Case Reports

Treatment of choriocarcinoma metastases by surgery and polychemotherapy – case report

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Summary

Choriocarcinoma is present in one out of every 40,000 pregnancies [1]. There is a great risk for incidence of the disease in women who become pregnant after 45 years of age. The clinical picture may vary and is related to the destruction of tissue and bleeding. New chemo protocols containing etoposide, cisplatin, ifosfamide, together with a resection of the focus resistant to chemotherapy, lead in most cases to the complete recovery [1, 2].

Key words: Choriocarcinoma; Polychemotherapy.

Introduction

Choriocarcinoma is a solid trophoblastic tumor primarily in myometrium or in distant organs and tissues [1]. It is constructed of syncytio- and cytotrophoblasts and shows no villus pattern [1]. Clinical symptoms are vaginal bleeding, enlarged uterus, high hCG titer, ovarian mass and an irregular basal body temperature chart. Choriocarcinoma is strongly indicated by the presence of metastasis found in the external genitalia or vaginal walls [1]. Multiple round radiological foci in the lungs show the progress of malignancy. Symptoms due to distant metastases suggest choriocarcinoma, e.g. abdominal pain and hemorrhage in hepatic lesions or persistent headache in brain metastases [1, 2]. It develops after evacuation of a hydatiform mole, abortion and delivery. The interval from an antecedent pregnancy is long, and can be more than one year in typical uterine choriocarcinoma [1, 2].

Choriocarcinoma is treated by primary chemotherapy, which is the first choice of chemotherapy for the treatment of choriocarcinoma. In most cases of metastatic choriocarcinoma, polychemotherapy and hysterectomy result in favorable remission [1, 2].

Case Report

A 47-year-old patient with two deliveries and five deliberate abortions was admitted to the Institute of Gynecology and Obstetrics, Clinical Center of Serbia because of uterine bleeding and also hematemesis and melena. Her last menstrual period was in April 1996, and irregular, brownish uterine bleeding appeared five months later. Explorative curettage was performed and choriocarcinoma was established by histological analysis.

Lung X-ray revealed bilateral nodular shadows, i.e. choriocarcinoma metastases. Beta subunits were 18,000 IU, and also the thyroid gland was hyperfunctioning with elevated hormone values.

Small pelvis ultrasound examination showed a 123 x 49 mm uterus, endometrial swelling with unclear hyperechogenic shadows on the posterior wall; a cyst was noted on the left ovary (37 mm), and right ovary appeared normal.

Abdominal echo imaging revealed secondary deposits in the right lobe of the liver in the form of hyperechogenic shadows.

Because of elevated ß hCG levels and her poor general condition, it was decided to correct the blood picture and then include polychemotherapy with decreased doses of cytotoxic drugs according to the MAC protocol. Chemotherapy was initiated in September 1996 during her first admission to the Institute. Then, in October, she received a second course of chemotherapy.

In view of the fact that the patient's general condition had improved, surgery with hysterectomy and bilateral salpingo-oophorectomy was performed in November 1996. Surgical findings were in favor of choriocarcinoma which had penetrated the uterine cavity and included not only uterine serosa but also other organs in the small pelvis. The uterus was soft and enlarged, bleed when touched and livid. There was also infiltration of the right parameters along the blood vessels. The histological finding after surgery was morphological changes corresponding to necrotizing choriocarcinoma.

The third course of chemotherapy according to the MAC protocol was induced after the surgery. In January 1997, because of repeated increased ß hCG levels, the fourth course of chemotherapy was induced according to the VBP protocol. In February, the patient received a fifth and in March a sixth course of chemotherapy according to the VBP protocol when ß hCG levels were 5 IU/ l. Thus we decided to follow beta subunits every three months. Repeated abdominal and lung X-ray imaging revealed regression of the previous changes. The patient was discharged in April 1997 with β hCG levels of 4 IU/l.

The patient was admitted again in November 1998 because during her regular checkup β hCG levels were 500 IU/l. It was thus decided to administer another four courses of chemotherapy over the following four months – polychemotherapies (EMACO, POMB, 5-fluorouracil). β hCG values decreased to 30 IU/l and small pelvis and abdomenal ultrasound, and also lung computed tomography (CT) did not show any focus with ectopic secretions of β hCG. Not until May 1999, when nuclear

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magnetic resonance (NMR) imaging was performed, did we find metastasis on the right adrenal gland (5 cm in diameter). In July 1999, the patient received four courses of polychemotherapy according to the ICE protocol, and afterwards the values of β hCG decreased to 100 IU/l. The patient was transferred to the Institute of Cardiovascular Diseases where she had surgical removal of the right adrenal gland tumor. Pathohistological findings confirmed adrenocortical carcinoma. Moreover, considering the postoperative increase of β hCG values, we asked for an expert opinion at the Institute of Oncology and Radiology, where it was confirmed that it was choriocarcinoma metastasis. After that, an immunohistochemical examination was performed which additionally confirmed the diagnosis. In the middle of February 2000, because of increased β hCG and general condition deterioration, the patient received another five courses of polychemotherapy according to the ICE protocol, ending in April 2000.

β hCG values decreased during the series from 31,800 IU/l before the therapy (February 2000) to 205 IU/l (April 2000) after the therapy. During this last polychemotherapy, pleural puncture was performed three times because of hemorrhage, and malignant cells were found.

The patient was discharged in good general condition and at the first checkup, after a month, β hCG values were under 5 IU/l.

During the consequent monthly, quarterly and later six-monthly checkups, the values of β hCG were never above 5 IU/l.

Discussion and conclusion

Choriocarcinoma presents in one of every 40,000 pregnancies [1]. There is a great risk for incidence of the disease in women who become pregnant after 45 years of age. At the time of diagnosis, our patient was 47 years old. The clinical picture may vary and is related to the destruction of tissue and bleeding. Vaginal bleeding or pus mixed with blood, together with abdominal pain and a palpated mass in the small pelvis, point to choriocarcinoma [1]. The first symptom in our patient was bleeding after amenorrhea. The diagnosis was established five months after the first symptoms. In one-third of the patients, the first symptoms are not gynecological but a consequence of distant metastases [1, 2].

Sometimes, in women with β hCG elevated levels, there could be a dysfunction of the thyroid gland because of a cross-reaction between hCG alpha subunits and thyroid stimulating hormone (TSH), which was the case in our patient [3]. Because of the often long period between previous pregnancy and clinical manifestation of the disease, and also the aggressive behavior of the tumor, spread dissemination is present in 60% of the cases [3]. The most common targets are the lungs, brain and liver [3]. In the literature data, adrenal dissemination is present in 10% of the cases, as was the case in our patient. Pulmonary metastases are relatively common in women with choriocarcinoma. According to recent publications, lung resection should be considered only in patients with chemoresistant disease and should be avoided in patients who respond to the therapy as evidenced by declining hCG levels, as in the case of our patient [4].

In the presence of liver metastasis whole liver irradiation or selective embolization of a metaststic liver lesion have been avocated according the recent literature [4].

Choriocarcinoma is often diagnosed by the analysis of increased β hCG values and in relation to metastatic lesions in other organs observed by radiography. In detection of metastatic foci, X-ray image in pulmonary lesions, CT in brain metastases, MRI in some soft tissues are useful [4].

Choriocarcinoma is treated by primary chemotherapy. In the past, hysterectomy was common but frequently followed by metastasis which was treated by chemotherapy [5]. Only chemotherapy-resistant metastasis or relapse associated with surgery, e.g. pulmonary lobectomy or craniotomy, and severe vaginal bleeding is treated by hysterectomy. However the combination of hysterectomy and chemotherapy has resulted in favorable remission [6, 7].

Women with metaststic choriocarcinoma should be treated initially with a multidrug combination chemotherapy. Several additional studies have confirmed the efficacy of the EMA/CO regimen, now the most commonly employed initial treatment for the management of high-risk gestational throphoblastic tumors [7, 8]. While EMA/CO has emerged as the treatment of choice, several modifications of the regimen have been proposed. Regimens containg cisplatin and etoposide are commonly employed for the treatment of persistent or relapsed throphoblastic tumors [7, 8]. After the succesfful use of bleomycin in the treatment of testicular neoplasmas, several investigators evaluated bleomycin-containing protocols for the treatment of refractory gestational trophoblastic disease. Also some authors have described ifosfamide for the treatment of refractory neoplasms [8].

Long-term follow-up of patients with choriocarcinoma indicates that the overall 5-year survival is now over 86% [8].

It is considered that the prognosis of patients with diseases refractory to chemotherapy is poor. A very small number of publications deal with treatment of refractory metastatic trophoblastic tumors. New technologies, application of factors stimulating the growth of colonies, have an important role in the future treatment of patients resistant to some drugs [8, 9].

New chemo protocols, containing etoposide, cisplatin, and ifosfamide, together with the resection of the focus resistant to the chemotherapy, lead in most cases to complete recovery [9, 10]. Now, with prompt diagnosis and multi-agent chemotherapy, even patients with widely metastatic diseases can be cured as was the case in our patient [10]. Adjuvant surgical and radiotherapeutic techniques have been refined. The remaining challenge that faces clinicians lies in the early recognition of patients with trophoblastic tumors and referal of such women to individuals with expertise in the management of gestational trophoblastic disease [10].

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