Mixed Non-Gestational Ovarian Choriocarcinoma: Relevance of Early Diagnosis in a Case Report

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Coriocarcinoma Ovariano Não Gestacional Misto: Relevância do Diagnóstico Precoce em um Relato de Caso

Coriocarcinoma Mixto de Ovario no Gestacional: Relevancia del Diagnóstico Precoz en un Informe de Caso

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ABSTRACT

Introduction: Non-gestational ovarian choriocarcinoma is a rare form of ovarian cancer, mainly affecting prepubertal women. It is considered an aggressive neoplasm and expansion to the lung is common in around 80% of patients, as in the following case. **Case report:** Female, 12 years old, with prolonged vaginal bleeding and abdominal distension. Computed tomography showed a large heterogeneous mass, predominantly cystic, with multiple coarse septa. The beta HCG level was 49,929.81 mUI/ml. She underwent median laparotomy for staging, with left adnexectomy plus resection of the retroperitoneal tumor and omentum, identifying stage IV. The histopathological examination concluded that it was a germ cell tumor of the ovary consisting of non-gestational choriocarcinoma. After being discharged from hospital, she underwent chemotherapy sessions. Subsequently, imaging showed nodules in both lungs, as well as expansive formations distributed in the liver parenchyma. In this context, pulmonary metastasectomy was performed months later. After this, new imaging tests were carried out to restage the disease and the following findings were seen: some residual pulmonary nodules and on the MRI of the skull, a sign of chronic hemorrhage. The patient's evolution was not favorable, her general condition worsened and she died one year after diagnosis. **Conclusion:** The aggressiveness of this disease is clear, especially in female pediatric patients, since early metastasis occurs in a significant percentage of cases, leading to an unfavorable prognosis.

Key words: choriocarcinoma, non-gestational; neoplasms; pediatrics.

RESUMO

Introdução: O coriocarcinoma ovariano não gestacional é uma apresentação rara de câncer de ovário, acometendo principalmente mulheres pré-púberes. É considerada uma neoplasia agressiva, sendo comum a ocorrência de expansão para o pulmão em cerca de 80% dos pacientes, como no caso a seguir. **Relato do caso:** Sexo feminino, 12 anos de idade, com sangramento vaginal e distensão abdominal prolongados. A tomografia computadorizada mostrou volumosa massa heterogênea predominantemente cística e múltiplos septos grosseiros de permeio. Dosagem do beta-HCG de 49.929,81 mUI/ml. Foi submetida à laparotomia mediana para estadiamento, com anexectomia esquerda mais ressecção do tumor retroperitoneal e do omento, identificando-se estádio IV. O exame histopatológico concluiu ser um tumor de células germinativas do ovário constituído por coriocarcinoma não gestacional. Após alta hospitalar, foi submetida a sessões de quimioterapia. Posteriormente, apresentou em exames de imagem nódulos em ambos os pulmões, além de formações expansivas distribuídas no parênquima hepático. Nesse contexto, foi realizada metastectomia pulmonar meses depois. Após isso, novos exames de imagem foram realizados para o reestadiamento da doença. Foram encontrados alguns nódulos pulmonares residuais e, na ressonância magnética de crânio, sinais de hemorragia crônica. A evolução da paciente não foi favorável, havendo agravamento do estado geral e óbito um ano após o diagnóstico. **Conclusão:** Compreende-se, desse modo, a agressividade dessa doença, em especial na faixa pediátrica feminina, uma vez que a metástase precoce ocorre em uma porcentagem significativa dos casos, levando a um prognóstico desfavorável.

Palavras-chave: coriocarcinoma não gestacional; neoplasias; pediatria.

RESUMEN

Introducción: El coriocarcinoma ovárico no gestacional es una presentación poco frecuente del cáncer de ovario, que afecta principalmente a mujeres prepúberes. Se considera una neoplasia agresiva y la expansión al pulmón es frecuente en alrededor del 80% de las pacientes, como en el caso siguiente. **Informe del caso:** Mujer de 12 años con hemorragia vaginal prolongada y distensión abdominal. La tomografía computarizada mostró una gran masa heterogénea, predominantemente quística, con múltiples septos gruesos. El nivel de beta HCG era de 49 929,81 mUI/ml. Se le practicó una laparotomía media para la estadificación, con anexectomía izquierda más resección del tumor retroperitoneal y del epiplón, identificándose un estadio IV. El examen histopatológico concluyó que se trataba de un tumor germinal de ovario consistente en un coriocarcinoma no gestacional. Tras el alta hospitalaria, se sometió a sesiones de quimioterapia. Posteriormente, el diagnóstico por imagen mostró nódulos en ambos pulmones, así como formaciones expansivas distribuidas en el parénquima hepático. En este contexto, meses más tarde se le practicó una metastasectomía pulmonar. Tras ésta, se realizaron nuevas pruebas de imagen para reestadificar la enfermedad y se observaron los siguientes hallazgos: algunos nódulos pulmonares residuales y, en la resonancia magnética del cráneo, una señal de hemorragia crónica. La evolución de la paciente no fue favorable, su estado general empeoró y falleció un año después del diagnóstico**. Conclusión:** Por lo tanto, es comprensible la agresividad de esta enfermedad, especialmente en las mujeres pediátricas, ya que en un porcentaje significativo de casos se producen metástasis tempranas, lo que conlleva un pronóstico desfavorable.

Palabras clave: coriocarcinoma, no gestacional; neoplasias; pediatría.

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INTRODUCTION

Non-gestational choriocarcinoma is a rare presentation of germ cell tumor in prepubertal women, its incidence is less than 0.6% in ovarian cancers[1-3]. With regard to the pediatric population, as in the present report, the peak incidence usually occupies a large part of this age group, since it usually occurs from 12 to 25 years old[2]. In addition, it is noteworthy that this tumor type can present in both pure and mixed forms, the latter being the worst prognosis, with only 50% of overall survival in three years[1,2,4].

In addition, it presents nonspecific clinical manifestations such as: vaginal bleeding, adnexal mass on ultrasound (USG), positive serum chorionic gonadotropin subunit beta (beta-HCG) and abdominal pain[2,4].

Treatment involves the combination of surgical intervention with chemotherapy (QT)[1,3]. The prognosis is reserved, as such tumor presents rapid growth, of an aggressive nature, with high chances of metastatic dissemination (hematological and local)[4,5]. Expansion into the lung occurs in more than half of the cases, as reported in the case in question[5].

This study was submitted to the Research Ethics Committee (CEP) of the Oswaldo Cruz University Hospital and approved under opinion number 6306631 (CAAE: 73028423.2.0000.5192), following all ethical requirements related to studies involving human beings, necessary for its success and protection related to the confidentiality of information, as evidenced in Resolution nº. 466/12[6] of the National Health Council (CNS).

CASE REPORT

A 12-year-old female patient was admitted to the oncology service of the Oswaldo Cruz University Hospital in July 2022 to investigate prolonged vaginal bleeding, lasting 21 days, and increased volume and abdominal pain for one month, in addition to constipation and weight loss. On admission physical examination, the patient was in good general condition, eupneic, acyanotic, pale (+/+4), afebrile to the touch, conscious and oriented. The abdomen was globose and depressible, with no signs of peritoneal irritation or visceromegaly, with extremities without edema and good peripheral perfusion. She had previously undergone USG and computed tomography (CT) of the total abdomen. Abdominal USG (Figure 1), in July 2022, showed a massive solid-cystic lesion, affecting the mesogastrium and epigastrium, measuring about 16.6 x 15.9 x 10.2 cm and 1,420 cm^3. CT of the total abdomen (Figure 2), in the same month, showed a large heterogeneous mass, well delimited margins and multiple coarse septa, with peripheral enhancement to the contrast medium, extending from the infrahepatic border to the pelvic region, measuring approximately 27.4 x 20 x 9.5 cm. CT also showed moderate ascites of loculated aspect, three hypoattenuating nodular images with peripheral contrast enhancement in the liver suggestive of lesions of secondary neoplastic etiology, present in segments VII, II and VI, the latter of greater dimension, with 1.4 x 1.1 cm, in addition to a small pulmonary nodule without calcium component, at the base of the right lung, of 5.0 mm, of indeterminate character. With regard to tumor markers, only beta-HCG was requested on the day, which presented a concentration of 49,929.81 mIU/ml, well above the reference value, suggesting, together with the results of the imaging tests, ovarian neoplasm.

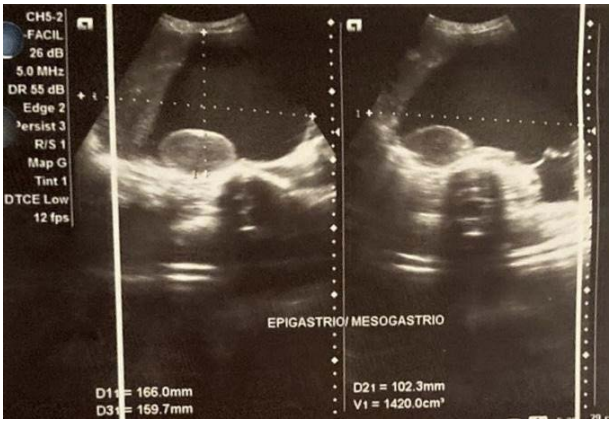

Figure 1. Abdominal USG (July 2022) showing a massive solid-cystic lesion, with involvement of the mesogastrium and epigastrium

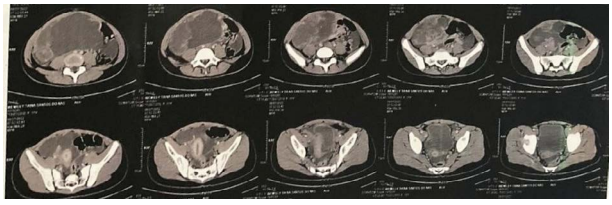

Figure 2. Total abdomen CT (July 2022) showing a large heterogeneous mass, predominantly cystic, with solid components, well delimited margins, and multiple coarse septa in between

The patient underwent median laparotomy two days later for staging of an ovarian tumor, which presented a lobulated solid-cystic tumor, with a rupture area at its upper pole, originating in the left ovary, with adhesion and involvement of the left horn; large omentum adhered to the tumor, especially in the zone of previous rupture; large volume of free fluid in the fluid and serohematic cavity. Left an annexectomy plus resection of the retroperitoneal tumor was performed, in addition to resection of the omentum. The staging found was IV. A new dosage of beta-HCG was performed, with a dosed value of 9,402 mIU/ml.

Histopathological analysis showed malignant neoplasm of germ cells, consisting of atypical mononucleated cells consistent with cytotrophoblast, arranged in a diffuse pattern of the intermediate syncytiotrophoblast. At the time, the left ovary weighed 1.836 g and measured 17.0 x 13.5 x 8.8 cm, with a smooth, grayish white external surface. The conclusion was a germ cell tumor (GCT) of the ovary consisting of non-gestational choriocarcinoma. Extensive areas of necrosis and hemorrhage, blood, and lymphatic vascular neoplastic embolization, as well as involvement of the cortical surface with direct neoplastic extension in the omentum were also observed. The lymph node identified in the omentum and the adhered uterine tube showed no evidence of neoplastic infiltration.

The immunohistochemical profile was compatible with the morphological diagnosis of non-gestational choriocarcinoma, but also showed a component of endodermal sinus tumor, of reticular and solid histological subtypes (Chart 1).

Chart 1. Immunohistochemical profile of the patient

Antigen	Clone	Result
Cytokeratins of 40, 48, 50 and 50.6 kDa	AEI/AE3	Positive
CD30 - KI-1 antigen	Ber-H2	Negative
AFP	Polyclonal	Positive
Beta hCG test	Polyclonal	Positive
Glypican-3, heparan sulfate proteoglycan	IGt2	Positive, rare cells
Germ cell transcription factor (OCT-¾)	C - 10	Negative
SALL-4 (*Zinc finger* TC, *Drosophila spalt* (salt) *gene*)	6E3	Positive

Captions: AFP = alpha-fetoprotein; Beta-HCG = chorionic gonadotropin beta subunit.

The patient was discharged three days after surgery, and the outpatient return was advised at the end of July 2022 to monitor the condition and, subsequently, to perform three cycles of adjuvant QT, based on the combined regimen of ifosfamide (2.0 g/m^2/day), cisplatin (40 mg/m^2/day) and etoposide (80 mg/m^2/day). She continued to be monitored in the service, with periodic hospitalizations for QT.

In July 2022, she underwent CT of the chest and upper abdomen, showing nodular formations in both lungs, with soft tissue attenuation and lobulated contours, suspected of secondary involvement. In addition, expansive formations distributed in the liver parenchyma were seen, hypoattenuating, suspected of metastasis. In this context, the first QT cycle was performed at the end of July 2022. The second QT cycle lasted five days and was performed the following month. He returned to the hospital in September to perform the third cycle of QT, with a beta-HCG dosage of 8.14 mIU/ml.

The new hospitalization occurred at the end of September to perform the fourth cycle of QT. The fifth QT cycle took place in October. At the end of December, the patient underwent a new hospitalization to start the tip protocol (paclitaxel, ifosfamide and cisplatin), presenting malaise during taxol infusion, but progressed well, with discharge in January 2023. In mid-January, it held the second tip, with discharge at the end of the month, in good condition. Then, the third and fourth tips were made. A CT scan of the chest, upper abdomen and pelvis was requested in April 2023, showing a nodule with soft tissue attenuation in the apical segment of the lower lobe of the left lung, paravertebral, in contact with the descending aorta, measuring 1.2 x 0.9 cm, a nodule with soft tissue attenuation, in a lingular segment, with irregular contours, measuring 0.7 x 0.5 cm and a similar-looking nodule located in the apical segment of the lower lobe of the left lung, measuring 0.5 x 0.4 cm, showing a volumetric reduction of such lesions. In the liver, a hypoattenuating nodular image was seen in the right lobe, measuring 1.2 cm. No mediastinal or lower abdominal lymph node enlargement was identified. No cystic formations were found in the right ovary. The most recent beta-HCG, from May 2023, was 2,373 mIU/ml, and alpha-fetoprotein, 2.0 ng/ml.

Due to the diagnosis of pulmonary and hepatic metastasis of the GCT, the patient was hospitalized again in June 2023 for left video thoracoscopy for pulmonary metastectomy. A mass in the left lower lobe was found in follow-up 10 of approximately 4 cm and a mass of 3 cm in the anterior basal segment of that same lobe. On palpation, there was a nodule of approximately 1 cm in the upper segment of the tongue. The lung presented firm adhesions from the left lower lobe to the chest wall in the topography of the descending aorta and esophagus to the diaphragm, determined by a larger mass. Pulmonary segmentectomy, pulmonary decortication, pleurectomy and thoracostomy with left-closed pleural drainage were performed. In the postoperative period, the patient evolved uneventfully, and respiratory and motor physiotherapy was performed to assist in her rehabilitation. The patient was discharged three days after surgery and was scheduled to return at the end of June 2023 for outpatient follow-up. At the next visit, new tests were requested for staging the disease: chest CT, skull magnetic resonance imaging

(MRI), bone scintigraphy and pet scan. On chest CT, some residual nodules were found; on skull MRI, a sign of chronic hemorrhage; on bone scintigraphy, there was a probable osteoarticular process on T4 on the right; and pet scan was not authorized. In addition, the beta-HCG value dosed on that day was 43,000 mIU/ml.

In July 2023, after discussion with the GTC protocol, he was talked to those responsible about the severity of the child's disease and the lack of cure conditions. Thus, it was decided to take palliative actions. Thus, the patient continued to be monitored regularly on an outpatient basis, returning to the service in early August 2023 with pain and enlargement of the abdomen, being hospitalized for support (blood transfusions) and ideal analgesia. The evolution of the patient was not favorable, with worsening of the general condition, resulting in death in the same month.

DISCUSSION

GCTs make up a large group of pathologies of diverse presentation in different age groups. Among adolescents and women of reproductive age, tumors such as teratomas (mature and immature), choriocarcinomas (gestational and non-gestational) and dysgerminomas are some examples of this neoplastic type[7].

Despite the low prevalence (less than 1% of GCTs), ovarian choriocarcinoma is a pediatric emergency of great clinical repercussion[7,8]. Because it is a rarity, its signs and symptoms are often non specific9.Associated with these factors, late diagnoses with severe disease presentations contribute to increased mortality in pediatric patients.

Serum beta-HCG level can be considered one of the most sensitive parameters to diagnose non-gestational choriocarcinoma and monitor response to treatment[8]. Since it usually arises from germ cells and behaves like GCT, the initial approach is surgery, by which the diagnosis is confirmed and treatment is started[8,9].

The staging of the disease is still uncertain. In cases of non-gestational ovarian choriocarcinoma, staging of ovarian cancer applies[8,10]. After surgical staging, adjuvant QT is indicated for patients at any stage. The response to treatment is evaluated through imaging exams such as: chest, abdominal and pelvic CT, MRI and pet scan images, depending on the clinical indication[8].

As for QT, it is known that gestational women are treated with methotrexate, adopting the EMA/CO regimen (etoposide, methotrexate/leucovorin and actinomycin-D, followed by one week of cyclophosphamide and vincristine). On the other hand, in recent years, there have been very few reported cases of the type of non-gestational neoplasm in women under the age of 20. In them, most underwent conservative surgery and multiple QT cycles. A significant percentage received methotrexate-based regimens, and a small percentage cisplatin-based. As a result, there was a good response to primary treatment[8]. In the case in question, the patient, after undergoing conservative surgery with preservation of the other ovary and uterus, underwent three cycles of QT based on the combination of ifosfamide, cisplatin and etoposide.

Non-gestational choriocarcinomas of the mixed type, reported in the present case, tend to have a poor prognosis. Early metastasis is commonly observed, unlike cases of ovarian mass in general, in which pediatric patients have a long-life expectancy after treatment, so post-surgical follow-up is relevant[9,10].

The lung is the main site of metastasis of non-gestational ovarian choriocarcinomas. In addition, liver, brain, pelvic and abdominal metastases can also occur, but to date their presentation has been limited[1,10].

Due to the rarity of this malignant tumor and the no specificity of its symptoms, especially in the pediatric group, one can see how challenging the diagnosis of this disease can be. Paradoxically, to achieve a better prognosis, early diagnosis is essential due to the high possibility of early metastasis. It is concluded, then, that non-gestational choriocarcinoma, especially mixed, has a significantly aggressive behavior in pediatric patients.

CONCLUSION

Non-gestational ovarian choriocarcinoma is a malignant neoplasm of low epidemiological incidence, but of high aggressiveness, representing a medical urgency. Given its complexity, an early and urgent diagnosis, in order to avoid surgery in a late time, and therefore an adequate treatment will directly reflect on the prognosis and survival of the patient. However, due to its high capacity for early metastases, therapeutic outcomes tend to have an unfavorable prognosis.

CONTRIBUTIONS

All the authors contributed substantially to the study design, analysis and/or interpretation of the data, wording and/or critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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