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Case Report

Metastatic germ cell tumor with complete response-7 years follow up

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ABSTRACT

Cancer of the testis is a relatively uncommon disease, accounting for approximately 1-1.5% of all cancers in males. 5% of the malignant germ cell tumors are made of extragonadal origin. Germ cell tumors occur in men younger, usually between 20 and 35 years old. We report a case of a patient with metastatic extragonadal germ cell tumor with multiple sites of metastases, and very high initial values of tumor marker human chorionic gonadotrophin (HCG)-1351308. At the time of diagnosis, the patient was in a very poor general condition. After the applied chemotherapy, there was a complete response and 7 years later the patient is without any symptoms of disease.

Keywords: Complete response, Germ cell tumor, Metastatic disease

INTRODUCTION

Testicular cancer represents overall 5% of urological tumors, with approximately 6,3 new cases occurring per 100000 males/per year in industrialized countries on the west, with data to 10 new cases/100000 males/per year in some Scandinavian countries. The vast majority of GCT arise in the testicles with ~5% occurring outside of the gonads, i.e. extragonadal germ cell tumor (EGGCT).[1,2]

EGGCT is by definition a germ cell neoplasm displaying one of the histologies associated with gonadal origin, but located outside of the gonads. This specific clinical entity was first described in the 19th century. Some autors suggest that this distribution is a consequence of abnormal cell migration during embryogenesis. They are rare tumors and usually found in the body's mid-line, e.g. retroperitoneum, mediastinum or cerebrum, sometimes posing diagnostic difficulties.[3] These tumors are still managed the same as testicular germ cell tumors.[4] Approximately 50% of the TGCTs are pure seminomas and 50% are non-seminomas.

CASE REPORT

The present study reports the case of a 42-year-old male with metastatic germ cell tumor, extragonadal. The patient was treated and followed up from 2010. During hospitalization in Clinic of Urology he underwent surgery (St. post orchiectomiam l.sin+biopsiam testis l.dex.). There was no palpabile and ultrasonografy detectable mass in testicles. On arrival at the Clinic of Oncology the patient was in very bad general condition, respiratory threatened and intoxicated, ECOG 4. CT scans showed multiple distant metastasis in lungs (Figure 1) and retroperitoneal lymh nodes. Serum level of human chorionic gonadotropin (HCG) was 1351308, LDH 1037 and AFP 2,6.

There was negative patohystological finding from orhiectomy. Typ of metastatic disease and levels of beta-HCG and LDH suggested that it may be metastatic nonseminomatous germ cell tumor.

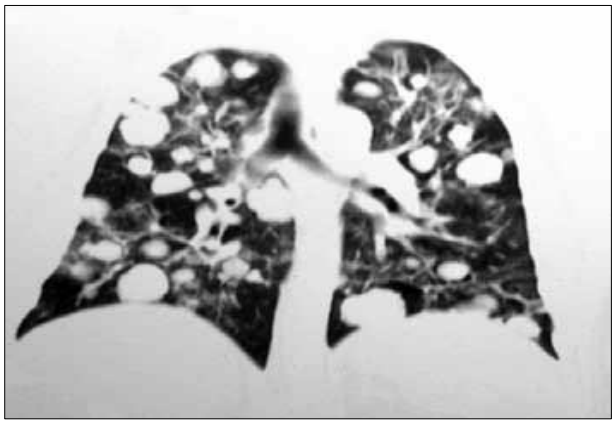

Figure 1. Multiple metastases in the lungs.

Oncological decision was to treat patient with PE chemotherapy (CHT) protocol, without Bleomicin due to respiratory deficiency (reduction in lung capacity). In 5/2010. the patient started chemotherapy with PE protocol, with aggressive premedication. Even though patient received antihyperuricemic agent before and during chemotherapy, tumor lysis syndrome developed. Also, leucopeny Gr 4 has occured after the first chemotherapy cycle and tremor of the left hand with paresis, so chemotherapy was stopped. He was treated with best supportive care: antibiotics, analgetics, hydration and compensation of electrolytes, corticosteroids, acidiuricum synthesis inhibitors, antiasthmatics, granulocytes stimulators and transfusions. From laboratory findings 5/2010.: HCG 1351308, AFP 2.6, LDH 1037, SE 53, Er 3.1, Hgb 82, Le 15, Plt 404, AST 45, ALT 15, Bilirubin total 34, Bilirubin direct 18, Glucosa 7, 8..5,3, urea 8..14..20..33, creatinin 116..156..202.

Endocranial CT scan was performed and showed right side subcortical parietal solitary meta, diameter 16 mm, with perifocal edema. Also, skeletal scyntigraphy was done and there was no spreading of disease in bones.

After prolonged hospitalization and symptomatic-supportive treatment, general condition of the patient was better, and chemotherapy was continued. Human chorionic gonadotropin level after second CHT was 19215, LDH level 503 and acidiuricum 248. Patient received 6 cycles with PE protocol with complete regression of retroperitoneal metastasis and partial regression of the lung metastases. Control laboratory findings - beta HCG 3.9, LDH 171, AFP 2.65, and ECOG 0.

The patient received second line chemotherapy with VEIP protocol, 4 cycles, that resulted with very good partial regression of pulmonary metastasis (Figure 2), with HCG - less than 2. From laboratory findings 3/2011: beta HCG 1.2 (Table 1).

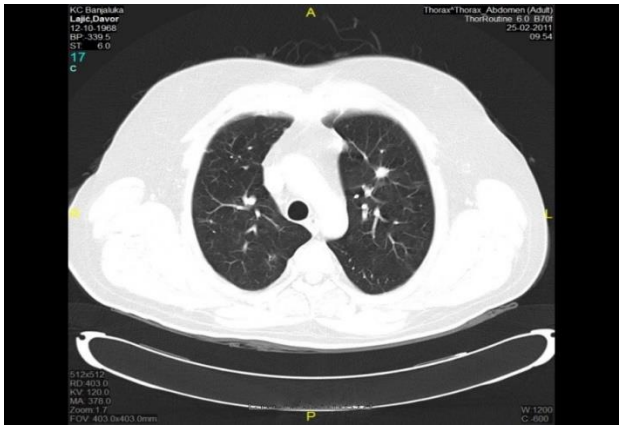

Figure 2: CT scan - regression of pulmonary metastasis.

Table 1: Tumor markers.

	Before CHT	After CHT No II	After CHT No VI	After second line CHT
HCG	1351308	19 215	3.9	1.2
LDH	1037	503	171	160
AFP	2.6	2.6	2.2	2.0

Control endocranial MRI was performed-the change described in brain parenchym in the right frontal gyrus precentralis, according to their MR characteristics could match the changes in which are observed the products of hem-can be present on the ground earlier described, the secondary deposits in the phase of regression (Figure 3). We consultet radiooncologyst-there is no indications of irradiation of endocranium.

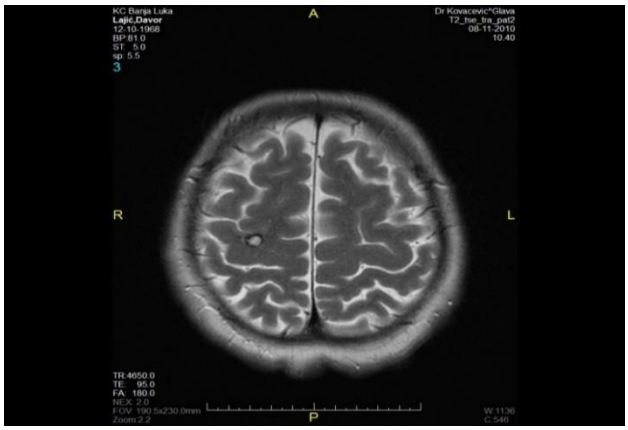

Figure 3: MR - regression of brain metastasis, products of HEM.

After all this threatment, he continued with regular follow up. One year after the specific oncological therapy was

finished, the patient returned to daily work, with a good quality of life. In the first two years patient was actively monitored for 2-3 months, and after that the next 5 years inspections of oncologist were carried out at 4-6 months, with relevant diagnostic tests. During follow-up, also our attention is focused on the possible occurrence of metachronous testicular tumors, and in the future occurrence of secondary malignancies. After 7 years of follow-up, done diagnostic imaging, there is no evidence of disease.

DISCUSSION

Approximately 30% of nonseminomatous germ-cell tumors (NSGCT) of the testis present with metastatic disease. Since the contributions of Einhorn and Donahue in 1977, platinum-based chemotherapy regimens have been standard therapy for patients with advanced disease.[5] The introduction of cisplatin-based combination chemotherapy resulted in a dramatic improvement in the prognosis of patients with metastatic germ cell tumors. In the pre-cisplatin era, cure rate for patients with advanced GCT was 5-10%. Standard recommended therapies are based on stage, serum tumor marker status, and IGCCCG risk classification. Patients with good-risk metastatic NSGCT have a five-year cancer-specific survival of 92% and may include patients from clinical stage (CS) IS to IIIA.[6] Cure rates approximate 100% in stage I disease and exceed 80% in metastatic cases.[7]

EGGCTs occur in several characteristic histological patterns that reflect the stages of normal embryonic and fetal development with seminomatous (germinoma/dysgerminoma) and nonseminomatous germ cell tumors. Histopathological pattern and tumor marker expression of α-fetoprotein (AFP), β human chorionic gonadotropin (β-HCG) and LDH, follow the same pattern as primary gonadal germ cell tumors.[8] As recommended by the ESMO Clinical Practice Guidelines biopsy of mid-line extragonadal tumors is mandatory, unless the patient is very sick and has high tumor markers. The biopsy should be recomended by testicular sonography to exclude a TGCT.[9]

Approximately 10% of all patients with advanced germ cell cancer present with brain metastases. Secondary deposit in the CNS usually occur as part of a systemic relapse of the disease. In patients with lung metastases it is necessary to do endocranial MR. Patients who have brain metastases at the time of initial diagnosis have a long-term survival probability of 30-40%. Patients mwho develop brain metastases during first line treatment have a 5-yr survival rate of only 2-5%.[10]

The cumulative risk of development of metachronous testicular cancer 10 years after diagnosis of EGGCT is about 10% according to the results from a meta-analysis by Hartmann et al. The rate of metachronous testicular cancer is higher among patients with nonseminomatous EGGCTs and retroperitoneal EGGCTs (14%), than in patients with seminomatous EGGCTs (1.4%) or seminomatous mediastinal EGGCTs (6.2%).[11] The risk of developing secondary non-germ cell solid tumors is not increased with an incidence of 2% after a median follow-up of 55 months.[12] However, there is an increased risk, in patients with mediastinal EGGCT, of developing acute megacaryoblastic leukemia or myelodysplasia with abnormal megacaryocytes (2% of patients).[13]

CONCLUSION

The present study represents an example of the excellent efficiency of CHT based on the cisplatinum in the treatment of advanced GCT, even with very bad performance status of patient. Also, our work has shown that the high value of HCG can be a reliable indicator of the presence of metastatic germ cell tumors. Regardless of oncology recommendations and protocols, sometimes the doctor must take great responsibility and make the difficult decision about the treatment of his patient.

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