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Research Article

Over the Counter Cisplatin-Etoposide Treatment for Primary Mediastinal Germ Cell Tumor

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- Yolk sac tumor
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Abstract

Background: Germ cell tumors are malignancies arising from gamete precursors usually located in the gonads or more rarely along the midline of the body including the anterior mediastinum. Primary mediastinal germ cell tumors are always of poor prognosis. In lack of validated treatment strategies the protocols of gonadic germ cell tumors are usually applied.

Methods: The case of a young male patient is reported who underwent 4 cycles of bleomycin-etoposide-cisplatin and 2 cycles of etoposide-cisplatin primary chemotherapy followed five weeks later by the resection of the residual mass of a primary mediastinal germ cell tumor measuring initially 11 cm of long axis.

Results: He was declared healthy after a five-year long relapse-free follow up.

Conclusion: Prolonging the advised 4 cycles of chemotherapy and programming the operation to 4-6 weeks after the first day of the last cycle of the chemotherapy seem to be reasonable therapeutic approaches.

INTRODUCTION

Germ cell tumors (GCTs) are malignancies arising from gamete precursors usually located in the gonads or more rarely along the midline of the body including the coccyx in children, retroperitoneum, anterior mediastinum and pineal gland. Risk classification of extragonadic GCTs is the same as of gonadic GCTs, with primary mediastinal GCTs being always of poor prognosis [1]. Due to the rarity of the disease prospective studies have not been realised. In lack of validated treatment strategies the protocols of gonadic GCTs are usually applied [1].

The creation of an international database has been proposed to obtain more information on these tumors [2].

MATERIALS AND METHODS

In the ten-year long oncologic practice of the regional hospital centre Petz Aladár, Hungary a single case of primary mediastinal GCT has been diagnosed. The management of this case is reported below.

Of note, there was a single case of primary retroperitoneal GCT in this period as well, whereas we treat 20-25 GCTs per year at our department of oncology.

CASE PRESENTATION

A 24-year-old male patient was admitted to another department for a mediastinal mass revealed by chest pain. The chest X-ray and CT showed an 11.0 cm large ovoid tumor in the anterior mediastinum (Figure 1). Varicocelectomy could be noted in his past medical history. Histological examination of the biopsy specimen diagnosed a clear yolk sac tumor (AFP+, Mib1: 80%). A spermatogram realised in the context of a cryopreservation showed azoospermia.

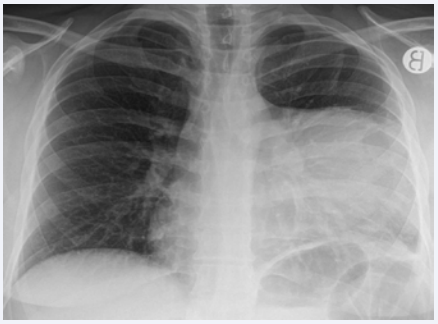

Figure 1 Chest X-ray of the mediastinal mass before the onset of the cytotoxic therapy.

He was transferred to our department for cytotoxic treatment. 4 cycles of BEP (bleomycin-etoposide-cisplatin) and additional 2 cycles of EP (etoposide-cisplatin) chemotherapy were administered. The initial level of alfa-foetoprotein (AFP) over 1000 ng/mL went down to 134 ng/mL at the end of the 3rd cycle and to 42 ng/mL at the end of the 5th cycle. (A haemoculture realised for fever during the 1st cycle came back positive for E.chloacae. He became apyretic under combined targeted parenteral antibiotic treatment.)

Control chest CT showed partial regression with a longest axial diameter of 8.0 cm. Tumor resection was realised from left axillary thoracotomy. Histological examination found an almost entirely necrotised tumor. However, the limiting zone composed of fibrotic tissue contained viable tumor cell islets typical for the earlier diagnosed yolk sac tumor. The resection was complete (R0). The slightly elevated preoperative tumor marker (AFP: 47 ng/mL) got normalised postoperatively (AFP: 6 ng/mL).

(On postoperative day 24 pulmonary embolism was diagnosed upon the onset of chest pain. Six-month long curative anticoagulant therapy was initiated with LMWH (low molecular weight heparin)).

Control chest CT at two months and six months did not show any recurrence. Further follow up was assumed by chest X-ray and tumor marker and no anomaly had been detected for 5 years. The patient was declared healthy and finishing of the oncologic follow up was offered.

DISCUSSION

A successful combined medical and surgical treatment is presented for a bulky non-metastatic primary mediastinal germ cell tumor.

The time from patient's presentation to treatment initiation was 24 days, although extreme elevation of the tumor marker was known within a week. The delay was essentially due to the asking for a second histological opinion. We wish the patient would have been presented to our department upon the receipt of the pathological AFP level. In that rare case, in the absence of alternative diagnosis the BEP therapy could have been started earlier, while the histological interpretation was ongoing.

The determination of AFP level is unfortunately limited at 1000 ng/mL in our hospital. Making impossible the correct initial IGCCCG (International Germ Cell Cancer Collaborative Group) risk classification of GCTs, the number of cycles of chemotherapy needed is estimated in certain cases by the marker kinetics. However, the primary mediastinal GCT is anyway of poor prognosis and 4 cycles of chemotherapy are recommended in the guidelines [1].

The recommendations do not help in cases when tumor marker levels do not sink to the normal range. We had earlier favourable experience with the use of additional 2 cycles of EP in the context of a non-seminomatous testicular GCT with giant retroperitoneal lymphadenomegaly where tumor markers remained high after 4 cycles of BEP and time gap to the retroperitoneal lymphadenectomy was fulfilled by the prolongation of the chemotherapy. Indeed, due to its pulmonary toxicity administration of bleomycin is limited to 4 cycles. In this case the additional treatment by EP allowed to maintain the AFP level stable (42-47 ng/mL) while waiting for surgery.

The main reason for the prolongation is to avoid that malignant cells get out of control of the cytotoxic treatment. A big surgery like the resection of a bulky mediastinal mass or a retroperitoneal lymphadenomegaly is not absolutely available within a short period of time. We believe that the optimal timing of surgery is 4 to 6 weeks after the first day of the last cycle of the primary systemic therapy. This interval may provide both, avoiding the risk of cytopenia and the tumor getting out of cytotoxic control.

It is interesting to note that primary mediastinal GCTs are so rare that no staging is univocally recognised [2]. In the absence of established staging the appreciation of treatment strategies may also be more flexible.

Finally, fertility preservation is a sensible issue with GCTs [3]. The patient was found to have azoospermia on the spermatogram realised in the context of the pretherapeutic cryo-conservation. The incidence of hypogonadism has been described to be higher in mediastinal GCTs but the relation to azoospermia is not clear [4]. Nevertheless, gonadic GCTs developed on cryptorchidism are known to be linked to azoospermia [5].

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