Pulmonary Metastatic Choriocarcinoma from a Burned-out Testicular Tumor

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Abstract

A 54-year-old man was referred to our hospital because of progressive dyspnea. Chest computed tomography showed multiple nodular shadows with a peripheral ground-glass halo. His clinical condition continued to deteriorate with the development of progressive respiratory failure requiring mechanical ventilation. A histological examination of a transbronchial lung biopsy revealed choriocarcinoma. The patient died within nine days of admission. A histological examination of the right testis during an autopsy revealed a burned-out testicular tumor consisting of a teratoma and a fibrous scar. We herein report a rare case of pulmonary multiple metastatic choriocarcinoma originating from a burned-out testicular tumor.

Key words: burned-out testicular tumor, choriocarcinoma, CT halo sign, multiple pulmonary metastasis

Introduction

Seminomas and nonseminomas (embryonal carcinoma, yolk sac tumors, teratomas, choriocarcinomas and mixed germ cell tumors) are the major histologic types of testicular germ cell tumors. Among these various germ cell tumors, choriocarcinoma is relatively rare, and mixed germ cell tumors that contain choriocarcinoma as one of the components comprise 8% of all testicular germ cell tumors, whereas its pure form represents less than 1% to 3% (1). Choriocarcinoma is the most aggressive type of germ cell tumor, characterized by a rapid proliferation and a greater propensity for distant metastases.

A burned-out testicular tumor refers to the presence of a metastatic extra-gonadal germ cell tumor with histological regression of the primary testicular lesion, and it is a rare form of testicular malignancy. This phenomenon in germ cell tumors is seen in choriocarcinomas (2, 3).

We herein report a rare case of pulmonary multiple metastatic choriocarcinoma originating from a burned-out testicular tumor.

Case Report

In March 2012, a 54-year-old man suffering from hemothorax and progressive dyspnea for one week visited our emergency center on foot. The findings of physical examinations conducted in the emergency room were as follows: Glasgow Coma Scale, 15 (eye opening, 4: verbal response, 5: motor response, 6); body temperature, 36.6 ºC; pulse rate, 125/min; blood pressure, 86/46 mmHg; and oxygen saturation, 50% on room air. Breathing sounds were weak and fine crackles were audible at end expiration in both lungs. The cardiac and abdominal examination results were normal. Gynecomastia and no peripheral lymphadenopathy were observed in the cervical, axillary and inguinal regions.

The white blood cell count was 23.1×10⁹/L with 94.0% neutrophils, 4.0% lymphocytes, 1.0% monocytes, 0.5% eosinophils, and 0.5% basophils. The C-reactive protein and lactate dehydrogenase levels were elevated at 21.11 mg/dL (normal range, 0-0.3 mg/dL) and 1,467 U/L (normal range, 110-230 U/L), respectively. Tumor markers, such as carcinoembryonic antigen and pro-gastrin-releasing peptide, were...
Figure 1. Chest roentgenogram showing multiple pulmonary nodules in both lung fields.

(normal, but the levels of soluble interleukin-2 receptor and cytokeratin 19 fragment were elevated, at 1,900 U/mL (normal range, 127-582 U/mL) and 51.9 ng/mL (normal range, 0-3.5 ng/mL), respectively. The results of an arterial gas analysis performed on room air were as follows: pH =7.458, partial pressure of arterial oxygen (PaO2) =38.5 mmHg, partial pressure of carbon dioxide in arterial blood (PaCO2) =26.1 mmHg and bicarbonate (HCO3) =18.1 mmol/L (Table). A chest roentgenogram showed multiple pulmonary nodules in both lung fields (Fig. 1). Computed tomography (CT) revealed multiple pulmonary nodules with a ground-glass opacity halo, and large low-density areas in the right swollen psoas muscle (Fig. 2). The patient was immediately admitted to our intensive care unit because of severe respiratory failure. Ventilatory assistance with non-invasive positive pressure ventilation was initiated. Empirical antibiotic therapy with parenteral meropenem (3.0 g/day) and liposomal amphotericin B (300 mg/day) was administered, but his arterial oxygen tension (PaO2)/inspiratory oxygen fraction (FiO2) (P/F) ratio rapidly deteriorated. On the third hospital day, he was intubated since he required mechanical ventilation and steroid pulse therapy, and methylprednisolone at a dose of 1 g/day was also administered for three days. A bronchoscopic examination was performed on the fourth hospital day, and a histological examination of transbronchial lung biopsy specimens obtained from the polypoid lesion at the orifice of the right B10 revealed choriocarcinoma on the sixth hospital day (Fig. 3). His serum beta-human chorionic gonadotropin (hCG) level was remarkably elevated at 6,100 ng/mL (normal range, 0-0.1 ng/mL). The patient died of multiple organ failure on the ninth hospital day (Fig. 4).

An autopsy revealed bilateral cryptorchidism, and a histological examination of the right testis revealed a burned-out testicular tumor consisting of a teratoma and a fibrous scar (Fig. 5), but no tumor was found in the left testis. There was evidence of metastatic lesions of choriocarcinoma in the lung, mediastinal and hilar lymph nodes, right kidney and right swollen psoas muscle.

Discussion

More than 90% of testicular tumors originate from germ cells, which are the principal cell type of the testis. The peak incidence of the diagnosis of and presentation with testicular germ cell tumors occurs between the ages of 15 and 35 years. The risk factors for testicular germ cell tumors include cryptorchidism, Klinefelter’s syndrome, a family history of testicular tumors, a prior history of a testicular tumor, infertility and sperm abnormalities (4-7). Seminomas and nonseminomas (embryonal carcinomas, yolk sac tumors, teratomas, choriocarcinomas and mixed germ cell tumors) are the major histologic types of testicular germ cell tumors.

| Hematology | Serology | Arterial blood gas analysis (room air) |
|------------|----------|--------------------------------------|
| WBC 23,100 /μL | CRP 21.11 mg/dL | pH 7.458 |
| Neut 94.0 % | IgG 892.0 mg/dL | pCO2 26.1 mmHg |
| Eosino 0.5 % | IgA 123.0 mg/dL | pO2 38.5 mmHg |
| Mono 1.0 % | IgM 4.0 mg/mL | HCO3 18.1 mmol/L |
| Lymph 4.0 % | β-D glucan < 6.0 pg/mL | BE -4.8 mmol/L |
| Baso 0.5 % | C3 109.0 mg/dL | |
| RBC 556×10^6 /μL | C4 27.9 mg/dL | |
| Hb 9.7 g/dL | CH50 >60.0 U/mL | |
| Ht 29.8 % | ANA < x 20 | Uric acid 1+ |
| Platelet 55.8×10^11 /μL | Normal flora | Sugar 4+ |

Biochemistry

| TP 6.4 g/dL | CEA 4.6 ng/mL | Protein 1+ |
| Alb 3.1 g/dL | SCC 0.5 ng/mL | Sugar 4+ |
| AST 27 IU/L | CYFRA 51.9 ng/mL | Blood 1+ |
| ALT 19 IU/L | PSA 0.97 ng/mL | WBC (-) |
| LDH 1,467 IU/L | CA19-9 5 U/mL | Ketone body 2+ |
| ALP 262 IU/L | Pro-GRP 27.2 pg/mL | Normal flora |
| BUN 35.5 mg/dL | slL2R 1,900 U/mL | Mycobacteria (-) |
| Cr 0.63 mg/dL | AFP 15.5 mg/mL | Cytology Class II |
| Na 134 mEq/L | hCG 550,000 U/mL | |
| K 5.2 mEq/L | Beta-hCG 6,100 mg/mL | |
| Cl 97 mEq/L | BS 221 mg/dL | |

Table. Laboratory Data.
Figure 2. Computed tomography (CT) showing multiple pulmonary nodules with a ground-glass opacity halo (A), and large low-density areas in the right swollen psoas muscle (B).

Figure 3. A: A histological examination of transbronchial lung biopsy specimens obtained from the polypoid lesion at the orifice of the right B10 revealing choriocarcinoma consisting of syncytiotrophoblasts and cytotrophoblasts. B: Immunohistochemical staining for human chorionic gonadotropin (hCG) performed on the biopsy specimen revealing positively stained syncytiotrophoblasts.

Figure 4. Clinical course.
Among these various germ cell tumors, choriocarcinoma is relatively rare. Eight percent of testicular germ cell tumors contain a choriocarcinoma component, and pure choriocarcinoma accounts for less than 1% to 3% of all primary testicular germ cell tumors (1). Testicular choriocarcinomas are highly malignant lesions with the potential for early, hematogenous metastases to the retroperitoneal lymph nodes, lung, liver, gastrointestinal tract and brain (1, 8).

A burned-out testicular tumor refers to the presence of a metastatic extra-gonadal germ cell tumor with histological regression of the primary testicular lesion. Histological features that are helpful for establishing a diagnosis of a burned-out testicular germ cell tumor include scar formation, intratubular calcifications, lymphoplasmacytic infiltrate, hemosiderin-containing macrophages and testicular atrophy (9). Scrotal sonography has been reported to be a relatively useful diagnostic tool for burned-out tumors. Sonographic findings of burned-out tumors of the testis include small, highly echogenic foci, hypoechoic areas, microlithiasis and macrocalcifications (10). This phenomenon in germ cell tumors is commonly seen either in choriocarcinomas (2, 3) or in association with a teratoma. The mechanism for this phenomenon has yet to be elucidated. One hypothesis suggests an immunological mechanism whereby common tumor antigens can be recognized by cytotoxic T lymphocytes after repeated exposure and then are subsequently replaced by fibrosis (11). Another hypothesis suggests that ischemia is caused by the tumor outgrowing its blood supply due to its high metabolic rate (12).

Choriocarcinoma has the worst prognosis of all germ cell tumors. This case was finally diagnosed as pTXNOM1bS3, stage IIIC, according to the 2010 American Joint Committee on Cancer/Tumor Nodes and Metastasis (AJCC/TNM) staging system of testicular tumors. The International Germ Cell Cancer Consensus Group (IGCCCG) published a consensus prognostic index for metastatic germ cell cancers in 1997 (13). This index stratifies patients into good-, intermediate- and poor-prognosis subgroups on the basis of three criteria: the primary tumor site, the levels of serum tumor markers, such as hCG, alpha-fetoprotein and lactic dehydrogenase, and the presence of extra-pulmonary visceral metastases. According to this index, this case fell into the poor-prognosis group. Four courses of chemotherapy consisting of intravenous bleomycin, etoposide and cisplatin are recommended for advanced disseminated germ cell tumors with a poor prognosis. Respiratory failure caused by the pulmonary metastasis of choriocarcinoma can progress rapidly.

In a previous report, 11% of the patients with the pulmonary metastasis of choriocarcinoma who presented with dyspnea died within one month of the start of therapy (14). As our patient quickly progressed to respiratory failure and, as a result, we were not able to administer the recommended chemotherapy. However, the IGCCCG reported that the five-year overall survival rate for patients with non-seminomatous germ cell tumors with a poor-prognosis was 48%, but it was more recently reported at 71% (15). As such, there has been a large increase in survival for patients with a poor prognosis. This increase is thought most likely to have been due to both more effective treatment strategies and more experience in treating patients with non-seminomatous germ cell tumors.

The halo sign is a circular area of ground-glass attenuation that is seen around pulmonary nodules on CT, as in this case. The CT halo sign is most often an indication of pulmonary hemorrhage, and it has also been reported with various diseases, such as infectious diseases, neoplastic diseases, and noninfectious and nontumoral diseases. A variety of lung tumor processes can cause hemorrhaging that appears as a halo around a pulmonary nodule on a CT chest scan. Such tumors are hypervascular with fragile neovascular tissue, the rupture of which causes pulmonary bleeding (16). Choriocarcinoma tumor cells have a characteristic ability to erode blood vessels, causing bleeding (17). Other examples include metastatic tumors in angiosarcoma, melanoma, osteosarcoma, and renal cell carcinoma (18). When a CT halo sign around circular nodules is observed, it is necessary to consider the possibility of pulmonary metastasis from choriocarcinoma in the differential diagnosis, even if it is a male patient. In addition, without a definite diagnosis of testicular choriocarcinoma, the phenomenon of burned-out tumors should be recognized.

The authors state that they have no Conflict of Interest (COI).

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