рабови и активно крвавење, а абдоминалниот ултразвук и компјутерската томографија покажаа крвавечка метастаска лезија во дуоденум, која пропагира и кон ретроперитонеум. По хируршкиот третман, хистопатолошкиот наод на ресецираниот примерок е во прилог на метастатски депозит на TMGCT. Последователно, туморот на тестисите беше потврден при физикален преглед и ултразвук, а потоа и хируршки отстранет. Следно, кај пациентот беа нотирани и повеќе метастатски депозити во белите дробови. Поради лошата општа состојба на пациентот, не беше започнат онколошки третман со хемотерапија. Пациентот почина три месеци по првично поставената дијагноза. Овој случај сугерира дека, иако дуоденалните метастатски TMGCT се ретки, тие треба да се земат предвид при диференцијалната дијагноза на гастроинтестиналното крвавење кај младите машки пациенти.

Клучни зборови: горно гастроинтестинално крвавење, дуоденални метастази, мешан тумор на герминативните клетки на тестисите