Developing retroperitoneal anaplastic carcinoma with choriocarcinoma focus after ovarian non-gestational choriocarcinoma: A case report

Razvoj retroperitonealnog anaplastičnog karcinoma sa horiokarcinomskim metastazama posle negestacijskog horiokarcinoma

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Abstract

Introduction. Choriocarcinoma is a malignant form of gestational trophoblastic neoplasm (GTN). It is a rare event but also a curable malignancy. In the majority of instances it develops after any gestational event. In some cases it develops as non-gestational extrauterine malignancy. Prognosis of choriocarcinoma is poor when invasion and metastases appear early and spread fast. This form of choriocarcinoma can lead to incurable and lethal outcome. Case report. We presented a 20-year-old patient with abdominal and retroperitoneal malignancy – anaplastic carcinoma combined with choriocarcinoma metastases. Tumor developed three months after left adnexectomy which had been done because of adnexal tumor. Choriocarcinoma was immunohistochemically confirmed in adnexal masses. Two courses of chemotherapy, metotrexate + folic acid (MTX+FA) regimen, were administrated. The initial serum beta human chorionic gonadotropin level stayed unknown as well as the last one after the treatment. The patient came from the other country and was hospitalized because of pelvic and abdominal pain and palpable abdominal masses in hypogastrium with progressive anemia. The human chorionic gonadotropin level was 38 mIU/L. Tumor biopsy was done and choriocarcinoma metastases were immunohistochemically confirmed with predominant anaplastic carcinoma. Five day course of MTX + cyclophosphamide regimen was administrated and the patient was prepared for operative treatment. Relaparotomy was performed and tumor completely exceeded. Tumor mass mostly developed retroperitoneally and partially in abdominal cavity infiltrating intestinal wall with rupture of sigmoid colon. Anaplastic carcinoma, with large fields of necrosis and bleeding, was confirmed after histological examination. Immunohistochemical examination excluded choriocarcinoma in tumor mass. After 20 blood units transfusion, one course of chemotherapy and tumor excision, the patient left hospital on the 9th postoperative day. The patient rejected chemotherapy which was recommended according to the protocol and died one month after the operation. Conclusion. Non-gestational metastatic choriocarcinoma complicated with another type of malignancy with early spread of the disease and low responsiveness to chemotherapy has poor prognosis and leads to lethal outcome.

Key words: choriocarcinoma; choriocarcinoma, non-gestational; carcinoma; diagnosis; drug therapy; digestive system surgical procedures; gynecologic surgical procedures; prognosis; treatment outcome.
Introduction

Gestational trophoblastic neoplasms (GTNs) can appear as benign GTNs (complete or partial hydatiform mole) as well as invasive mole, choriocarcinoma or placental site trophoblastic tumor as malignant GTNs. Among GTNs, choriocarcinoma is a highly potent malignancy of trophoblastic origin and usually represents disturbance of fertilization. Choriocarcinoma is a rare event, highly malignant tumor and in the majority of instances its localization is intratubal and of gestational origin. Choriocarcinoma usually occurs after normal pregnancies, after term pregnancies and after molar pregnancies. It can also occur after nongestational events. Serum beta human chorionic gonadotropin (HCG) elevation depends on hormone secretion component of choriocarcinoma (syncytiotrophoblast). Extratubal localization of choriocarcinoma is rare and can develop on ectopic pregnancy. It is believed that some malignant non-gestational trophoblastic malignancies especially choriocarcinoma can develop from pluripotent germ cells in the gonads. If non-gestational choriocarcinoma invades and metastatises early and rapidly without specific clinical manifestation it may have a poor prognosis. Diagnosis can be confirmed after histological and immunohistochemical examinations. This means that poorly differentiated carcinomas may show focal area of choriocarcinomatous differentiation.

Case report

A 20-year-old patient presented with abdominal and retroperitoneal malignancy – anaplastic carcinoma (gravida 1, parity 1). The tumor developed three months after left adnexectomy because of cystic tumor and normal uterus without pathological masses and there was a heterogenous mass dimensions partly in abdominal and retroperitoneal tumor mass.

The patient came to our hospital with a history of pelvic pain and developing abdominal and left retroperitoneal tumor 3 months after left adnexectomy and 2 courses of chemotherapy. Right adnexectomy was done one year before this operation and histopathological findings confirmed borderline cystadenoma ovarii.

On admission to hospital the patient had palpable abdominal masses, pelvic and abdominal pain and progressive anemia. The tumor that developed 3 months after left adnexectomy and 2 courses of chemotherapy because of the confirmed non-gestational choriocarcinoma spreaded retroperitonealy and also in the abdominal cavity. We checked HCG and it was 38 mlU/L. Tumor marker CA-125 and alpha-fetoprotein (AFP) levels were in normal ranges. Transvaginal Doppler ultrasonographic examination was done and normal uterus without pelvic masses was seen. Hyperechoinic masses were suspected on the left lateral and back retroperitoneal and invaded to the left subphrenium.

This was confirmed on computed tomography (CT) scans of abdomen and pelvis. CT scans of the pelvis showed the normal uterus without pathological masses and there was a heterogenous mass dimensions partly in abdominal and pelvic regions. The patient was therefore treated in another country. Two courses of chemotherapy, methotrexate 50 mg/m² iv on the days 1, 3, 5, 7 + folic acid 30 mg iv on the days 2, 4, 6, 8 (MTX + FA), were administrated without checking initial HCG level.
dominal cavity and mostly invaded left retroperitonealy (Figure 2). Brain and lung metastases were excluded after X-ray examination.

Fig. 2 – Computed tomography (CT) scan of an abdominal and retroperitoneal tumor mass

The patient had progressive anemia with hematocrite (hct) 29%–19% (reference values 37.0%–51.0%) and hypoalbuminemia 25–27 g/L (reference values 32–50 g/L). During the first 4 days the patient got 8 blood units and 12 units of fresh frozen plasma (FFP). Broad spectrum antibiotics administrated on the second day of hospitalisation when the patient became febrile (38–39.5°C) with increasing leukocytes (> 12 \times 10^9/L), platelets (> 400 \times 10^9/L) and also increasing CRP > 165 mg/L (reference value < 5.0 mg/L).

To prevent multiorgan failure, endotoxic shock or/and disseminated intravascular coagulation caused by hemorrhage and infection in tumor mass we decided to exceed the tumor mass. Because of the great risk of hemorrhage biopsy of metastasis is not recommended in patients with metastatic choriocarcinoma. We decided to do it in spite of the risks, so we could make the right decision for the final treatment and to find the source of hemorrhage and suspected developing infection. Tumor biopsy was done and metastatic choriocarcinoma with predominant anaplastic carcinoma was confirmed (Figure 3). According to this and also ultrasonographic and CT findings we prepared the patient for radical tumor excision. Preparation included administrating appropriate chemotherapy regimen. Suggested chemotherapy regimens for choriocarcinoma treatment include the following: MAC regimen – metotrextate (MTX) + actinomycin-d + cyclophosphamid, then EMA/CO – etoposide + metotrextate + actinomycin-d + cyclophosphamid + vincristin. Unfortunately, these protocols could not be administrated in Serbia because actinomycin-d is not registrated.

That means that chemotherapy regimen was modified and 5 days metotrextate + cyclophosphamid regimen was administrated before total tumor excision. This therapy showed to be effective and one week later beta HCG was 2 mlU/L. Because of immunohistochemically confirmed metastatic focus of choriocarcinoma in predominant anaplastic carcinoma and only one positive HCG level of 38 mlU/mL, 5 day chemotherapy (metotrextate 15 mg IV + cyclophosphamide 300 mg IV) was administrated according to the protocol.

One week after chemotherapy serum HCG was below 5 mlU/mL. During and after chemotherapy the patient got 8 blood units and 9 units of FFP. Broad spectrum antibiotics continued administrating. The operative treatment was done in collaboration with vascular surgeon. Rupture of sigmoid colon and hemorrhage in tumor mass were found. The tumor had been exceeded in toto (Figure 4). On the day before and during the operation, 12 doses of blood were transfused and 6 doses of FFP. Immunohistochemical examination excluded metastases of choriocarcinoma in the exceeded tumor mass. After chemotherapy and total tumor excision anaplastic carcinoma was confirmed with intestinal infiltration and large fields of necrosis and bleeding. Tumor cells were CK7,
CK20, beta HCG, PLAP, inhibin and p63 negative. Our patient had nongestational choriocarcinoma with poor prognosis. The patient had early and extensive development of anaplastic carcinoma with choriocarcinoma foci complicated with ruptured sigmoid colon, infection and hemorrhage in tumor tissue. This explains progressive anemia, infection and febrile state. Nine days after the operation the patient went home recovered but died one month later because had rejected chemotherapy recommended according to the protocol.

**Discussion**

Non-gestational choriocarcinoma is a rare trophoblastic malignancy. If diagnosed on time and treated it can also be curable. If it does not invade nor metastasize early the prognosis can be better and the treatment more successful. Sometimes it spreads in the abdomen and also retroperitoneally. Non-gestational choriocarcinoma are followed with significantly lower serum beta HCG than in postgestational choriocarcinoma. That is the reason for poor prognosis in the time of diagnosis with following complications and lethal outcome. Because of the great risk of hemorrhage biopsy of metastases is not recommended in patients with metastatic choriocarcinoma. Destruction of local tissue and organs can be followed with progressive anemia caused by local hemorrhage in tumor, abdomen or retroperitoneum. Concomitant infection with high temperature needs antibiotic treatment and supportive therapy.

Chest and brain X-ray have to be done to exclude metastases in non-gestational as well as in gestational choriocarcinoma. Ultrasonography and CT are also of a great diagnostic value. Suggested chemotherapy regimens for choriocarcinoma treatment include following: MAC regimen – metotrexate (MTX) + actinomycin-d + cyclophosphamid, then EMA/CO – etoposide + metotrexate + actinomycin-d + cyclophosphamid + vincristin. Unfortunately, these protocols could not be administrated in Serbia because actinomycin-d is not registrated.

In the presented patient the effective chemotherapy regimen was a modified one: 5 days metotrexate 15 mg iv + cyclophosphamid 300 mg iv were administrated before the operation and tumor excision. This therapy showed to be effective for choriocarcinoma foci in anaplastic carcinoma and one week later beta human chornic gonadotropin was 2 mIU/L. Prognosis of non-gestational metastatic choriocarcinoma depends on the diagnosis as well as on treatment response. Delayed diagnosis and low responsiveness to chemotherapy and early extensive spread of disease mean poor prognosis and lead to lethal outcome.

**Conclusion**

Non-gestational metastatic choriocarcinoma complicated with another type of malignancy with early spread of the disease and low responsiveness to chemotherapy has poor prognosis and leads to lethal outcome.

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**REFERENCES**
