RECURRENT OVARIAN YOLK SAC TUMOUR IN AN 11-YEAR OLD GIRL – CASE REPORT

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Abstract: Ovarian cancer is responsible for 1-2% of all childhood malignancies, in children up to 85% of ovarian malignancies are histologically found to be germ cell tumors. Yolk sac tumors are the second most common subtype of germ cell tumors, they are aggressive rapidly growing and with frequent metastasis to other organs, and associated with elevated levels of alpha-fetoprotein.

We present the case of an 11-year-old girl that was admitted to our hospital for abdominal pain, and a large abdominal tumor that occupied the whole hypogastric region of the abdomen. MRI showed a right ovarian tumor; tumor markers were obtained prior to surgery. Histological diagnosis of ovarian Yolk Sac Tumor was made and the patient was scheduled for chemotherapy. The patient and family interrupted all medical treatment and follow-up, presenting 5 months later, with recurrence on the contralateral ovary. Even if the ovarian yolk sac tumor has a good survival rate, the delay in starting chemotherapy and lack of compliance to treatment can give it a poor prognosis, and lead to recurrence or metastasis.

Keywords: Ovarian tumor, Yolk-sac, Alfa-fetoprotein, Delayed chemotherapy

1. Introduction

Ovarian cancer is responsible for 1-2% of all childhood malignancies, between 1-15 years of age. [12]

Histologically, germ cell tumors account for 85% of neoplasia of the ovary in the paediatric population, and only 3-5% of all malignant ovarian neoplasms, [12], [4] yolk sac tumors being the second most common subtype, comprising about 1% of all ovarian malignancies. [5], [8]

Yolk sac tumors also called Endodermal sinus tumor or recently recommended – primitive endodermal tumor, are rare, highly aggressive and malignant that can be present in children and young adults [16] [10]. Alfa-fetoprotein is usually elevated in patients with ovarian yolk sac tumors and may aid in the diagnosis of such malignancies, it can be correlated with the severity of the disease, as well as

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in the follow-up of the patients in diagnosing recurrence. [8]

Alfa-fetoprotein has a half-life of about 5 days so it can be useful in predicting residual malignant tissue after surgical resection. [3]

Before the introduction of chemotherapy yolk sac tumors had a 5-year survival rate of about 15%, nowadays this improved to about 90% with combination chemotherapy such as BEP (Bleomycin, Etoposide and Cisplatin). [4]

2. Case Presentation

We present the case of an 11-year-old female patient admitted to the Paediatric Surgery Department for abdominal pain and the presence of a large mass in the hypogastric area that extended cranially to the level of the umbilicus.

The clinical examination revealed a firm fixed, large palpable mass that occupied the hypogastric region situated on the midline of the abdomen, affirmatively the patient noticed the growth of the mass 3 months ago. (Figure 1)

Tumor markers were carried out showing an alpha-fetoprotein of 15647ng/ml (n 0.6–6.7), a beta-HCG of 1.20 mUI/ml (n<5) and CA125 of 257U/mL (n<35), Biochemistry and Complete blood count showed a C Reactive Protein of 9.5 mg/dL (n<1) and a Haemoglobin of 11.7 g/dL (n 12-15).

Ultrasonography of the abdomen showed a defined mass that measured about 12/7cm with a heterogeneous structure, with cystic areas, and calcifications (isoechoic, hypo and hyperechoic), in close relation to the uterus suggesting a tumor of the right ovary, also free fluid was found in the peritoneal cavity (Figure 2).

An MRI scan of the abdomen and pelvis was ordered, that showed a large pelvic and abdominal tumor arising from the right ovary that measured 13/11/8cm that had a heterogeneous structure, predominantly cystic, with multiple septa, necrotic and haemorrhage areas. The left ovary had a normal size with few follicular cysts under 2cm, and no enlarged lymph nodes, or other secondary determinations, but ascites was noted. (Figure 3)
A laparotomy was performed: at entry in the peritoneal cavity, hemoperitoneum was noted, after peritoneal washings were obtained for cytology, the tumor was inspected, and this showed a rupture in the capsule prior to surgery.

According to the operative guidelines for ovarian tumors of the Children’s Oncology Group [15] the peritoneal surface and liver was examined - without any suspicious lesions; the contralateral ovary was of normal appearance – so no biopsy was obtained; the omentum was not adherent to the tumor and no nodules were present – omentectomy was not performed; and no suspicious or enlarged retroperitoneal or pelvic lymph nodes were found – biopsy was not performed.

Thus, a fertility sparing surgery was decided, with a right side salpingo-oophorectomy being performed removing the tumor that measured 13/13/10 cm. (Figure 4)

According to the staging system for ovarian germ cell tumors of the Children’s Oncology Group the patient was staged as Stage I – Limited to the ovary, with no other evidence of disease beyond the ovaries. [15]

The histological examination revealed a yolk sac tumor of the ovary, with immunohistochemistry confirmation, with a Ki67 protein present in about 60% of the tumor cells, Ki67 being a marker of proliferation and mitosis. [2]

After discharge, the patient was referred to our Paediatric Oncology Department where she was scheduled for chemotherapy treatment with Bleomycin, Etoposide and Cisplatin (BEP) on the following week, but failed to present for treatment.

3 months later the patient was admitted in our hospital for abdominal pain, and a diagnosis of ascariasis was made and she received treatment with albendazole, while being admitted in the Oncology unit for malignancy re-evaluation.

A contrast CT scan of the thorax abdomen and pelvis was performed, where no signs of malignancy were observed, the left ovary was 3.8/2.8 cm with follicular cysts under 1.7 cm, and no free fluid in the peritoneal cavity.

Tumor markers showed an alpha-fetoprotein of 389 ng/mL (n 0.6-6.7) beta-HCG 1.20 mU/mL (n<5), LDH 180U/L (n 135-225).
The patient was again scheduled for chemotherapy the following week and again, failed to present for treatment.

58 days from the last check-up, and about 5 months from initial surgery, the patient presents to our hospital with abdominal pain and a large mass in the hypogastric region, slightly deviated to the left side of the abdomen. (Figure 5)

Ultrasonography described a large mass similar with the previous one that measured about 15/9 cm that had a bylobed shape, the structure was heterogeneous hypo and isoechoic with multiple transonic areas (necrosis). (Figure 6)

Tumor markers showed an increase in Alpha-fetoprotein to 25017ng/mL (n 0.6-6.7), Beta-HCG 2.3 mUI/mL (n<5), LDH 365 U/L (n 135–225)

Blood tests showed a decreased haemoglobin 10.9 g/dL (n 12-15) and an elevated C-reactive protein of 6.6 mg/dL (n< 1).

A contrast MRI of the abdomen and pelvis was obtained that highlighted a large tumor arising from the left ovary, comprised of two masses joined together, with multiple septa, predominantly cystic with solid components and with moderate ascites. The size of the mass was described as 9/12/16 cm. (Figure 7)
The ethics and the tumor board committee explained to the parents the prognosis and the need for a bilateral salpingo-oophorectomy in addition to chemotherapy, as well as life-long hormonal replacement therapy.

Laparotomy was performed and hemoperitoneum was found, the tumor capsule was once again ruptured prior to surgery, a large tumor was identified that was adherent to the omentum, ileum, and parietal peritoneum of the anterior abdominal wall, after lysis of the adherences a left side salpingo-oophorectomy was performed, also a resection of the omentum, and multiple biopsies were made from the parietal peritoneum. No enlarged lymph nodes were detected. The resected tumor was 17/10/9 cm. (Figure 8)

Fig. 8. Macroscopic aspect of the secondary left ovarian tumor, note omentum intimately adherent to cranial pole

Considering the visceral involvement of omentum and intestine the tumor was staged as a Stage III tumor and was referred to 3 to 4 cycles of BEP, according to the European Society for Medical Oncology guidelines (ESMO), [6] in our Oncology Department without being discharged prior to chemotherapy. Alpha-fetoprotein levels dropped to 5856 ng/ml one week after surgery suggesting possible residual malignant tissue. After the first cycle of BEP alpha-fetoprotein levels were 214ng/mL, and the patient is currently still under BEP treatment, on the second cycle.

3. Discussions

Malignant germ cell tumors of the ovary often present with abdominal pain and the presence of a mass in the hypogastric region, or even acute abdomen caused by torsion or tumor rupture. [3] [7]

A study published in 2017 by Nasioudis et al. analyzed 561 women with yolk sac tumors of the ovary, the majority of patients presented with an early stage, I or II – about 60%, Stage III was found in 30% and only about 10% had a Stage IV of the disease. Also, the 5-year survival rate was 95% for stage I but much lower, of 70% in stage III and only 50% in stage IV. [14]

Thus, it is of uttermost importance to diagnose the disease in an early stage and start chemotherapy after the resection of the tumor.

Before 1970 most childhood germ cell tumors turned out to be fatal, but after the introduction of Cisplatin the survival rate started to rise, to this day BEP is the standard protocol regarding germ cell tumors. [12]

Fertility sparing surgery is nowadays advised in Yolk sac tumors, when associated with BEP it leads to a good prognosis.
regarding menstruation, pregnancy and offspring. Numerous studies describing patients that had normal ovarian function and gave birth to normal developed babies. [9][17][11]

A lower education background can lead to a lack in compliance with treatment, a study published in 2016 by Mangili et al. showed that out of 44 patients, that should have received chemotherapy after a malignant ovarian germ cell tumor, 23 had a recurrence, out of which 7 patients died eventually. More than half of the patients, 4 of them, had ovarian Yolk sac tumors, proving that this histology usually has the worst prognosis. [13]

In our patient we can see that without adjuvant chemotherapy recurrence was present on the contralateral ovary, the fact that not even 2 months before the recurrence she had a normal CT scan and then a 17cm tumor raises awareness of the aggressive nature, fast growth and high malignant potential of the yolk sac tumors.

Even if Mahadik et al. states that a female patient that has an ovarian malignancy could be lucky if this malignancy proves to be a germ cell tumor, because of the good prognostic regarding survival and potential fertility after surgical and adjuvant BEP treatment [12], still yolk sac tumors larger than 16cm, like in our patient, could have a poor outcome, as stated by the Children’s Cancer Study Group. [1]

4. Conclusions

It is of uttermost importance to raise awareness especially in parents of paediatric patients, about the importance of an early diagnosis of ovarian tumors - that treated in stage I could lead to a 5-year survival rate of more than 95%.

Alpha-fetoprotein is a crucial tumor marker in the diagnosis and especially in the follow-up of yolk sac tumors, being a predictive factor of residual malignant tissue and of recurrence.

Adjuvant chemotherapy should be used in 3-4 cycles of Bleomycin, Etoposide and Cisplatin (BEP) after surgical resection, to improve outcome and overall survival rate.

Parents should be counselled and they need to understand that even if surgery was performed it is of great importance that the adjuvant chemotherapy should be followed thoroughly to minimize recurrence and increase the overall survival of their offspring.

References

