Case report - Thoracic oncologic

Mediastinal germ cell tumor with acute myeloid leukemia and growing teratoma syndrome

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Abstract

A 39-year-old man was referred to hospital with a giant mediastinal mass, thrombocytopenia and high levels of serum tumor markers. Flow cytometry of bone marrow and peripheral blood samples led to the diagnosis of a mediastinal germ cell tumor associated with hematologic neoplasia. He was treated with combination chemotherapy for a germ cell tumor and acute myeloid leukemia. After chemotherapy, the tumor was enlarged, although serum tumor marker levels had decreased. After induction therapy, the tumor was surgically resected. This syndrome is rare, and more cases need to be studied to enable effective treatment.

Keywords: Malignant germ cell tumor; Acute myeloid leukemia; Growing teratoma syndrome

1. Introduction

The association of mediastinal germ cell tumors with hematological malignancies has been recognized for more than 20 years [1, 2]. In 1990, Nichols et al. established this association as a clinical entity. However, the neoplastic processes involved are unknown [3].

A previously healthy 39-year-old man was referred to our hospital with persistent fever and chest pain. A chest X-ray revealed a large mass extending from the mediastinum into the right lung field (Fig. 1a) and enhanced computed tomography confirmed a large mass (115 × 86 mm) extending from the anterior mediastinum into the right hemithorax, and stenosis of the superior vena cava (Fig. 1b).

Serological studies showed a serum α-fetoprotein (AFP) level of 1536 ng/ml (normal range 0–20), a β-subunit of human chorionic gonadotropin (β-HCG) level of 114.5 mIU/ml (normal range 0–0.5), and a lactate dehydrogenase level of 2468 IU/l (normal range 119–229). Laboratory tests showed the following: a hemoglobin level of 17.8 g/dl; hematocrit of 52.4%; white blood cell count of 6200 (60% neutrophils, 18% lymphocytes, 5% monocytes, and 15% neoplastic cells); and a platelet count of 4000/µl. A tumor biopsy was not performed because of severe thrombocytopenia. Due to a dry tap, no bone marrow aspiration biopsy data were obtained. Cytogenetic analysis revealed multiple aberrations (61, XY, −X, −3, −4, −5, −6, −8, −9, +10, −11, −12, −13, +15, −16, −17, +19, +mar1). Both bone marrow and peripheral blood samples showed the presence of blasts positive for CD41 and GP-A. This led to a diagnosis of ‘the syndrome of mediastinal germ cell tumor associated with hematologic neoplasia’ (M6 and M7).

The patient was treated with a combination of cytarabine, daunorubicin, cisplatin, and etoposide. The chemotherapy was administered every four weeks without significant toxicity other than severe pancytopenia. After two cycles of chemotherapy both AFP and β-HCG levels had returned to normal (Fig. 2), and flow cytometry of the bone marrow showed 3.5% blasts. However, the mediastinal mass had increased in size. The patient underwent another round of brachytherapy, combined with cytarabine and etoposide for blast control, but the tumor did not shrink. After three months of induction therapy, the tumor was surgically removed, because the tumor had been growing and became symptomatic.

The tumor presented as a fibrotic capsule, firmly attached to (and invading) the pericardium (Fig. 1c). An ‘en block’ resection of the lesion and other involved structures including the pericardium, the left brachiocephalic vein, the thymus, and a portion of the right upper pulmonary lobe was performed, and pathologic examination showed a mature teratoma with necrotic tissue without malignant elements. The patient was discharged from the hospital two weeks after surgery. However, the patient had a recurrence at four weeks after the surgery, and died from progression of leukemia.

2. Comment

The syndrome of mediastinal germ cell tumor associated with hematologic neoplasia is rare, and few cases have been reported. Almost all patients with germ cell tumors complicated with hematologic malignancy die of leukemia. However, there was a case of a mediastinal germ cell tumor...
Fig. 1. (a) Chest roentgenogram on admission. (b) Computed tomography scan of the chest showing a mediastinal mass extending from the anterior mediastinum into the right hemithorax, and stenosis of superior vena cava. (c) Intraoperative field. The tumor was invading to the pericardium and pericardial fat.

other agents were set at 60% doses compared with the standard regimens for AML and extragonadal non-seminomatous germ cell tumors to avoid a fatal adverse event.

After two cycles of chemotherapy the tumor had increased in size despite a reduction in serum tumor marker levels. This situation was first described by Logothetis et al. in 1982 and is known as the ‘growing teratoma syndrome’ [5]. In that particular case, the increase in size was due to a mature teratoma.

In the current case, an additional round of brachytherapy failed to halt tumor growth, although tumor markers remained low. Microscopic analysis of the surgically excised tissue showed a mature teratoma with necrotic tissue. This suggests that, in cases, such as this, it might be not necessary to perform additional rounds of brachytherapy if the increased mass is due to the mature teratoma.

In conclusion, ‘the syndrome with mediastinal germ cell tumor associated with hematologic neoplasia’ is rare and a standard treatment protocol has not been established. In most of the reported cases, the patients died after treatment. Further studies are needed to improve the outcome for patients with this syndrome.

References