

CASE REPORT

Optimal management and the role of radiotherapy in the complex treatment of primary mediastinal seminoma: A clinical case with literature review

Lena Marinova^{1*} Rositsa Krasteva² Zahari Zahariev²

Abstract: The Primary Mediastinal Seminoma (PMS) is a rare extragonadal malignant germ-cell tumor. We report a clinical case of our practice, which is the reason for this literature review and try to find the optimal multimodal therapeutic option and the role of radiotherapy.

Keywords: seminoma, mediastinum, complex treatment, radiotherapy

1 Introduction

Seminoma is a rarely diagnosed extragonadal germ-cell tumor, which occurs in three ectopic places: the pineal gland^[1], retroperitoneal space^[2] and mediastinum^[3].

The mediastinum is the most frequent place for this localization (25%-30%). Due to the rarely diagnosed cases, insufficiently studied origin and more specific biological behaviour, mediastinal seminoma poses a number of unresolved therapeutic problems. Therapeutic problems are related to the multimodal treatment approach and the location of each of the oncological methods: surgery, radiotherapy and chemotherapy.

2 Case presentation

A 32-year old male was diagnosed with vena cava syndrome and enlarged supraclavicular lymph node. Not reported for concomitant oncological diseases. Thorax CT showed a big tumour mass occupying the anterior portion of the mediastinum, infiltrating 2/3 of the right lung and compressing the trachea, vena cava and vena azygos, clearly indicated in Figure 1.

The biopsy of the supraclavicular lymph nodes permitted the diagnosis of seminoma.

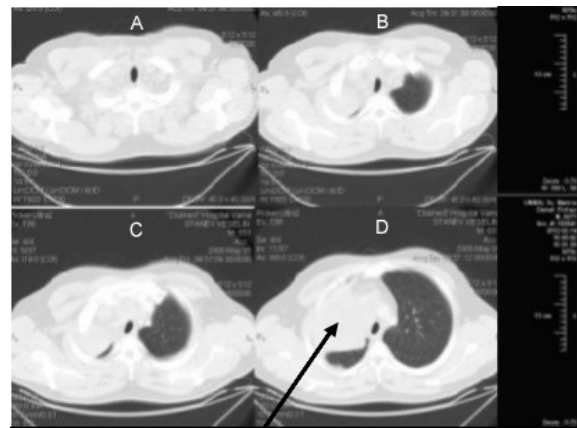


Figure 1. Thorax CT before chemotherapy and radiotherapy (A→B→C→D stand for the different levels from top to the bottom of the chest)

Blood laboratory tests for β -subunit human chorionic gonadotropin (b-hCG) and Alpha Fetoprotein (AFP) before chemotherapy were in normal ranges (b-hCG, 5 IU/l; AFP, 4.03 IU/ml). Bone scan with gama-camera (Tc 99 m and abdominal ultrasonography) were also normal. The treatment started with chemotherapy with PVB-Carboplatin (200 mg/m²) on day 1, Vinblastine (0.15 mg/m²) on days 1 and 2, Bleomycin (15 U/m²) on days 1 and 2 (every 21 days, 6 cycles were done). Due to partial response (PR) that decrease in the initial tumour volume to 50%, chemotherapy was followed by radiotherapy (Figure 2).

At the first stage of radiotherapy the whole mediastinum was irradiated of telegamatherapy with single dose (2 Gy) to a total dose (TD, 42 Gy). For the supraclavicular region and neck lymph nodes were implemented TD (40 Gy) with a single dose (2 Gy). Control CT of the

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*Correspondence to: Lena Marinova, Department of Radiotherapy, Oncology Center, Russe, Bulgaria; Email: rad_marinova@abv.bg

¹ Department of Radiotherapy, Oncology Center, Russe, Bulgaria

² Clinic of Radiotherapy and Oncology, Uni Hospital, Panagyurishte, Bulgaria

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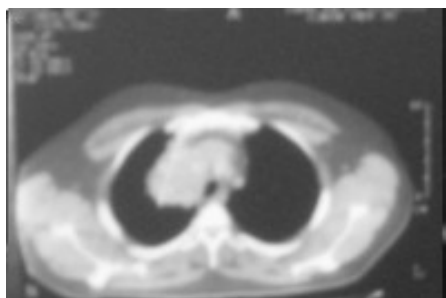


Figure 2. Control CT of the chest after 6 cycles of chemotherapy (similar to Stage II)

chest was performed after the first stage and the image revealed residual tumour mass in the mediastinum (Figure 3).

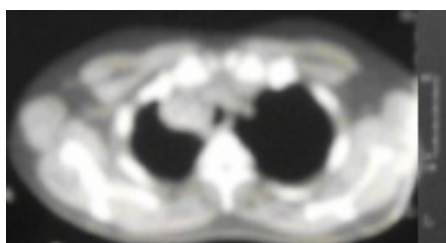


Figure 3. Control CT of the chest after 6 cycles of chemotherapy and radiotherapy of the mediastinum to total dose 42 Gy (similar to Stage II)

At the second stage of radiotherapy was implemented boost to the TD (56 Gy) in the residual tumour mediastinal mass. New control chest CT will be performed two months after the radiotherapy. If the tumour persists, maybe surgery will be a good option?

3 Discussion

For determination of the optimal treatment management in PMS, it is necessary to consider all characteristics of this rare extragonadal germ-cell tumor.

Malignant Mediastinal Germ-cell Tumors (MMGT) are 3%-10% of all mediastinal tumors and only 1%-5% of Germ-cells tumors. Primary Mediastinal Seminoma is 52% of all MMGT. This cancer can occur at any age, but is most common between the ages of 20 and 40. The patient complains of dyspnea, retrosternal pain or heaviness in this area, cough, fever, gynecomasty and weight loss. In 10% of the patients superior vena cava syndrome develops^[4,5].

PMS is a slowly increasing tumor that reaches up to 20-30 cm in diameter^[6]. Most often this is a bulky disease with large, heterogenic tumor masses in the anterior mediastinum and very rarely in the middle mediastinum^[7].

These tumours can infiltrate the neighboring tissues

and organs: lung, heart, chest wall. They can lead to obstruction of pulmonary arteries and to infiltration of the pericardium^[8]. The dissemination is usually present with symptoms from lymphatic infiltration (supraclavicular and neck lymph nodes on both sides).

In 30%-40% of the cases the disease is localized without distant metastases. It is possible to have hematogenic dissemination, most often in the bone^[9], lung and intrathoracic structures and rarely in the retroperitoneum and in the brain^[10].

Laboratory blood tests and biochemistry are in normal ranges. Serum levels of b-hCG and AFP are in normal ranges too. In the 10% of the locally advanced PMS /pure seminoma/ there may be elevation of b-hCG levels, but not AFT. A significant elevation of AFT levels (up to 100 ng/ml) usually indicates the presence of the nonseminomatous germ-cell elements. AFP levels may be elevated in patients with liver dysfunction or hepatitis.

Germ-cell neoplasms are classified into two broad histologic categories: seminoma and non-seminomatous germ-cell tumours. Pure seminoma is the most common single histology, accounting for 30% of all germ-cell tumours^[7]. Germ-cell tumors are composed of round, large pleomorphic cells with clear or granular cytoplasm with large centrally situated nucleoli.

The principal objective of the staging evaluation is to ascertain whether the patient has an early-stage disease or disseminated disease.

A chest-X-ray can determine a tumor mass in the mediastinum without calcifications and compression into trachea and bronchi. Chest CT in most cases reveals tumor mass in the anterior mediastinum, situated around the trachea, superior vena cava, vena azygos with infiltration of these structures. CT imaging is non specific and that's why it is difficult to differentiate PMS from other mediastinal tumors. Using MRI, it is possible to differentiate seminoma and nonseminoma germ-cell tumors.

For exact staging the following are necessary: testicular ultrasonography, abdominal ultrasonography, chest CT, abdominopelvic CT and PET-CT with Gallium-67^[11].

Treatment options are surgery, radiotherapy, chemotherapy and complex therapy. In literature there are cases of local surgery, excision of the primary mediastinal tumour, including with thymectomy^[7]. With regard to thymectomy, it is not indicated, since the previous notions are rejected, that the tumor originates from the thymus or from its embryonic chins. Radical inguinal orchiectomy is a rejected method too, because the old statement that PMS are metastases from degenerative occult primary testicular tumours is not acceptable now. In pathology reports after autopsy no changes are found in the testis or in the retroperitoneal lymph nodes^[12, 13].

The modern opinion on the role of surgery in PMS is as “salvage surgery”: (1) In case of residual mediastinal tumour masses after chemotherapy^[14,15,31]; (2) Relapses despite the achieved local tumour control after chemotherapy^[16]. Resection of the residual tumour masses with a diameter of less than 3 cm after chemotherapy should be fine-tuned, as the pathologists often report lack of tumour cells. The residual tumor masses after chemotherapy must be over 3 cm in order to require a “salvage surgery”^[17].

Seminomas are radiosensitive tumors. Radiotherapy alone in PMS achieves a disease-free progression period (FDP) up to 54%-62% and overall survival of up to 69%^[18,19]. The standard radiotherapy plan, Clinical Target Volume (CTV), includes mediastinum, supraclavicular and neck lymph nodes with TD (40-50 Gy)^[29]. In neck lymph nodes metastases, some oncologists expand the volume of radiotherapy, including axillary lymph nodes. Total dose with cancer eradicating effect in PMS when the radiotherapy is applied alone is 45 to 60 Gy. 1/3 Of the patients after radiotherapy have distant metastases or local relapse^[20]. The most frequent reason for relapse is the bulky disease and the systemic characteristics of this illness. Chances to cure PMS patients only with radiotherapy and to confirm local tumour control (LTC) are slim.

Since 1970, the standard medical treatment in PMS is 4 to 6 cycles of chemotherapy with Cisplatin^[16,21,22] or PVB. Tumor evaluation after chemotherapy in most cases reports remission of the disease. High dose chemotherapy followed by bone marrow transplantation is given in dissemination diseases^[24-27]. Chemotherapy alone achieves high therapeutically results that 5 years of FDP is 86%-90%^[19,28]. Liu TZ, *et al.* recommended that chemotherapy combined with a local therapy such as surgery or radiotherapy is a reasonable treatment strategy^[32]. In the presented clinical case, it concerns locally advanced mediastinal seminoma with vena cava syndrome and partial tumour response after chemotherapy, similar to other authors^[29]. In the residual tumour mass, we realized TD 56 Gy. This radiotherapy is necessary, because surgery was impossible and it is the only follow-up treatment in the present case. There is no significant shrink in the tumour volume after chemotherapy and also after radiotherapy to TD 42 Gy which is a sign of moderate chemo- and radioresistance. Despite normal levels of β -HCG, in the tumour there may be present a small amount of syncytiotrophoblastic cell component, which does not increase the tumour marker. This is the reason for the second stage to raise the mediastinal TD to 56 Gy.

PMS is a bulky disease with systemic characteristics. For maximal treatment effect it is necessary to combine

three oncological methods: chemotherapy, radiotherapy and salvage surgery^[30]. In all cases one should start with chemotherapy, and after that proceed with radiotherapy like an additive method. Because of radio sensitivity and accumulation of side effects of radio and chemotherapy, the TD must be up to 54-56 Gy. The patient follow-up is every 2 months including chest CT and serum markers.

4 Conclusion

(1) PMS is a systemic disease with a high chance to be cured.

(2) The role of radiotherapy is additive local treatment method following chemotherapy.

(3) An open question remains whether the salvage surgery should be performed with a residual tumor after chemo and radiotherapy.

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