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Krukenberg Tumor in A 26-Year-Old Young Patient with Primary Location in the Stomach: A Case Report

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ABSTRACT

Objective: *Report a case of a 26-year-old patient diagnosed with Krukenberg tumor with the primary site localized in the stomach.*

Methods: *The researchers obtained the information through a review of the medical record, an interview with the patient, a photographic record of the diagnostic methods to which the patient was submitted, and a literature review.*

Final Considerations: *The case reported and publications raised expand knowledge regarding the course and management of the disease in young patients, which still needs to be clarified in the medical community and needs more studies.*

Keywords

Krukenberg Tumor, Neoplasm Metastasis, Young Adult.

Introduction

First described in 1896 by Friedrich Ernst Krukenberg (1871-1946) [1], Krukenberg tumor is a rare pathology secondary to a neoplasm that can have its primary origin in various places in the human body, such as the gastrointestinal tract (GIT), the breast or the thyroid. This tumor is usually bilateral, voluminous, and asymptomatic and usually affects slightly older women, especially in the premenopausal period. It has a worse prognosis when its primary origin is in the GIT compared to other primary sites in which it can originate [2].

Gastric cancer spreads via hematogenous, lymphatic, and surface implantation routes, considering that the rate of lymphatic metastasis to the ovary from gastric cancer is higher when compared to colorectal or biliary cancer. It is relevant to highlight that metastases from gastric cancer to the female genital tract are rare but significantly worsen patients' prognosis, especially when the metastases involve the ovaries [3].

The diagnosis of Krukenberg's tumor follows the World Health Organization (WHO) diagnostic criteria, which includes stromal involvement, the presence of mucin-producing neoplastic signet ring cells, and sarcomatoid proliferation of the ovarian stroma, or it can also be clinically defined as any metastatic ovarian carcinoma derived from other body sites [2]. This tumor can be asymptomatic

or manifest with unspecific symptoms, such as the appearance of a pelvic mass, abdominal pain or pelvic pain, back pain, generalized edema, ascites, and dyspareunia [4]. Faced with unspecific signs and symptoms, the investigation of this intriguing disease involves obtaining images to aid diagnosis, which include Ultrasonography (USG) of the abdomen and pelvis, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) [5].

An ideal treatment strategy for these tumors has yet to be established. To date, there are some alternatives for therapy, such as cytoreductive surgery, adjuvant chemotherapy, or intraperitoneal hyperthermic chemotherapy. However, it has yet to be defined which treatment or combination of treatments is related to higher survival rates for patients with this pathology [6].

Case Report

TOM, 26 years old, white, with two pregnancies, one vaginal delivery, and one miscarriage (G2P1+1), in use of an intrauterine device (Mirena). She had no comorbidities, allergies, or addictions and denied any medication intake. She was admitted to the Gynecological Emergency Department of the Santa Casa de Misericórdia de Vitória Hospital (HSCMV), complaining of an increasing abdominal volume observed 15 days ago, associated with nausea and pelvic pain. Physical examination on admission: the patient is in good general condition, alert, oriented, ruddy, hydrated, anicteric, acyanotic, and afebrile. Abdominal examination: soft, nontender, and nondistended abdomen with a hardened, fixed mass extending from the pubic symphysis to the umbilical scar, painless on superficial and deep palpation, no signs of peritoneal irritation. Speculum examination: vagina with preserved roughness and elasticity, no lesions with the rotation of the speculum, epithelialized cervix, no visible lesions, no abnormal discharge or bleeding. No Intrauterine Device (IUD) thread was visible. A mass bulging in the rectouterine pouch interfered with this examination. Bimanual examination revealed a large palpable mass on the anterior vaginal wall and rectouterine pouch. At the time she was first seen, the patient already had a total abdominal ultrasonography (USG) showing a solid mass containing cysts in the hypogastric region with regular contours, hypervascularized, measuring 14x12x9 cm, as well as another mass with the same characteristics in the rectouterine pouch, measuring 7.5x5.2x4.5 cm and a slight ascites. The patient also had previous laboratory tests showing an increase in the enzyme alkaline phosphatase (1003 U/L). Given the clinical picture, the patient was admitted to the hospital for further investigation, and we ordered new laboratory tests, including tumor markers and a new Doppler Transvaginal USG (USG-TV). During the first few days in the hospital, the patient complained of lower back pain, besides the pelvic pain and malaise already reported in the admission. The USG-TV carried out at the service showed two complex images, predominantly solid, with well-defined boundaries and large solid areas, intensely vascularized on color Doppler, one of them located in the posterior region on the right, measuring 98x82x77 mm, with a volume of 328.81 cc and the other in the anterior area on the left, measuring 170x121x138 mm, with a volume of 1847 cc. Free fluid was noted in the abdominal cavity (compatible with ascites) and both costophrenic sinuses (compatible with pleural effusion). In addition, the new laboratory tests requested showed maintaining alteration in the alkaline phosphatase enzyme (789 U/L), as well as an alteration in hemoglobin (9.2 g/dL), CA19-9 (589.27 U/mL) and CEA (36.01 ng/mL) markers and a significant thrombocytopenia of 66,000/mm3. Given the thrombocytopenia and the patient's back pain, the assistant team suggested the hypothesis of medullary infiltration due to the ovarian mass seen on the USG.

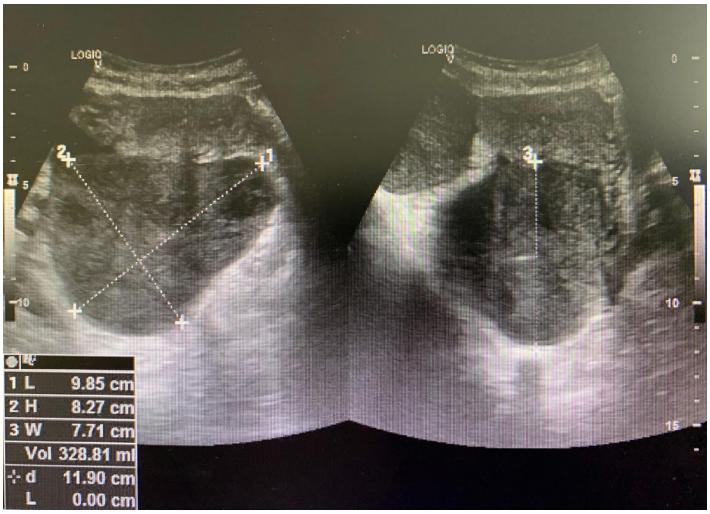

Figure 1: Transvaginal ultrasound showing two complex images, predominantly solid, with well-defined boundaries, and large solid areas, intensely vascularized on color Doppler.

For further investigation of the ovarian mass, the attending medical team ordered Computadorized Tomographies (CT scan) of the chest, abdomen, and pelvis. The CT scans of the abdomen and pelvis showed a large, mixed, heterogeneous mass, with solid lumps and dense material in between, with some septations and peripheral enhancement by the contrast, with a heterogeneous density predominantly of thick liquid, located in the pelvic cavity anteriorly, extending from the supravesical region to the supraumbilical, measuring approximately 17x13.9x6.8 cm in its longest axes. In the same CT scan, another mass with the same characteristics was seen in the hypogastric region, measuring approximately 8.3x9.75x7.1 cm. The chest CT scan showed a bilateral pleural effusion, more extensive on the right, but with a thickness of only 3.3 cm, associated with atelectasis of the lung bases in correspondence. Therefore, the team decided not to indicate relief thoracentesis at the moment.

The patient was referred to the operating room for an exploratory laparotomy due to the bilateral ovarian mass shown on imaging tests. An inventory of the cavity revealed an asymmetrical bilateral ovarian mass and a small amount of ascitic fluid. The surgery team performed a right oophorectomy and sent the specimen for flash freezing. They also collected the ascitic fluid and sent it for laboratory analysis. At the time of freezing, a pathologist analyzed the sections of the removed specimen, which showed signs of malignancy, suggesting a diagnosis of Krukenberg tumor. A left oophorectomy was also performed. After the approach, all the material removed was sent for histopathological analysis, and the

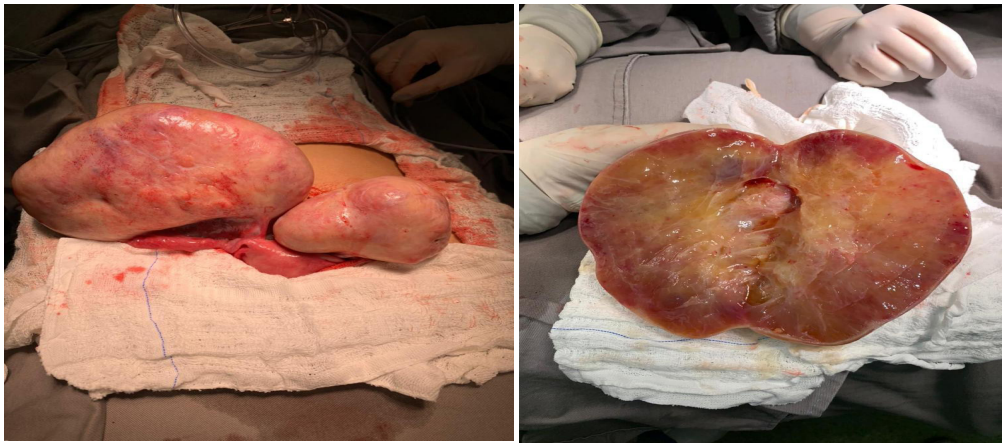

Figure 2: Ovarian masses removed in the operating room and sent for histological analysis.

patient went to the ward.

Two days after the surgical procedure, the patient was discharged from the hospital under the supervision of the gynecology team, as she remained asymptomatic after the surgery and had no complications. She was instructed to maintain post-operative and investigative follow-up with the gynecology team on an outpatient basis and to carry out endoscopic research on the gastric mucosa and other sites of metastasis. Three days after discharge, the patient returned to the gynecological emergency room complaining of low back pain and hypogastric pain refractory to pain medicines associated with episodes of nausea. The team requested new laboratory tests that showed a significant drop in hemoglobin (5.1 g/dl) and thrombocytopenia (73,000 thousand/mm3). The pain kept refractory to the medicines prescribed in the emergency room. The attending team decided to readmit the patient, prioritizing pain control. They also prescribed two red blood cell concentrates and ordered a new CT scan of the abdomen and pelvis, as well as upper digestive endoscopy (EGD) and colonoscopy to investigate the primary site of the tumor, the origin of the bleeding, and possible metastases. These imaging tests had already been requested and were scheduled but had not yet been carried out by the patient. The colonoscopy showed no significant alterations, but the EGD revealed moderate endoscopic enanthematous pangastritis with Sakita A1 ulcers in the gastric antrum, proceeding with a biopsy of the ulcerated lesion.

The new CT scan of the abdomen and pelvis revealed bilateral pleural effusion, a small sheet of pneumopericardium, thickening of the inter- and intra-lobular septa compromising the bilateral lung bases, suggestive of lymphangitis, apparent parietal thickening with a reduction in the lumen in the region of the gastric body and antrum, an unchanged uterus, the presence of an IUD and free fluid in the rectouterine pouch, as well as multiple lytic lesions involving the vertebral bodies, sacrum, ilia, and sternum. Histopathological analysis of the specimens removed in the operating room revealed the presence of adenocarcinoma with signet ring cells infiltrating ovarian tissue associated with intense fibrosis, characterizing desmoplasia and absence of involvement of the ovarian surface, confirming the diagnosis of Krukenberg tumor.

The result of the biopsy of the gastric ulcer performed during the EGD showed a poorly differentiated diffuse-type adenocarcinoma composed with signet ring cells, confirming the primary site of the tumor. After establishing the diagnosis, the gastric tumor was classified as stage IV due to the presence of bone metastases shown on the CT scan. After staging, the patient continued her treatment with the HSCMV's Clinical Oncology team, which provided comfort and a better explanation of the disease. After that, the oncology team, alongside the patient, decided to start chemotherapy (CTx). After starting CTx and stabilizing her condition, the patient was discharged from the service with guidance and all the necessary support for outpatient follow-up. However, 12 days after discharge, the patient returned to the HSCMV emergency room with severe back pain, refractory to morphine, and significant anemia. She was admitted again for pain control and a blood transfusion. During this new hospitalization, the patient evolved with clinical decompensation, presenting moments of dyspnea, as well as anemia refractory to blood transfusion and pain complaints refractory to medications such as high-dose morphine, methadone, gabapentin, midazolam, and dipyrone. In this context, the attending team decided to call in the Palliative Care team, who assessed the condition and managed the patient in palliative care only. The patient in question ended up dying within seven days due to an irreversible neoplastic disease diagnosed at an advanced stage.

Discussion

Gastric cancer is one of the most common cancers worldwide. It generally affects patients over 65, and its incidence is higher in Asian countries. Metastases and recurrences are the major causes of a poor prognosis for this disease. Ovarian metastases from gastric cancer, known as Krukenberg tumor, also point to a worse prognosis and are one of the main reasons for gastric cancer treatment failure [7].

Currently, the literature shows that around 76% of Krukenberg tumors originate from the stomach, 11% from the colorectal segment, 4% from the breasts, 3% from the biliary system, and the last 3% from the pancreas, uterine cervix, bladder, renal pelvis,

and thyroid all together [8]. In some cases, it is challenging to differentiate the primary tumor from a metastatic ovarian tumor, highlighting that the margin of error in diagnosis is considerably high [9].

The "Krukenberg tumors of gastric origin versus colorectal origin" study showed that the survival rate after resection of metastatic ovarian tumors with a primary site in the stomach was approximately 22.7 months, corroborating other studies analyzed. In contrast, the survival rate for the colorectal primary site was significantly higher [10]. Generally, the mortality rate is high, and the average survival after the diagnosis is 14 months [11]. However, the patient in this report showed a much lower survival rate than expected, given that the disease was already at an advanced stage at the diagnosis. It should be mentioned that the evolution of Krukenberg tumors in younger patients, such as the patient in this report, is generally faster and more aggressive [2].

When it comes to an unfavorable prognosis related to the Krukenberg tumor, the following should be considered in particular: peritoneal involvement, synchronous presentation, the presence of ascites, and high levels of tumor markers, such as CEA [12]. It is also possible to observe that synchronous tumors originating in colorectal cancer had a longer survival time than those originating in gastric cancer [10]. Currently, the diagnosis of Krukenberg tumor follows the criteria of the WHO, based on the histopathological description, in which Serov and Scully classified tumors according to anatomical site, histological type, and degree of malignancy [13]. Regarding the treatment, there is still no ideal therapy, which depends on the particularities of each event, the primary site of the tumor, and the staging of each case. However, it is known that when metastases are limited to the ovaries, bilateral ovarian surgical resection increases overall survival time [11]. Therefore, when diagnosed with the Krukenberg tumor, bilateral oophorectomy is recommended to prevent and reduce the risk of contralateral tumors, aiming to reduce morbidity [11]. In this case, the patient underwent bilateral oophorectomy due to the extent of her ovarian lesions.

Another relevant point is the importance of complementary approaches to surgical treatment, which have proven to be more effective in Krukenberg tumors. In 20 retrospective studies with a sample of 1533 cases of Krukenberg tumors, the protocols used consisted of adjuvant chemotherapy, cytoreductive surgery, hyperthermic intraperitoneal chemotherapy (HIPEC), and neoadjuvant chemotherapy. The analysis of these studies showed that most cases diagnosed at an early stage showed a significant increase in survival with cytoreductive surgery associated with adjuvant chemotherapy [6].

Conclusion

Krukenberg tumor is a rare bilateral metastatic ovarian adenocarcinoma, even rarer to find in young patients, which can have a primary carcinoma coming from different places in the body. Usually, it has a late diagnosis, given that the patient's initial symptoms are nonspecific and vague. This report corroborates studies that showed an unfavorable prognosis associated with this type of tumor, with modest survival rates, especially in young patients with distant metastases at the time of diagnosis.

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