

Primary Malignant Mediastinal Germ Cell Tumors

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Abstract

Primary malignant mediastinal germ cell tumors are the most common extragonadal germ cell tumors in young adults (PMMGCT). We review in our report the clinical features and therapeutic strategies and outcome of three patients diagnosed with PMMGCT at the department of medical oncology at Hassan II University Hospital of Fez, Morocco and we review briefly the existing literature data.

Keywords: Germ cell tumors; Mediastinum; Treatment

Introduction

Primary Malignant Mediastinal Germ Cell Tumors (PMMGCT) are the most common extragonadal germ cell tumors in young adults [1,2]. They are a diagnostic challenge and have a worse prognosis than their gonadal counterparts. In this report, we review the clinical features, therapeutic strategies and outcome of three patients with PMMGCT treated at the department of medical oncology at Hassan II University Hospital of FEZ, Morocco between January 2007 and December 2015.

Case Reports

The first case was a 23-year-old male, without particular past medical history who was diagnosed with mediastinal immature teratoma. At the time of diagnosis, the patient presented with complaints of dyspnea, hemoptysis and weight loss. His physical examination was unrevealing, and the testicles were normal. Patient's computed tomography (CT) scans of chest abdomen and pelvis revealed a large mass in the anterosuperior mediastinum with diffuse pulmonary metastases. Ultrasound examination of the scrotum was normal. The diagnosis was established by the elevated AFP concentration and histological examination by fine needle biopsy. Palliative chemotherapy based on cisplatin, etoposide and bleomycin (BEP) regimen was started. After 6 cycles of treatment, the patient developed diffuse brain metastases. He underwent brain radiotherapy and died few days later from the decline of his overall health status.

The second case was a 32-year-old smoker male who was worked up at the department of pneumology for an incidental bulky anterior mediastinal mass involving mediastinal vessels and right hemithorax along the pleural surface. Elevated serum level of BHCG, normal AFP and needle biopsy supported the diagnosis of pure seminoma. His CT scans did not reveal distant metastases. Ultrasound examination of the scrotum was done as well, results of which were negative. The patient received BEP chemotherapy. After a total of four cycles of treatment, a biological and radiological partial remission were observed with a residual mass of 3 cm versus 11 cm. PET scan was negative, and the patient underwent a careful monitoring. He remained disease-free for 29 months.

The third case was a 27-year-old male, drinker and smoker who presented with a four months medical history of hoarseness and dyspnea. His physical examination was normal. The CT scans showed an anterior large mediastinal mass without distant metastasis. Test for AFP was elevated. A testis primary was excluded by sonographic investigation of the testis. Pathology was consistent with a yolk sac mediastinal tumor. The patient was treated with initial BEP chemotherapy. Radiologic partial response and negativation of serum markers was achieved after 4 cycles and the patient underwent complete resection. He is disease free for 25 months.

Discussion

Primary Malignant Germ Cell Tumors (PMGCT) of the mediastinum are the most common extragonadal germ cell tumors. They account for less than 6% of all germ cell malignancies and represent approximately 12% of all malignant mediastinal primitive tumors [3-5]. The origin of these tumors is thought to be the cessation of the migration of embryonic cell toward gonads along the median line; other authors suggest the reactivation of genes, normally active only during the embryonic life, which confers pluripotent properties to a small amount of cells [6]. Histologically, PMMGCT are similar to those that occur in gonads. These are categorized into three different entities: seminomas, immature teratomas, nonseminomatous tumors including yolk sac tumor, embryonal carcinoma, choriocarcinoma, teratocarcinoma and mixed tumors [7,8]. Seminomas are the most common mediastinal malignant germ cell tumors [7]. The clinical symptoms are nonspecific, reason for which MGCT are prone to be misdiagnosed. The most common presenting symptoms are cough, chest pain, hemoptysis, dyspnea, night sweat, or weight loss and rarely symptoms of superior vena cava compression. Sometimes, the patient is asymptomatic, and the diagnosis is made by routine examination or elevations in serum alpha-fetoprotein (AFP) and/or beta-human chorionic gonadotropin (beta-hCG) which will ultimately favor a diagnosis of NSGCT [5].

However, a tissue diagnosis is required for definitive diagnosis of Mediastinal malignant GCT before treatment unless the patient requires emergent treatment, and the diagnosis is obvious by tumor markers and the distribution of disease. Also, Extragonadal germ cell tumors are considered metastases from occult or gonadal cancer until proved otherwise [9].

In the last two decades, cisplatin-based chemotherapy has become the standard therapy for PMMGCT, and the role of surgical resection has been changed into multimodal therapy because surgery alone has resulted in a poor prognosis to the patients with PMMGCT [10-12]. Pure seminomas are sensitive to both chemotherapy and radiotherapy; they have good prognosis regardless of location and Long-term disease-

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free survival is achieved in roughly 90 percent of patients treated with chemotherapy [12-14], The best therapeutic sequence of surgery, chemotherapy and radiotherapy has not been evaluated in controlled trials. However, most centers recommend primary cisplatin based chemotherapy rather than radiotherapy or surgery. In those patients who are not candidates to chemotherapy, primary radiations have been effective in the local control of the tumors, and are an acceptable option in the absence of bulky or metastatic disease [13]. The optimal treatment of residual masses is a subject of contention. Optional approaches include careful monitoring with periodic CT scans, open biopsy of the mass, and 18-fluoro-2-deoxyglucose (FDG) positron emission tomography (PET) scan. Masses fixed with PET CT should be resected whenever possible.

NSGCT are aggressive tumors that are often metastatic at presentation. They are relatively resistant to radiotherapy which is not recommended [15,16]. Multimodality treatment utilizing primary chemotherapy followed by surgery to resect any residual masses has become the best approach to improve the survival of these patients [17]. Residual masses contain tumor residues in nearly 50% of cases even in the absence of elevation of tumor markers. A complete response is then obtained in 45 to 55% of the cases [18]. Nevertheless, NSGCT have an unfavorable prognosis due to the low rate of complete response, a high risk of relapse and the late occurrence of secondary hemopathies [19].

Conclusion

In conclusion, the prognosis of patients with seminomas is significantly better than that of patients with NSGCT. The results of multidimensional therapy for PMMGCT depend on both successful chemotherapy and surgery. However, further studies are needed for the identification of clinical, biological and even cytogenetic prognostic factors which would allow a more adapted multimodality treatment strategy to improve the survival.

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