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Spontaneous regression of anterior mediastinal seminoma with normalization of β-human chorionic gonadotropin levels

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ABSTRACT

INTRODUCTION: Although spontaneous regression (SR) of anterior mediastinal seminoma is very rare with normalization of β-human chorionic gonadotropin (β-hCG) level, video-assisted thoracic surgery (VATS) is the most effective solution for definite diagnosis of indeterminate anterior mediastinal masses.
DIAGNOSIS, THERAPEUTIC INTERVENTIONS, AND OUTCOMES: A rare case of an asymptomatic 37-year-old man with an anterior mediastinal mass that was detected on a routine chest X-ray is presented. Computed tomography (CT) showed a large anterior mediastinal tumor with superior vena cava invasion and SR before VATS for definitive diagnosis. On pathology, the definitive diagnosis was seminoma. Microscopic examination showed abundant apoptotic cells within the tumor. Chemotherapy (bleomycin 30 mg/day, etoposide 200 mg/day, cisplatin 40 mg/day) was given to this patient, and the tumor showed high sensitivity.
CONCLUSION: Anterior mediastinal seminoma showing SR induced by spontaneous apoptosis of tumor cells may have good sensitivity to chemotherapy, and a good clinical outcome may be achieved in these patients. This case also highlights that VATS is the most effective solution for definite diagnosis of indeterminate anterior mediastinal masses.

1. Introduction

Spontaneous regression (SR) of cancer is defined as the complete or partial, permanent or temporary disappearance of malignant disease without any treatment. However, the mechanism of SR remains unclear [1]. Primary extragonadal seminoma is usually located in the anterior mediastinum without any specific signs or symptoms [2] and usually shows elevated levels of β-human chorionic gonadotropin (β-hCG) [3]. An extremely rare case of anterior mediastinal seminoma that showed SR before surgery is performed.

2. Presentation of case

A 37-year-old man was admitted to our hospital for evaluation of an anterior mediastinal mass in July 2013. The tumor was detected on routine chest X-ray and chest computed tomography (CT) (Fig. 1A). The patient complained of anterior chest discomfort when he bent forward. Laboratory studies showed normal blood cell counts and chemistry profiles, except for a slightly elevated serum β-hCG (5.9 mIU/mL, normal level <1.0 mIU/mL) and soluble interleukin-2 receptor (IL-2R, 456 U/mL, normal range 145–519 U/mL). The chest X-ray showed a nodular shadow and widening of the mediastinum. Chest CT demonstrated rapid growth of the tumor from 75 mm to 83 mm. The tumor was heterogeneous, located at the anterior side of the superior vena cava (Fig. 1B). On admission, the β-hCG level (0.9 mIU/mL) became normal. The tumor size decreased from 83 mm to 65 mm on chest CT, even though the patient received neither chemotherapy nor irradiation (Fig. 1C).

Tentative diagnoses were invasive thymoma, malignant lymphoma, and germ cell tumor. To obtain a definitive diagnosis, video-assisted thoracoscopic biopsy was performed. The tumor occupied the greater part of the left thoracic cavity and had invaded to the superior vena cava. Two blocks were obtained from the surface of the tumor without necrotic sections. Pathological examination demonstrated that the tumor cells had clear and spacious cytoplasm, with a small, centrally located nucleus coarse-clumped by chromatin, and glycogen granules (Fig. 2A). Immunohistochemically, the tumor cells stained positively for β-hCG, placental-like alkaline phosphatase (PLAP), cytokeratin CAM5/2, and OCT3/4 (Fig. 2B). The cellular surface markers CD3/5/15 were negative. A definitive diagnosis of primary seminoma in the anterior mediastinum was made. To evaluate apoptosis, the specimen was investigated by hematoxylin-eosin (H&E) staining and TUNEL

Abbreviations: β-hCG, β-human chorionic gonadotropin; CT, computed tomography; SR, spontaneous regression; IL-2R, interleukin-2 receptor; EGGCTs, extragonadal germ cell tumors.

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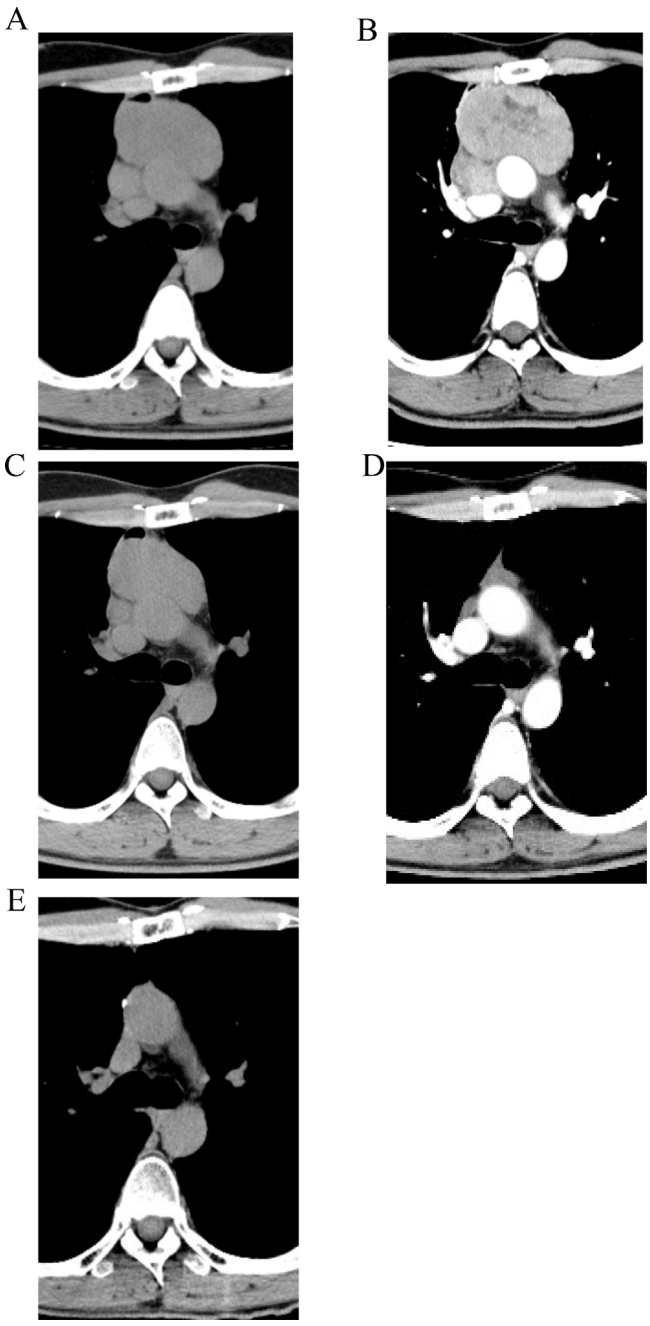

Fig. 1. (A) Initial chest computed tomography (CT) without IV contrast ordered by the patient's initial physician shows a large tumor ($75 \times 69 \times 68\ mm^3$) in front of the ascending aorta. (B) Follow up chest CT with IV contrast 5 weeks later shows interval tumor size increase ($83 \times 75 \times 65\ mm^3$) with possible invasion of the superior vena cava. (C) Chest CT without IV contrast before biopsy shows spontaneous regression to $65 \times 65 \times 29\ mm^3$ without any treatment 7 weeks later. (D) Chest CT with IV contrast showed that the tumor became smaller after two months of chemotherapy (E) Chest CT without IV contrast after resection of tumor two years ago shows no recurrence of tumor.

staining. Abundant apoptosis was detected in the biopsied specimen with slight necrosis (Fig. 3).

The patient was referred to the urology department of our hospital; chemotherapy with bleomycin 30 mg/day, etoposide 200 mg/day, cisplatin 40 mg/day (BEP chemotherapy) was performed. Chest CT showed that the tumor became smaller after two months of chemotherapy (Fig. 1D), and the residual tumor was radically resected by median sternotomy approach. The patient is currently free of tumor, 2 years after resection, without any abnormal findings on chest CT (Fig. 1E) or serum tumor markers.

3. Discussion

Primary extragonadal germ cell tumors usually arise in the mediastinum [4]. The most common histology is seminoma. The anterior mediastinum is the most common primary extragonadal site for seminoma, which occurs mostly in young males [2]. However, at the initial diagnosis, patients do not have specific symptoms such as chest pain, dyspnea, and so on [5]. On CT scan, seminomas usually show a large and coarsely lobulated mass with slight enhancement [6]. The classical treatment includes surgery and radiotherapy. Liu et al. showed that patients with chemotherapy plus surgery or radiotherapy had good long-term survival [7]. Presently, cisplatin-based chemotherapy is performed for seminoma followed by adjuvant surgery, and it achieves good clinical outcomes [8].

The diagnosis of seminoma is very difficult because it has no specific symptoms. Junuzovic reported that the level of β-hCG was elevated in 53% of patients with seminoma [9]; therefore, β-hCG is currently used in the evaluation of surgical or chemotherapy treatment of seminoma [10,11]. To the best of our knowledge, there have been no previous cases of normalization of elevated β-hCG levels without any treatment. In the present case, the internal heterogeneous area of the tumor became smaller on chest CT before surgery, suggesting that central necrosis or differentiation of malignant cells to a normal phenotype may be a basic biological pathway for normalization of elevated β-hCG levels. However, there is insufficient evidence to prove the relationship between spontaneous regression (SR) of tumor and normalization of elevated β-hCG levels. Previous studies showed that patients with elevated β-hCG levels had worse clinical outcomes [12,13]. This case, which showed normalization of elevated β-hCG levels, would be expected to have a good clinical outcome.

For testicular seminoma, tumor burn out has been reported. This rare form of testicular germ cell neoplasm usually presents at the metastatic stage, typically accompanying extragonadal germ cell tumors (EGGCTs), occasionally with traces of tumor in the testis. Minamida et al. reported spontaneous regression without accompanying metastatic lesions [14]. Spontaneous regression of invasive thymoma and mediastinal lymphoma has also been reported [1,12]. Cole reported that SR of cancer is rare, with an estimated incidence of less than 1 in 60,000–100,000 cases, and that more than half of the cases are renal cell cancer, neuroblastoma, malignant melanoma, and choriocarcinoma [12]. SR of malignancies is apparently mediated by two basic biological pathways: differentiation of malignant cells to a normal phenotype, and cell death either by apoptosis or inflammatory necrosis [1]. The postulated mechanisms include modification of immunological factors and concomitant viral or bacterial infections, hormonal factors, and elimination of carcinogens [14]. In the present case, the tumor became smaller on chest CT before surgery without any treatment. Unfortunately, it was not possible to obtain enough evidence to elucidate the mechanism of SR of the tumor. Moran and Vadeeswar reported that SR of thymomas with cystic and hemorrhagic lesions is associated with necrosis because of ischemia and so on, but the mechanism of necrosis remains unclear [3,13]. Several reports showed that patients with spontaneous regression had good long-term survival [15,16]. In the present case, pathological studies with H&E staining were performed to see whether necrosis had occurred and affected the SR of the tumor. Because tissue was obtained from the surface of the tumor, increased eosinophilia, glassy cytoplasm, and myelin figures were not detected. Although there was insufficient proof to confirm clearly that necrosis affected SR in this case, necrosis may

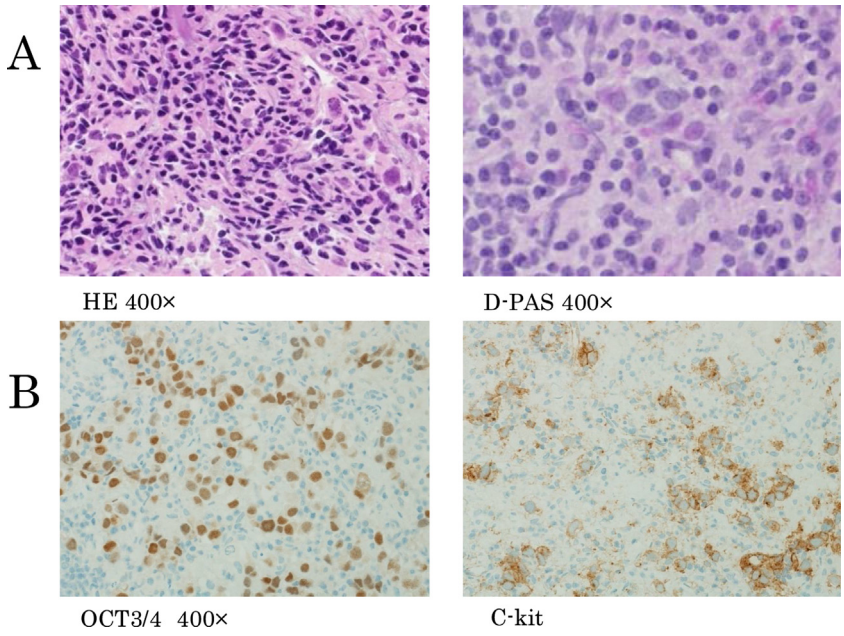

Fig. 2. (A) The tumor consists of round and large cells. Cells have clear and spacious cytoplasm, with a small, centrally located nucleus coarse-clumped by chromatin, and abundant glycogen granules. (B) Immunohistochemically, the tumor cells stain positively for β-hCG, C-kit, placental-like alkaline phosphatase (PLAP), cytokeratin CAM5/2, and OCT3/4. The cellular surface markers CD3/5/15 were negative (data not shown). The final diagnosis was primary seminoma in the anterior mediastinum.

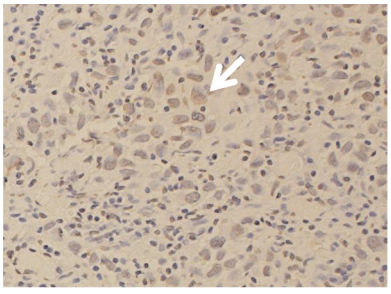

Fig. 3. Microscopic examination of the specimen shows abundant apoptotic cells on TUNEL staining. Apoptotic cells (white arrowhead) are stained brown.

have occurred in the center of the tumor because of ischemia. The tissue stained positive with TUNEL staining, which indicates that apoptosis was accelerated by ischemia or other factors. Apoptosis may have been a major pathway of SR in the present case.

This case highlights that anterior mediastinal seminoma with SR induced by apoptosis and normalization of β-hCG level shows higher sensitive to chemotherapy than others, and good clinical outcome is forecasted from these observations. VAST is the most effective solution for definite diagnosis of indeterminate anterior mediastinal masses. Our work has been reported in line with the SCARE criteria [17].

Conflicts of interest

There are no any conflicts of interest to disclose.

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There are no any sources of funding for this study to declare.

Ethical approval

This study had got ethical approval.

Consent

Written, informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Authors' information

Zaiqiang Yu and Daisuke Kimura performed the surgery.

Zaiqiang Yu and Daisuke Kimura drafted the manuscript. All authors read and approved the final manuscript.

Guarantor

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