Metastatic choriocarcinoma with tumour lysis syndrome

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Abstract
We report on a 32-year-old woman, gravida 5, para 2 who presented with a rapidly growing process of a choriocarcinoma after spontaneous birth. Two weeks after delivery, the patient suffered from dyspnoea, tachycardia and two large ovarian cysts. Diagnostic showed a metastasis choriocarcinoma in the lung. After the first application of chemotherapy according to the EMACO protocol the patient degraded quickly. She had a respiratory distress syndrome and an endotracheal intubation was necessary. We suspected a massive tumour cell lysis with haemorrhage after chemotherapy. Tumourlysis syndrome in choriocarcinoma is a rare complication as it is in solid tumours. Treatment in the intensive care unit allowed continuation of chemotherapy with EMACO. The general health state of the patient improves slowly and β-HCG falled. After 78 days of hospitalization the patient was able to be discharged from hospital.

Introduction
Choriocarcinoma is a gestational trophoblastic disease (GTD). It is a malignant cancer usually of the placenta. This type of malignancy is characterized by intimately related syncytiotrophoblasts and cytotrophoblasts with extensive haemorrhage. Two types can be differentiated: low and high risk. The dissemination of metastasis is typical for high-risk choriocarcinoma. 25% of choriocarcinoma occur after spontaneous birth; the others, after an extra uterine pregnancy and miscarriage. In Europe, there are only rare cases of choriocarcinoma whereas in Asia and Africa the incidence is much higher [1,2]. The cure rates are good, when therapy starts quickly. In high risk choriocarcinoma the gold standard for treatment is a multi-agent chemotherapy with etoposide, actinomycin D, methotrexate, cyclophophamid and vincristine (EMACO).

A monotherapy with etoposide has also good effects on metastatic choriocarcinoma and can be discussed [3]. Surgery does not play a major role.

Case report
A 32-year-old woman G5 P2 after spontaneous birth with 40+0 week of pregnancy presented with tachycardia and shivering during postnatal hospitalization. The results in blood examination showed a hyperthyroidism (TSH 0,01 IU/ml, fT3 19,95 pg/ml, fT4 6,28 ng/dl) and the IRM revealed bilateral multicompartment cys from the ovaries (10×10 cm).

According to the patient's history these cys had been diagnosed during pregnancy already. The symptoms were tolerable for the patient and she wished to breast feed her child. A treatment with Thiamazol and Propanolol for hyperthyreosis was refused. One week later the patient came to the emergency room with lower abdominal pain. The examination showed a patient in a reduced general condition with tachycardia and dyspnea at rest. The lochia were normal, there were no abnormal bleedings. The bilateral multicompartment cys were stable and without signs of torsion. The further radiological diagnostics revealed multiple metastasis in the lungs, suspect nodules in mediastinum, and no metastasis in brain. Since the patient's mother had had a thyroid cancer and she presented with the signs of hyperthyroidism we suspected a thyroid cancer. However, further diagnostics (sonography of thyroid and scintigraphy of the thyroid) were unremarkable. High β-hcg serum values (149074 mU/ml) led the way to diagnosis. According to the staging the patient has a FIGO III choriocarcinoma with a WHO-Score of 14; so it must be considered as a high-risk carcinoma. Based on this diagnosis a multi-agent chemotherapy with etoposide, actinomycin D, methotrexate, cyclophosphamid and vincristine was started immediately. After the first administration, the general condition of the patient worsened. The dyspnea at rest aggravated and the patient had to be intubated. The patient presented an acute respiratory distress syndrome (ARDS) and needed an extracorporeal membrane oxygenation (ECMO). We supposed a tumour lysis syndrome. The multiagent chemotherapy was continued under extracorporeal membrane oxygenation. Finally, the patient stabilized and was extubated. The value of β-hcg decreased (see below). 78 days after diagnosis the patient went home in good general condition (Table 1).

Discussion
The tumour lysis syndrome (TLS) is an oncological emergency which is caused by massive tumour cell lysis at the first application of chemotherapy. The danger of TLS is especially high when the proliferation rate from the tumour is high and when a rapid response of chemotherapy is to be expected. It showed hyperphosphatemia with hypocalcaemia, hyperuricemia and hyperkalaemia. These

| Period | Dosage   |
|--------|----------|
| Day 1 (before chemotherapy) | 150000 mU/ml |
| Day 6 (before chemotherapy) | 1600.000 mU/ml |
| Day 12 (4 days after chemotherapy) | 511.00 mU/ml |
| Day 47 | 155 mU/ml |

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electrolyte and metabolic disturbances can progress to clinical toxic effects, including renal insufficiency, cardiac arrhythmias, seizures and death to multiorgan failure. Therefore, an immediate handling in intensive care is needed.

**TLS appears primarily in lymphatic or hematopoietic cancers, in solid tumours it’s unusual [4,5].**

When risk factors (mass of tumour, renal insufficiency, preexisting hyperuricemia, cardiovascular disease, exsiccosis, elevated LDH) exist, a prevention for TLS is recommended. It is recommended to avoid nephrotoxic substances, to avoid potassium sparing diuretics and to avoid too much phosphate supply. It is important to supply liquids (3 l per day) and to start a treatment with Allopurinol or better Uratoxidase (Rasburicase) as a prophylactic treatment. The main goal of treatment is to prevent the occurrence of renal dysfunction which is associated with heavy morbidity and mortality [6].

**Especially the treatment with Uratoxidase (Rasburicase) is effective. It decreases the need for dialysis [7].**

Our patient didn't show any sign of kidney failure, but an acute respiratory distress syndrome which needed an extracorporeal membrane oxygenation (ECMO). In the FIGO cancer report from 2018 [8] an ultrahigh risk group with a WHO risk score of 13 or greater is identified. It is recommended that for those with massive disease it could be better to start with an initial gentle chemotherapy with Etoposide 100 mg/m² and Cisplatin 20 mg/m² on days 1-2, repeated weekly for 1-3 weeks, before starting normal chemotherapy [9,10]. The identification of high-risk patients of a TLS is indispensable before beginning a chemotherapy. Then it needs to be discussed if a preventive treatment with Uratoxidase (Rasburicase) and/or a gentle induction chemotherapy should be done.

**Conclusion**

Our case report shows a quickly processing choriocarcinoma and the complication of a TLS, which is rare in choriocarcinoma. The vaginal bleeding was not the main symptom, but hyperthyroidism which is a consequence of a choriocarcinoma and the large ovarian cysts. One can learn from this case that it is important to identify the risk factors from TLS before starting treatment and to discuss a prevention treatment with Uratoxidase (Rasburicase) and a gentle induction chemotherapy to avoid an eventual hospitalization in intensive care unit.

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