Krukenberg Tumor in Long-Term Remission: Case Report

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Tumor de Krukenberg em Longo Tempo de Remissão: Relato de Caso

Tumor de Krukenberg en Largo Período de Remisión: Informe de Caso

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ABSTRACT

Introduction: Krukenberg tumor is a rare and aggressive metastatic tumor that is part of the differential diagnosis of ovarian masses. It originates mainly from the gastrointestinal tract, especially the stomach and colon. Its median survival at diagnosis is 16 months. **Case report:** A 35-year-old healthy patient complained of lower abdominal pain and dyspareunia for one year, with a transvaginal ultrasound showing an extensive mass in the left ovary. Through the investigation, a colonoscopy was performed revealing rectosigmoid adenocarcinoma. The subsequent evaluation included analysis of the genetic panel, the result of which was negative, and the revelation of metastases in the liver, peritoneum, and ovary, the latter called Krukenberg tumor. After treatment involving chemotherapy, rectosigmoidectomy with lymphadenectomy and bilateral salpingo-oophorectomy, peritoneal cytoreduction, and hepatic metastasectomy surgeries, the latter two associated with hyperthermic intraperitoneal chemotherapy, the patient is asymptomatic, with quality of life and in complete remission five years after diagnosis. **Conclusion:** Case report of Krukenberg tumor with a longer remission time than described in the literature, possibly due to the combined therapies used and favorable molecular profile.

Key words: Krukenberg Tumor/diagnosis; Ovarian Diseases; Survival; Neoplasm Metastasis.

RESUMO

Introdução: O tumor de Krukenberg compreende um tumor metastático raro e agressivo que faz parte dos diagnósticos diferenciais das massas ovarianas. Origina-se principalmente do trato gastrointestinal, especialmente do estômago e cólon. Sua sobrevida mediana ao diagnóstico é de 16 meses. **Relato do caso:** Paciente de 35 anos, hígida, queixava-se de dor abdominal baixa e dispareunia há um ano, com ultrassonografia transvaginal evidenciando massa extensa em ovário esquerdo. Por meio da investigação, foi realizada colonoscopia revelando adenocarcinoma de retossigmoide. A avaliação posterior compreendeu a análise do painel genético cujo resultado foi negativo e a revelação de metástase no fígado, no peritônio e no ovário, este último denominado tumor de Krukenberg. Após tratamento envolvendo quimioterapia, cirurgias de retossigmoidectomia com linfadenectomia e salpingo-oforectomia bilateral, cirurgias de citorredução peritoneal e de metastasectomia hepática, as duas últimas associadas à quimioterapia intraperitoneal hipertérmica, encontra-se assintomática, com qualidade de vida e em remissão completa cinco anos após o diagnóstico. **Conclusão:** Relatar o caso de tumor de Krukenberg com tempo de remissão mais prolongado do que o descrito em literatura, possivelmente pelas terapias combinadas utilizadas e perfil molecular favorável.

Palavras-chave: Tumor de Krukenberg/diagnóstico; Doenças Ovarianas; Sobrevida; Metástase Neoplásica.

RESUMEN

Introducción: El tumor de Krukenberg es un tumor metastásico raro y agresivo que forma parte del diagnóstico diferencial de las masas ováricas. Se origina principalmente en el tracto gastrointestinal, especialmente en el estómago y el colon. Su mediana de supervivencia al momento del diagnóstico es de 16 meses. **Informe del caso:** Paciente sana de 35 años, que consultó por dolor abdominal bajo y dispareunia de un año de evolución, con ecografía transvaginal que mostró masa extensa en ovario izquierdo. A través de la investigación, se realizó una colonoscopía que reveló un adenocarcinoma rectosigmoideo. La evaluación posterior incluyó el análisis del panel genético, cuyo resultado fue negativo y la revelación de metástasis en hígado, peritoneo y ovario, este último denominado tumor de Krukenberg. Luego de un tratamiento que incluyó quimioterapia, cirugías de rectosigmoidectomía con linfadenectomía y salpingooforectomía bilateral, cirugía de citorreducción peritoneal y metastasectomía hepática, estas dos últimas asociadas a quimioterapia intraperitoneal hipertérmica, la paciente se encuentra asintomática, con calidad de vida y en remisión completa a cinco años del diagnóstico. **Conclusión:** Se reporta un caso de tumor de Krukenberg con tiempo de remisión mayor al descrito en la literatura, posiblemente debido a las terapias combinadas utilizadas y al perfil molecular favorable.

Palabras clave: Tumor de Krukenberg/diagnóstico; Enfermedades del Ovario; Sobrevida; Metástasis de la Neoplasia.

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INTRODUCTION

Krukenberg tumor is a rare metastatic tumor form that affects the ovaries, usually originating from the gastrointestinal tract, especially the stomach and colon[1]. Although the stomach is still the most prevalent primary location organ (76%)[2,3], the colon has become increasingly relevant[4] due to increasing incidence of colorectal cancer. It is histologically characterized by mucin-producing signet ring cells[5], and a differential diagnosis of ovarian masses is important[6].

The downregulation of E-cadherin in the primary location is believed to contribute to metastasis in the ovaries[7]. There are four means of propagation: continuity, contiguity, hematogenous, or lymphatic[8], depending on the primary location[6]. Gastric tumors are prone to use the lymphatic route, while colon adenocarcinomas propagate through hematogenesis due to its intense intestinal vascularization[8].

The median diagnosis age is 48 years, usually during perimenopause[9]. Bilateral tumors are common[9], and bilateral oophorectomy is part of the treatment[10]. Median survival is 16 months[9], but factors such as metastatic extension and therapeutic approach significantly influence the prognosis[9]. The median increases to 23 months when the metastasis is confined to the ovary and reduces to 13.5 months when the metastasis is in other sites besides the ovary[9]. In addition to the metastasis extension, other factors related to a worse survival are the presence of ascites and primary gastric site[9]. Some factors that increase survival and are related to the disease treatment include metastasectomy[11], surgical resection of primary tumor[12], cytoreductive surgery[13-15], and hyperthermic intraperitoneal chemotherapy (HIPEC)[15], in addition to chemotherapy treatment[16].

The objective of the present study is to report a case of a patient who had a Krukenberg tumor over more than five years ago and is currently in clinical remission, presenting considerably higher survival than the median described in the scientific literature. This research has been approved by the Research Ethics Committee of the *Centro de Pesquisas Oncológicas (Cepon)*, report number 6.995.879 (CAAE (submission for ethical review): 81627524.2.0000.5355), in compliance with Resolution number 466/2012[17] of the National Health Council.

CASE REPORT

Female patient, 35 years, previously healthy, who had two pregnancies, one birth, one miscarriage, and a history of miscarriage one year ago. Complained of intense pain in the lower abdomen and deep dyspareunia. A transvaginal ultrasound (USG-TV) was performed in January 2019, which showed a heterogeneous adnexal collection in the left ovary measuring 7.4 x 5.4 x 8.4 cm. The hypothesis of a post-miscarriage corpus luteum cyst was raised, and medroxyprogesterone acetate was prescribed, but the patient showed no improvement. A new USG-TV was prescribed in three months, showing the permanence of the adnexal mass to the left, with projection to the posterior rectouterine pouch. Due to the lesion's expansiveness, upper digestive endoscopy and colonoscopy were performed, this last one pointing to an ulcerovegetative lesion in rectosigmoid junction, whose biopsy revealed a moderately differentiated ulcerated carcinoma, infiltrating the lamina propria. At the time of diagnosis, the patient reported having lost 3 kg over the previous week and previous episodes of hematochezia, previously associated with hemorrhoidal disease. Later, possible neoplastic implants were revealed in a computerized tomography (CT) of the abdomen and pelvis: a hypodense liver lesion in addition to a cystic pelvic lesion (Figure 1) — characterized as a Krukenberg tumor. Two weeks after the initial diagnosis, a rectosigmoidectomy with lymphadenectomy and bilateral salpingo-oophorectomy was performed in February 2019, in addition to a peritoneal implant resection in the Douglas cul-de-sac. From the surgical pieces obtained, the pathological staging pT4apN2bpM1c was defined, with neoplasm-free surgical resection margins. Molecular profiling was performed by pyrosequencing, resulting in wild-type KRAS and NRAS, a hereditary cancer panel with no pathogenic variant, and negative microsatellite instability research with a single finding of a variant of uncertain clinical significance (VUS) in the BLM gene. After 11 adjuvant chemotherapy cycles performed every fifteen days from March to August 2019 using the FOLFOX (folinic acid, 5-fluorouracil, and oxaliplatin) + cetuximab protocol, there was a partial response detected by the remnant liver metastases on abdominal magnetic resonance imaging (MRI).

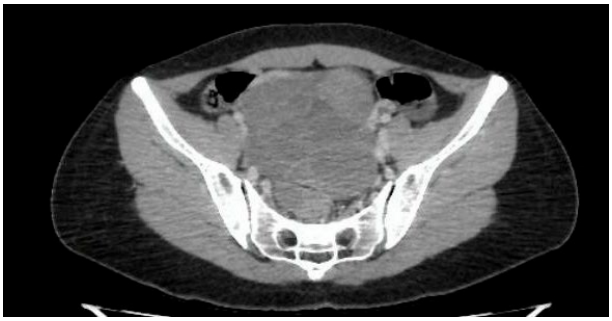

Figure 1. (1/31/2019): Voluminous pelvic lesion of multiloculated cystic aspect, measuring approximately 12.0 x 11.1 x 9.2 cm. Keeps close contact with the anteroinferior wall of the rectosigmoid, without evident cleavage plane to the method

Due to the presented response and considering resection of metastases, after eight months of diagnosis after adjuvant chemotherapy, the patient was submitted to oxiplatin HIPEC in September 2019 in addition to partial hepatectomy and peritoneectomy, whose anatomopathological showed complete response in the peritoneum. In July 2020, due to a recurrence of neoplastic implant in the liver, in addition to a presacral implant showed in a new PET-CT ten months after HIPEC, cytoreductive surgery with resection of metastases was performed in addition to a new HIPEC, now with mitomycin. Following the last surgery, between October 2020 and April 2021, the patient was prescribed 13 FOLFOX chemotherapy cycles, followed by the removal of oxaliplatin and maintenance with 5-fluorouracil + folinic acid for six sessions. In August 2021, a chest CT and abdomen MRI showed no signs of the disease, and the patient achieved a complete response to the treatment. There was a subsequent change to oral chemotherapy with capecitabine to ensure greater comfort for the patient. Five years after diagnosis, the patient is asymptomatic and in complete remission for over three years, with no signs of the disease.

DISCUSSION

This case is worth highlighting due to its prolonged remission of Krukenberg tumor, presenting a median survival rate much higher than that reported in scientific literature. Despite the unfavorable presentation of the patient at first, there was a noticeable response to treatment. After five years of diagnosis the patient has shown no signs of the disease for three years and her quality of life is preserved. This outcome is attributed to factors such as wild-type KRAS[18,19] and the adopted therapy approach[11-16], including surgical cytoreduction, metastases resection, and chemotherapy.

The report contrasts positively with the median survival documented in the literature, which is often limited. Moreover, while the median age at diagnosis is 48 years, with a high prevalence in patients undergoing perimenopause[9], the case described involves a 35-year-old patient, highlighting the relevancy of considering this diagnosis even in younger ages. The presence of bilateral metastases, typical in up to 80% of cases[10], was also observed, reinforcing the characteristic presentation, although in an atypical age group.

At the molecular level, the wild-type KRAS identified in the patient is associated with a better response to cetuximab[19], a monoclonal antibody used to treat colorectal cancer, which probably contributed to the favorable prognosis. In contrast, mutations in this gene are related to a reduced survival rate[18].

The chosen therapeutic approaches determined the achieved results. Surgical cytoreduction is highlighted as an essential approach to improve outcomes, present in multiple stages of this case, including rectosigmoidectomy, bilateral salpingo-oophorectomy, and partial hepatectomies. HIPEC[15], effective in reducing the peritoneal tumoral load, was also successfully used. The combination of FOLFOX and HIPEC protocols illustrates the integration of therapies to optimize results, which is in line with recommendations from the most recent literature[13].

This report emphasizes the relevancy of advanced diagnostic and therapeutic strategies for Krukenberg tumor, highlighting the possibility of favorable outcomes even in complex scenarios.

CONCLUSION

Krukenberg tumor represents a significant clinical challenge, both at diagnosis and treatment levels, given its metastatic origin and complex factors that influence the survival of patients. Health professionals must consider this possibility when assessing differential ovarian masses to ensure an appropriate treatment approach and improve patients' prognoses.

CONTRIBUTIONS

Both authors have substantially contributed to the study design, acquisition, analysis and interpretation of the data, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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