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Case Report

Is There a Bridge Between Systemic Lupus Erythematosus and Thymomas?

Sistemik Lupus Eritematöz ve Timoma Arasında Bir Köprü Var mı?

Xie QIBING,[1] Yin HENG,[2] Tao YE,[2] Chen XI,[1] Yin GENG[1]

[1]*Department of Rheumatology and Immunology, West China Hospital, Sichuan University, Chengdu, China*
[2]*Department of Nephrology, West China Hospital, Sichuan University, Chengdu, China*

In this report, we describe a 21-year-old male patient who developed a type C thymoma (undifferentiated carcinoma) after five years of stabilized systemic lupus erythematosus (SLE) activity. The patient remained stable even after chemoradiotherapy for the thymoma, and at the one-year follow-up, treatment had no effect on the progression of the SLE. Previous data regarding the coexistence of SLE and thymomas suggested that interaction occurs between these two diseases through some implicit mechanisms. However, we believe that no interaction takes place between two diseases, based on our experience and related literature data.

Key words: Systemic lupus erythematosus; thymectomy; thymoma.

Bu makalede, sistemik lupus eritematöz (SLE) aktivitesi stabil olduktan beş yıl sonra tip C timoma (diferansiye olmamış karsinom) gelişen 21 yaşında erkek bir olgu sunulmaktadır. Hasta timoma için verilen kemoterapiden sonra bile stabil kaldı ve bir yıllık takip sürecinde uygulanan tedavi SLE progresyonunu etkilemedi. Sistemik lupus eritematöz ve timoma birlikteliğine ilişkin daha önceki veriler, kesin olarak anlaşılamayan bazı mekanizmalar ile bu iki hastalığın birbirleriyle etkileştiğini işaret etmektedir. Ancak deneyimimiz ve ilgili literature verilerine dayanarak, bu iki hastalık arasında herhangi bir etkileşim olmadığı kanısındayız.

Anahtar sözcükler: Sistemik lupus eritematöz; timektomi; timoma.

Systemic lupus erythematosus (SLE) is associated with several immune abnormalities involving both T and B lymphocytes.[1] A thymoma is the only tumor that has been proven to generate mature T cells from immature precursors.[2] Many people have suspected that the association between thymomas and SLE is not incidental[3-7] due to the primary immunological role of the thymus and the purported abnormal functioning of the T lymphocytes in SLE. However, in our patient, the thymoma developed after five years of stabilized SLE activity, and the treatment for the thymoma did not change the state of the SLE. Therefore, in spite of what has been presupposed, we hypothesize that there is no interaction between these two diseases.

CASE REPORT

For the past five years, a 21-year-old male patient with a past history of SLE had been receiving treatment with prednisone and hydroxychloroquine (200 mg bid) therapy at the rheumatology department of West China Hospital. The first onset of symptoms included oral ulcers, multiple serositis, multiple inflammatory synovitis, urine protein levels

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Correspondence: Xie Qibing, M.D. Department of Rheumatology and Immunology, West China Hospital, Sichuan University, 610041 Chengdu, China. Tel: 86-18980601299 e-mail: xieqibing1971@163.com

of 1.1 g/24 hours, positive anti-nuclear antibodies (ANA: 1:3200; speckled), and anti-double stranded DNA (anti-dsDNA) above the laboratory reference range (1:320), all of which fulfilled the criteria for SLE.

The patient was admitted to the rheumatology department at our West China Hospital in June of 2012 due to a two-month history of left chest pain accompanied by fatigue, accidental palpitation, and dyspnea. His lupus status was inactive at that time with a Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score of 4 due to pleurisy and pericarditis. After thoracic computed tomography (CT), the existence of a tumor measuring 7.5x11.5 cm was confirmed in the anterior mediastinum (Figure 1). A percutaneous biopsy also suggested a type C thymoma (undifferentiated carcinoma) (Figure 2).[8] As a preoperative therapy, the patient had undergone four rounds of chemotherapy and 11 rounds of radiotherapy. At the one-year follow-up, his SLE was stable with a SLEDAI-2K score of 0.

DISCUSSION

In the past, some in vitro and in vivo experiments suggested that thymic abnormalities could play in role in the appearance of autoimmune diseases.[6,7] In addition, some research declared that intratumor thymopoiesis could generate impaired T cells or alter the T cell repertoire and create a greater potential for the onset of autoimmune diseases such as SLE.[2,3] In fact, it has been accepted as truth that thymomas can affect autoimmune diseases like SLE through some unknown mechanisms.[3-7] If we follow this path of thought, it is also easy to deduce that for patients with both autoimmune diseases and thymomas, the treatment given for thymomas, (i.e., a thymectomy) would improve the clinical outcomes of autoimmune diseases since there is a relationship between the two. Furthermore if there are some immunoregulations associated with both SLE and thymomas, then these two diseases are most likely to occur or, if already present, accelerate under dramatic changes such as when a thymectomy is performed or when the SLE is in the active stage. However, none of these hypothetical manifestations were observed in our patient. Meanwhile, a recent meta-analysis of thymoma-associated SLE suggested that variable outcomes are seen with this disease after thyroidectomies rather that the previously assumed improvement.[9] Hence, we began to doubt the accepted assumptions regarding the connection between immunoregulations and thymomas and SLE.[3-7]

Additionally, we reviewed 24 cases in the literature published in English along with our own case, all of which had relatively detailed information about the patients' clinical features (Table 1),[4,5,10-24] and discovered that most of the patients underwent surgery as the primary treatment for the thymoma, with some combining the surgery with radiotherapy and/or chemotherapy. The outcome of SLE varied after the treatment with remission in five of the 24 patients, exacerbation in seven others, no reported changes in five more, and SLE occurrence in the other six. We also noticed that there were no specific features in these patients with the different outcomes.

Therefore, we argue that the so-called interaction between thymomas and SLE does not exist. If this was the case, then the SLE would have accelerated after

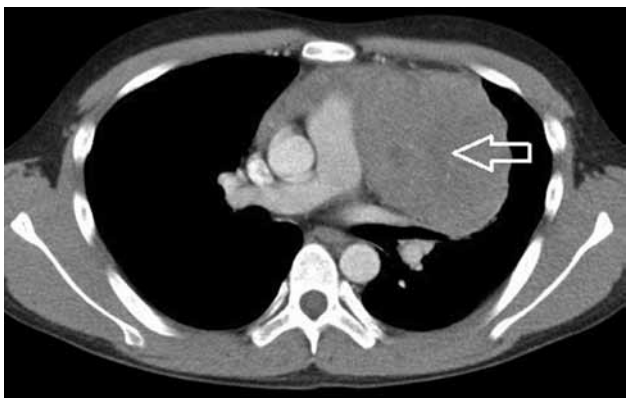

Figure 1. Thoracic contrast-enhanced computed tomography showing a mass of soft tissue density in the anterior mediastinum (white arrow).

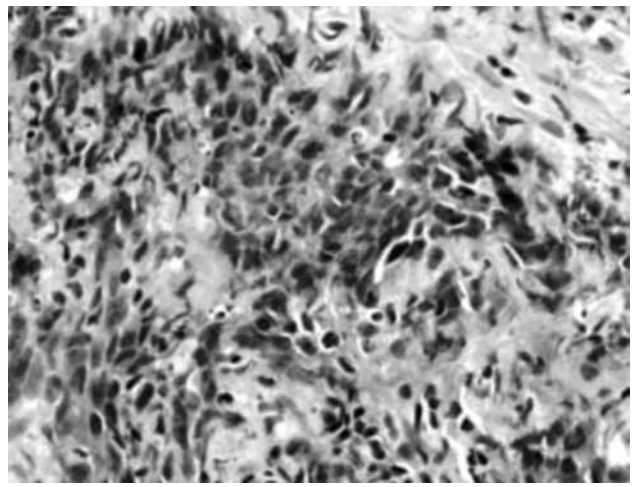

Figure 2. Undifferentiatied cell type seen in the thymoma (H-E x 40).

Table 1. Characteristics of the 24 patients with both a thymoma and systemic lupus erythematosus

Author	Gender/age at diagnosis of SLE	Age at discovery of the thymoma	Other autoimmune disease	Treatment for the thymoma	SLE outcome
Mastaglia, et al.[10]	F/53	55	No	Surgery	Remission
Mala et al.[11]	F/36	36	No	Radiotherapy	No change
Mizon et al.[12]	F/49	49	MG	Surgery an radiotherapy	Occurrence
Calabrese et al.[13]	M/18	21	No	Surgery	Occurrence
Claudy et al.[14]	F/65	67	No	Surgery	No change
	F/68	68	No	-	Decreased
	F/55	57	No	Surgery	Exacerbation
Steven et al.[5]	F/49	50	No	Surgery and radiotherapy	Exacerbation
	F/48	50	No	Surgery and radiotherapy	Exacerbation
Simeone et al.[15]	Not reported	One year after diagnosis of SLE	No	Surgery and radiotherapy	Remission
Cruz et al.[16]	F/57	57	MG, pemphigus erythematosus	Not reported	No change
Fournel et al.[17]	F/57	57	No	Chemotherapy	No change
Ogawa et al.[18]	F/50	49	No	Surgery	Exacerbation
Menon et al.[19]	F/62	62	No	Surgery	Remission
Rosman et al.[20]	F/42	38	No	Chemoradiotherapy	Occurrence
Zandman et al.[21]	F/30	30	No	Surgery	Remission
	F/48	48	No	Surgery	Exacerbation
Mevorach et al.[22]	F/66	66	No	Surgery	Occurrence
	F/66	61	No	Surgery	Occurrence
	F/26	24	MG	Surgery	Occurrence
Duchman et al.[23]	F/53	63	Pure red cell aplasia	Surgery and radiotherapy	Remission
Boonen et al.[4]	F/76	76	No	Surgery	Exacerbation
Bozzolo et al.[24]	F/27	27	No	Surgery	Exacerbation
Our patient	M/16	21	No	Chemoradiotherapy	No change

SLE: Systemic lupus erythematosus; MG: Myosthenia gravis.

the onset of the thymoma or been alleviated after treatment for this tumor. At the very least, the outcome of SLE after a thymectomy ought to be unanimous, but none of these scenarios occurred in our patient or in the cases that we reviewed in the literature.

Finally, though we doubt that the relationship between SLE and thymomas is as close as was previously presumed, further studies with more evidence are needed to prove our hypothesis. However, our findings indicate that clinicians should not overlook the variable prognosis of SLE after treatment for thymomas.

Declaration of conflicting interests

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