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Case Report

Composite type A thymoma and diffuse large B-cell lymphoma

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ABSTRACT

The concurrent occurrence of thymoma and diffuse large B-cell lymphoma in the thymus has not been previously reported. We describe a 74-year-old man who presented with general weakness, neck lymphadenopathy, night sweats, and body weight loss. A right anterior mediastinal mass was found on computed tomography of the chest. The immunohistochemical stains AE1/AE3, CD20, CD3, and MUM-1 confirmed the different components of the mediastinal tumor. A heavy-chain gene clonality assay and light-chain gene clonality assay confirmed the B-cell clonality of the mediastinal tumor and neck lymph node. The patient had received a complete course of chemotherapy, and the result of positron emission tomography–computed tomography showed complete remission. The pathologic report of this mass revealed composite type A thymoma and diffuse large B-cell lymphoma. If concurrent or composite thymoma and lymphoma are suspected, a thorough examination of the thymoma with a combination of ancillary studies is recommended to rule out the possibility of concurrent lymphoma.

1. Introduction

The most common thymic tumors in adults are thymomas, followed by mediastinal lymphomas, some of which arise from the mediastinal lymph nodes [1]. Patients with thymomas have been reported to have an increased incidence of subsequent malignancy, or concurrent malignant neoplasms. Engels et al [2] published a large population-based study that reported that 9% of patients with invasive thymoma had subsequent malignancies, a risk that significantly increased in digestive site cancers (2.5%), non-Hodgkin's lymphoma (1%), and soft tissue sarcoma (0.3%). Four of seven patients with non-Hodgkin's lymphoma in the above study had B-cell tumors diagnosed by immunophenotyping [2]. Khoury et al also described secondary malignant neoplasms in 8–31% of patients with thymoma [3]. The most common concurrent or composite lymphoma in the thymus associated with a thymoma is T-cell lymphoma/leukemia. To the best of our knowledge, there are only two case reports of composite B-cell lymphomas and thymomas. We describe a case of a thymic tumor composed of a type A thymoma and a diffuse large B-cell lymphoma (DLBCL).

2. Case Report

A 74-year-old man with a history of hypertension, benign prostate hyperplasia and gouty arthritis came to the outpatient clinic of Kaohsiung Municipal Ta-Tung Hospital for a persistent productive cough with whitish sputum for 1 month. Other associated symptoms and signs included dizziness, general weakness, night sweats, poor appetite, and body weight loss of about 3 kg in 1 month (60–57 kg). His physical examination revealed right posterior supraclavicular lymphadenopathy. Both chest radiography and chest computed tomography showed a right side anterior mediastinal mass. He was transferred to our hospital for further evaluation. Routine preoperative laboratory test results revealed normocytic anemia with a red blood cell count of 2.18 $\times$ 10^{12}/L (male reference range, 4.5–5.9 $\times$ 10^{12}/L), hemoglobin of 6.5 g/L (male reference range, 14–17.5 g/L), hematocrit of 18.9% (male reference range, 41.5–50.4 %), and mean corpuscular volume of

Conflicts of interest: none.

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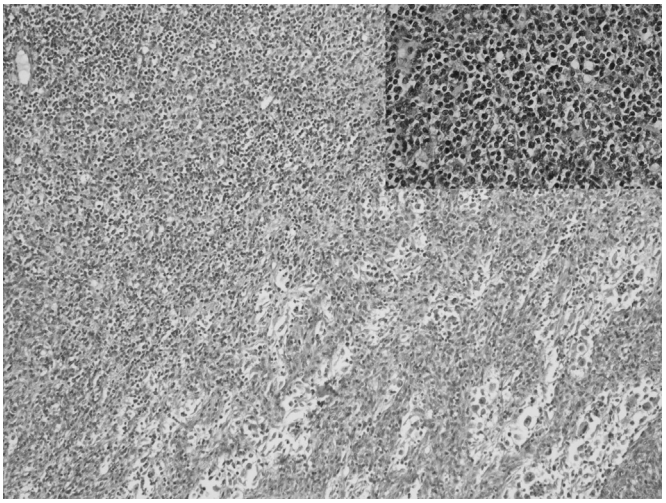

Fig. 1. The mediastinal tumor is composed of two distinct cell populations, spindle cells (right lower) and lymphocytic cells (left upper). The spindle cells have pale eosinophilic cytoplasm and spindle nuclei. The lymphocytes are large, with angulated and vesicular nuclei, occasionally prominent nucleoli, and scant cytoplasm. Hematoxylin–eosin stain, original magnification 100× and 400× (inset).

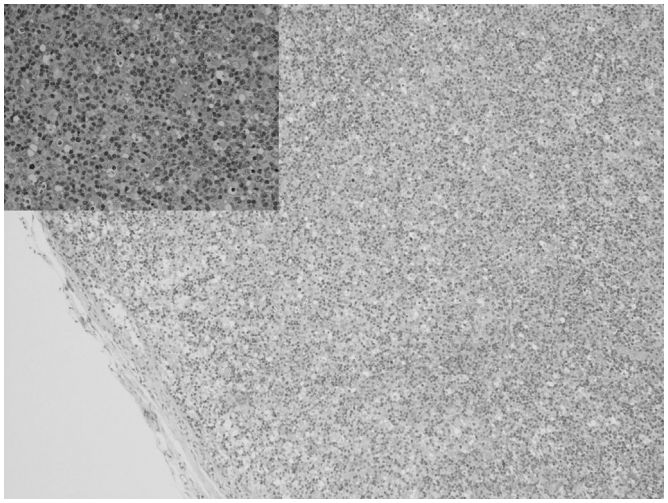

Fig. 3. The supraclavicular lymph node has an effaced nodal architecture and is infiltrated by large lymphoid cells. Hematoxylin–eosin stain, original magnification 100× and 400× (inset).

86.7 fL (reference range, 80.0–96.1 fL). The total white blood cell count was 5.9 × 10^9/L (reference range, 4.4–11.3 × 10^9/L) with 22.0% lymphocytes (reference range, 20–50%), which were within normal limits. Under the impression of a thymoma or thymic carcinoma with supraclavicular lymph node metastasis, the patient underwent surgical excision of the anterior mediastinal mass and excisional biopsy of the right supraclavicular lymph nodes.

Surgical findings included a 6.7 cm × 4.7 cm × 3.0 cm, 45.0 g anterior mediastinal tumor, and right supraclavicular lymph nodes consisting of four tissue fragments, up to 1.5 cm × 1.3 cm × 0.8 cm. Grossly, the anterior mediastinal tumor was grayish and elastic with a ruptured capsule. On microscopic examination, sections of the thymus showed a spindle cell tumor with hemangiopericytoma-like vascular hyperplasia. These spindle tumor cells contained bland nuclei, dispersed chromatin and inconspicuous nucleoli arranged in solid sheets or in a storiform pattern. The spindle tumor cells were positive for AE1/AE3, but negative for CD34, smooth muscle actin, S-100 protein and CD117. These findings supported a diagnosis of type A thymoma.

In addition, dense lymphoid infiltrates composed of mixed small and large lymphoid cells were seen at the peripheral soft tissue surrounding the thymic tumor or intrathymic tumor infiltrate (Fig. 1). The larger lymphoid cells showed centroblastic or immunoblastic morphology with some Hodgkin-like cells. Increased mitotic figures were also noted. The large lymphoid cells were positive for CD20 (Fig. 2), MUM-1, bcl-2 and bcl-6 (focal), but negative for AE1/AE3, CD3, CD5, CD10, CD30 and CD15. The Ki-67 index was about 70%. Epstein–Barr encoding region *in situ* hybridization was negative. A section of the right supraclavicular lymph nodes also showed infiltration of atypical large lymphoid cells with focal preserved nodal architecture (Fig. 3). These large lymphoid cells revealed the same results as the immunohistochemical study of the thymus.

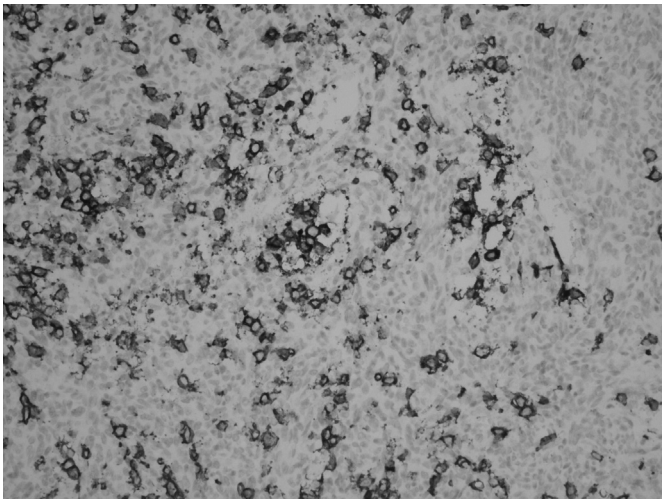

Fig. 2. CD20 is positive in the lymphoid infiltrate and negative in the spindle component. Immunoperoxidase with hematoxylin counterstain, original magnification 200×.

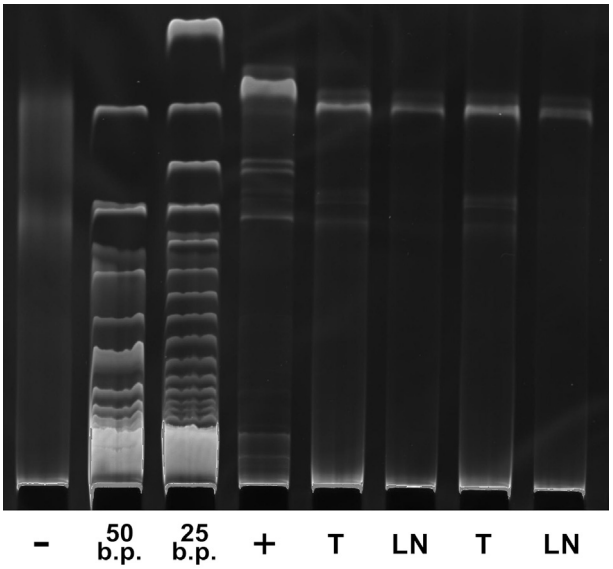

Fig. 4. Immunoglobulin κ light chain gene clonality assay of the anterior mediastinal tumor and right supraclavicular lymph node. + = positive control; − = negative control; T = anterior mediastinal tumor; LN = *supraclavicular* lymph node.

Table 1
Literature reports in English of concurrent thymoma and lymphoma.

Authors	Age/Sex	Thymoma type	Lymphoma type
Cory et al (2012) [5]	59/F	Invasive lymphocyte-rich thymoma (WHO type B1)	Peripheral T-cell lymphoma NOS
Francesca et al (2003) [7]	65/M	Epithelial thymoma (WHO type AB)	T-cell lymphoblastic lymphoma
Joseph et al (2003) [3]	62/M	NS	CLL/SLL
Barton (1997) [8]	NR *	Invasive lymphocyte-rich thymoma (WHO type B1)	Peripheral T-cell lymphocytosis
Nishioka (1995) [9]	43/M	Type 1 thymoma	T-lymphoblastic leukemia/lymphoma after resection of thymoma
Friedman et al (1994) [6]	95/M	Invasive thymoma, predominantly spindle cell type	T-lymphoblastic leukemia/lymphoma
Lishner et al (1994) [10]	42/M	Lymphocytic-type thymoma (WHO type B1)	T-γ/δ leukemia/lymphoma
Smith et al (1994) [11]	(I) 30/F (II) 55/F	Invasive thymoma, predominantly lymphocytic-rich cortical type (WHO type B1)	Peripheral T-cell lymphocytosis
Macon et al (1991) [12]	64/F	Lymphocyte-rich thymoma	T-lymphoblastic leukemia/lymphoma at time of recurrent thymoma
Doll et al (1991) [13]	(I) 77/M (II) 43/M (III) 55/M	Malignant thymoma, predominantly lymphocytic	Peripheral T-cell lymphocytosis
Nemoto et al (1987) [4]	62/M	Spindle cell thymoma (WHO type B3)	Hodgkin's disease
Thomas et al (1983) [14]	40/M	Invasive thymoma	T-cell chronic lymphocytic leukemia
Skinnider et al (1982) [15]	(I) 65/M (II) 33/M	(I) Epithelial thymoma (WHO type B3) (II) Mixed lymphoepithelial thymoma (WHO type AB)	(I) 'Histiocytic lymphoma' (II) Poorly differentiated lymphocytic lymphoma
Gould et al (1977) [16]	64/M	Prevalent epithelial	Lymphocytic lymphoma

CLL/SLL = chronic lymphocytic leukemia/small lymphocytic lymphoma; NOS = not otherwise specified; NR = not reported; NS = not specified.

The B-cell clonality assay, immunoglobulin heavy chain gene clonality assay (tube B) and immunoglobulin κ light chain gene clonality assay (tube A), were performed for both the right mediastinal tumor and supraclavicular lymph node. Both tissues showed VH-FR2 and JH heavy chain gene rearrangements (not shown) and Vκ and Jκ light chain gene rearrangement (Fig. 4).

A bone marrow biopsy showed negative results. Thus diffuse large B-cell lymphoma Ann Arbor stage IIE was diagnosed.

The patient received complete chemotherapy with a regimen of rituximab, cyclophosphamide, hydroxyl daunorubicin, vincristine, and prednisone over 5 months. Two months later, positron emission tomography–computed tomography revealed complete remission.

3. Discussion

During the past 5 decades, there have been sporadic reports of thymomas associated with hematopoietic neoplasms (Table 1) [3–16]. So far, the most common association is with T-cell neoplasms, including T-cell leukemia/lymphoma and T-cell lymphoproliferative disorders. There are only isolated reports in English of thymoma coexisting with B-cell lymphoma, one case with chronic lymphocytic leukemia/small lymphocytic lymphoma [3], and one with classic Hodgkin's lymphoma [4]. In these published cases, the most common subtype of thymoma associated with concurrent or composite hematopoietic neoplasms was type B1 thymoma.

There are two hypotheses regarding the relationship between thymomas and lymphoproliferative disorders. One is that the abnormal B-cell clone arises from aberrant stimulation or failed suppression by abnormal T cells that mature in a dysfunctional thymoma environment. This hypothesis is supported by the strong association between T-cell immunodeficiency and B-cell malignant neoplasms [5]. The other hypothesis is that the epithelium of the thymoma retains the ability to stimulate T-cells, and this ongoing stimulation predisposes to neoplasia [6]. In addition, association with maturation of B-cells is via T helper cells (Th cells); T-cell immunodeficiency may be more related to Th cells than T cytotoxic cells (Tc cells).

Composite thymoma and lymphoma may be difficult to diagnose, especially in lymphocyte-rich thymomas. By definition, reactive lymphocytic proliferation is polyclonal. Hence, a combination of ancillary studies, such as flow cytometric analysis, T-cell receptor gene rearrangement analysis, B-cell clonality assay, immunohistochemical study, and cytogenetic study, is necessary to exclude a monoclonal lymphoproliferative disorder [3,5].

In conclusion, we describe a rare case of composite type A thymoma and DLBCL involving the anterior mediastinum with right supraclavicular lymph node involvement. If composite thymoma and lymphoma are suspected, a thorough examination of the thymoma with a combination of ancillary studies is recommended to rule out the possibility of concurrent lymphoma.

Acknowledgments

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