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Case Report

Late and Rapid Relapse in Mediastinum from Testicular Germ Cell Tumor Stage I Over 13 Years after Surgery

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Keywords
Mediastinal lymph node metastasis · Late relapse · Germ cell tumor · Testicular seminoma

Abstract
Patients with stage I testicular germ cell tumors have a long life expectancy, but the tumors have a potential to relapse after treatment. Although relapse is observed within a few years in most cases, late relapse over 10 years after initial treatment has also been reported in patients with stage I testicular germ cell tumors. We encountered a case of testicular seminoma that developed mediastinal lymph node metastasis 13 years after radical surgery for the primary tumor. The relapsed disease progressed rapidly and the patient died within 1 month due to respiratory failure without any chance for therapy. On postmortem examination, the thoracic lesions were pathologically confirmed to be metastases from the testicular seminoma with yolk sac tumor. Here, we report the clinical course and a review of the relevant literature. Based on our experience, we emphasize long-term follow-up and/or careful examination in patients with stage I testicular germ cell tumors.

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Introduction

Testicular germ cell tumors represent only around 1% of all male cancers, but they are the most common malignancies in young adult men [1]. Of all testicular germ cell tumors, seminomas are the most common. Around 75% of seminoma patients present with stage I disease, i.e., no clinical evidence of metastasis [1]. Standard treatment is inguinal orchiectomy, followed by surveillance or adjuvant therapy, consisting of either radiotherapy or chemotherapy. Although it is regarded as a curable disease, the reported relapse rate is 4% – 15% even in stage I seminoma [2–10].

In general, patients with stage I testicular germ cell tumors show relapse within 2–3 years after orchiectomy [2–6]. Although late relapse of testicular seminoma has been reported in the literature [7–12], it is extremely rare. In particular, relapse over 10 years after treatment is extremely rare. Furthermore, the most frequent site of late relapse is the retroperitoneal space [6–10].

We encountered an unusual case of testicular seminoma with syncytiotrophoblastic giant cells (STGC) that developed mediastinal lymph node metastasis 13 years after high inguinal orchiectomy. The patient was managed by surveillance without any adjuvant therapies. However, the disease relapsed rapidly and he died of respiratory failure within 1 month after onset of symptoms without any chance for therapy. On postmortem examination, the thoracic lesions were pathologically confirmed to be metastases from the testicular seminoma combined with yolk sac tumor and STGC. Here, we report the clinical course and present a review of the relevant literature.

Case Presentation

A 56-year-old man with a history of stage I seminoma with STGC of the left testicle 13 years ago was referred to our hospital for further examination of mediastinal tumor. He was treated with high inguinal orchiectomy and serum human chorionic gonadotropin (HCG) beta-subunit level was 0.2 ng/mL at the time. The testicular tumor size measured 5 cm × 5 cm and was pathologically diagnosed as stage I seminoma with STGC without rete testis invasion. On histological analysis, the majority of the tissue was seminoma (>95%) with rare STGC (Fig. 1a, b). Although the patient had been managed by surveillance without adjuvant therapy for 3 years after orchiectomy, he did not visit the hospital subsequently.

The patient complained of dry cough and dysphagia for over the 1 month and presented with body weight loss. Chest computed tomography (CT) revealed a large mediastinal mass compressing the left atrium, esophagus, and both main bronchi (Fig. 2). Serum alpha-fetoprotein was elevated (359.1 ng/mL) and HCG was slightly elevated (1,011 mIU/mL). Transesophageal tumor needle biopsy was performed. However, the patient was hospitalized because of progressive respiratory distress. He died 1 week after hospitalization without any chances for chemotherapy. Autopsy was performed and indicated that the median-posterior mediastinal tumor had infiltrated and proliferated in the pericardium and myocardium and invaded into the pericardial cavity. The histological features were similar to those of previous testicular surgical specimens (Fig. 3). Immunohistochemical analysis indicated that the tumor cells were positive for Sal-like protein 4 (SALL4) and placental alkaline phosphatase (PLAP) and focally positive for HCG (Fig. 3b). The tumor consisted of seminoma (>95%) and yolk sac tumor (5%) with rare STGC components. There were no other metastatic lesions, including retroperitoneal or paraaortic lymph nodes, liver, right testicle, etc.

Discussion

Here, we reported a case of late relapse in the thoracic space more than 10 years after orchiectomy for stage I testicular germ cell tumor, which resulted in fatal outcome These findings are extremely rare in cases of stage I testicular germ cell tumors.

Cummins et al. [2] summarized 164 cases of stage I seminoma and reported that 22 (13%) patients had relapsed at a median of 15.5 months (range: 6–55) after orchiectomy. After a median follow-up period of 13 years, the recurrence and disease-specific mortality rates were 13 and 1.3%, respectively. Sogani et al. [3] reported that no patients with non-seminomatous germ cell tumor of the testis had relapsed beyond 24 months with a median follow-up of 11.3 years. In addition, they summarized previous cohort studies of surveillance protocols and reported that relapse beyond 24 months was observed in only 0.5% of cases [3]. Therefore, 2 years of relapse-free survival after orchiectomy for stage I testicular germ cell tumor is generally considered to be equivalent to cure.

However, several cases of late relapse in patients with stage I testicular germ cell tumor have been reported. Based on the report by Oldenburg et al. [7], the incidence rates were 1.4 and 3.2% in pure seminoma and nonseminoma patients, respectively. In addition, Mukhtar et al. [11] and Pavic et al. [12] reported cases of late recurrence after 43 years and 32 years, respectively. Therefore, clinicians should be aware of the possibility of late relapse after successful treatment in patients with stage I testicular germ cell tumor.

Several management options are available in patients with stage I testicular seminoma, including surveillance, adjuvant radiotherapy, and chemotherapy. In a previous large pooled analysis, tumor size >4 cm and invasion of the rete testis were suggested to be predictors of relapse [5]. As initial testicular tumor size in the present case was 5 cm, our patient may have been at increased risk of relapse. However, it remains unclear whether these predictive factors are related to late relapse. Several case reports of late relapse showed pathological differentiation to yolk sac tumor [11] or malignant teratoma [12]. Indeed, pathological findings in our case also indicated a yolk sac tumor, although the component was small. We speculate that biological multiformity in germ cell tumor cells is related to late relapse.

Relapse has been reported to occur in various sites, including the contralateral testis, inguinal lymph nodes, retroperitoneum, mediastinum, and lung [6, 14]. Although the retroperitoneum was the most frequent site of late relapse, the frequencies of relapse in the mediastinum and lung were reported to be 11.5 and 15.2%, respectively [7]. According to Williams et al. [13], metastatic mediastinal tumors from testicular seminoma were observed in the middle and posterior mediastinum, which was similar to the radiographic findings in our case. As primary mediastinal seminoma involves the anterior mediastinum, it is important for physicians to consider the metastatic germ cell tumors in cases presenting with middle and posterior mediastinal masses in patients with a prior history of testicular germ cell tumor.

In the present case, the metastatic mediastinal tumor rapidly caused cardiorespiratory distress, and unfortunately the patient died before the disease could be treated. Several studies indicated the usefulness of salvage chemotherapy or radiotherapy for relapsed disease [6–10]. Even in cases of late relapse, chemotherapy-naïve surveillance patients have a good prognosis and their characteristics do not differ from patients with early relapse [7–10]. Thus, the conditional risk of late relapse is minimal. Nevertheless, patients and physicians should be aware of a prior history of stage I testicular seminoma. In addition, we should inform patients about the possibility of late relapse even 10 years after successful treatment. Such care and information may avoid delay in proper diagnosis and treatment in cases of relapsed disease.

In summary, the present case suggested that patients with testicular germ cell tumors have the potential to develop late relapse and/or distant metastases during the clinical course, even many years after orchiectomy. We emphasize long-term follow-up and/or careful examination in patients with testicular germ cell tumors.

Statement of Ethics

Ethical approval was not relevant or applicable to this case report. Full informed consent to publish manuscript and images obtained from the patient's family.

Disclosure Statement

The authors declare that there are no conflicts of interest in the present study.

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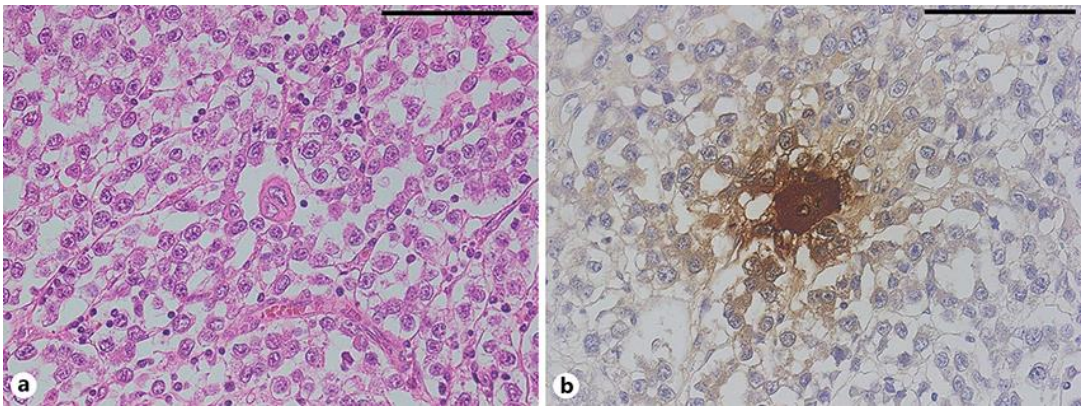

Fig. 1. Pathological findings on hematoxylin and eosin (H&E) and HCG immunohistochemical staining in resected testicular tumor. (**a**) H&E, (**b**) HCG immunohistochemical staining of the testicular mass (40×).

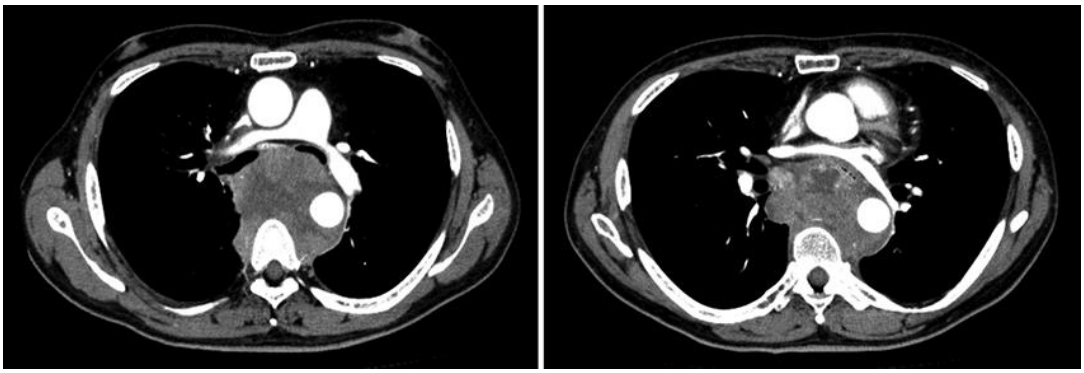

Fig. 2. Chest computed tomography findings at relapse in the present case. The mediastinal tumor extended to both the bronchi, pulmonary artery, left atrium and pericardium.

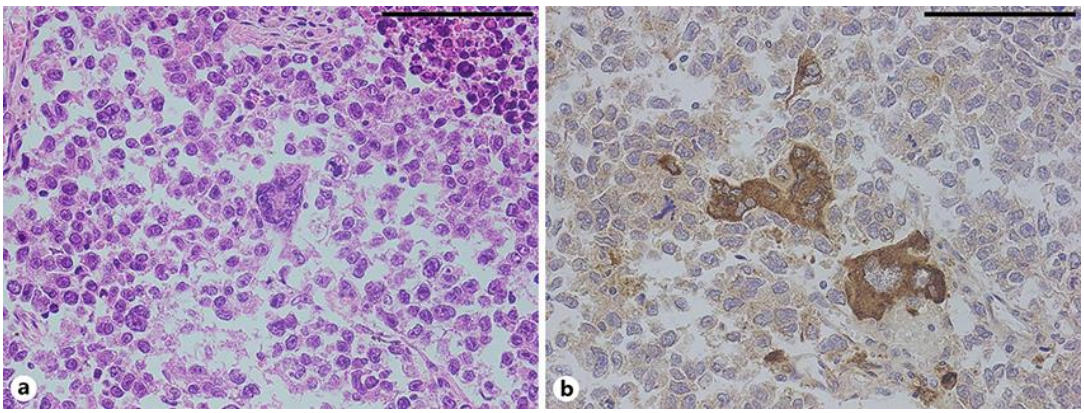

Fig. 3. Postmortem pathological findings on hematoxylin and eosin (H&E) and HCG immunohistochemical staining in the mediastinal mass. (**a**) H&E, (**b**) HCG immunohistochemical staining of the mediastinal mass.