CASE REPORT

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Systemic *lupus erythematosus* and *thymus persistens* – A case report

Sistemski eritemski lupus i perzistentni timus

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Abstract

Introduction. Thymus plays an important role in the maturation of T-lymphocytes and in the development of immune tolerance. Its involution comes after puberty. If thymic tissue remains preserved in an advanced age it is considered to be the *thymus persistens*. According to the available data, 5% of patients with a thymoma have some of the autoimmune disorders. Medical data on the systemic *lupus erythematosus* (SLE) association with the *thymus persistens* are scarce. **Case report**. A 29-year-old patient was diagnosed with SLE at the age of 12. She was treated with continuous doses of corticosteroids and an antimalarial drug (chloroquine). After ten years, the first, and then two more recurrences of the disease with the last recurrence in 2011 occurred. The performed laboratory analyses indicated the disease activity. The radiography of thorax showed a change on the right lung, with enlarged mediastinal shadow. Therefore the multislice computed tomography (MSCT) of thorax was made. The pathohistology findings confirmed that the change on the right lung was focus of chronic pneumonitis, while the change in mediastinum was *thymus persistens*. The thymectomy was performed. Due to pneumonitis, the treatment of SLE was continued with corticosteroids, antimalarial drug and pulse doses of cyclophosphamide. The patient received six monthly and six quarterly pulsed doses of the drug. The remission of the disease maintained all the time. **Conclusion**. The disorder of thymic function should be considered as a possible cause in the development of SLE. Though the effect of thymectomy is difficult to assess, patients should be carefully monitored.

Keywords:
lupus erythematosus, systemic; thymus gland; comorbidity; diagnosis, differential; drug therapy.

Apstrakt

Uvod. Timus ima važnu ulogu u sazrevanju T limfocita i razvoju imunološke tolerancije. Nakon puberteta dolazi do njegove involucije. Ukoliko tkivo timusa ostane očuvano i u odmaklom životnom dobu govorimo o perzistentnom timusu (*thymus persistens*). Prema dostupnoj literaturi 5% bolesnika sa timomom ima neki od autoimunskih poremećaja. Podaci o udruženosti sistemskog eritemskog lupusa (SLE) i pezistentnog timusa su oskudni. **Prikaz bolesnika**. Prikazali smo bolesnicu staru 29 godina kod koje je dijagnoza SLE postavljena u 12. godini života. Lečena je kontinuiranim dozama kortikosteroida i antimalarikom hlorokinom. Nakon deset godina dolazi do prvog, a zatim još dva recidiva bolesti. Poslednji recidiv bio je 2011. godine. Učinjene laboratorijske analize ukazivale su na aktivnost bolesti. Tada je na radiografiji pluća uočena promena u desnom plućnom krilu i proširena senka medijastinuma, zbog čega je učinjen multislajsna kompjuterizovana tomografija (MSCT) grudnog koša. Biopsijom je utvrđeno da je promena u desnom plućnom krilu žarište pneumonitisa, a promena u medijastinumu perzistentni timus. Učinjena je timektomija. Lečenje SLE je zbog pneumonitisa nastavljeno kortikosteroidima, antimalarikom i pulsnim dozama ciklofosfamida. Bolesnica je primila šest mesečnih i šest tromesečnih pulsnih doza leka. Sve vreme održava se remisija bolesti. **Zaključak**. Poremećaj funkcije timusa treba razmatrati kao mogući uzrok nastanka SLE. Koliko timektomija utiče na tok autoimunske bolesti teško je proceniti, ali bolesnike svakako treba pažljivo pratiti.

Ključne reči:
lupus, eritematozni, sistematski; timus; komorbiditet; dijagnoza, diferencijalna; lečenje lekovima.

Introduction

Systemic *lupus erythematosus* (SLE) is a chronic inflammatory disease caused by unknown etiology. Its main characteristic is a tissue and cell damage, which is caused by immune complexes and pathogenic autoantibodies. A disorder of immune response regulation with a development of the phenomenon of autoimmunity plays an important role in the pathogenesis. The disease is characterized by the permanent creation of pathogenic autoantibodies to certain cellular components as well as by the formation of immune complexes. A hyperactivity of autoreactive B- and T- cells is expressed, which is caused by a series of disorders. A clinical profile of this multisystem disease is quite diverse. At the

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beginning, it may appear either as a disease of one organ or as a multisystem disease. Skin, joints, serous membranes, hematopoietic tissue, kidneys and central nervous system are the most frequently affected [1]. The thymus plays an important role in the maturation of T lymphocytes and in the development of immune tolerance. The thymus function disorder is often a cause of some autoimmune diseases [2]. Thymomas are the most common tumors of the anterior mediastinum [3]. The percutaneous needle biopsy or parasternotomy are usually used as diagnostic tools of this tumor, after radiographic examination of the thorax. This diagnostic reveals thymoma in cytological or histological findings. The association of SLE and thymoma is something which is known these days [4, 5]. We report a case of a patient with SLE who was diagnosed the *thymus persistens*.

Case report

A 29-year-old patient was diagnosed with SLE at the age of 12 based on polyarthralgia, skin changes, bicytopenia (leuko-lymphopenia and thrombocytopenia) and positive antinuclear antibodies (ANA). She was treated with continuous doses of corticosteroids and an antimalarial drug. After ten years there was the first, and then two more recurrences of the disease. She was hospitalized in the Clinic for Rheumatology and Clinical Immunology at the Military Medical Academy in Belgrade after the last recurrence in 2011. She was subjectively without symptoms, objective admission findings were normal. Laboratory analysis showed positive inflammatory syndrome - an elevated erythrocyte count (Er) sedimentation rate (123 mm/h), Coombs positive anemia [Er 3.61 × 10^{12}/L, hemoglobin (Hgb) 106 g/L], leukopenia (leukocytes 1.7 × 10^{9}/L) and lymphopenia (absolute lymphocyte count 0.170 × 10^{9}/L), hypocomplementemia - complement component 4 (C4 = 0.06 g/L), hypergammaglobulinemia polyclonal type (gamma fractions of protein electrophoresis - 46%), increased values of IgG 46.1 g/L, high rheumatoid factor (838 IU/mL) and in immunoserological analyses: ANA 2+ homogeneously/blotchy type, anti-dsDNA 152 IU/mL, anti- Ro 208 IU/mL, anti-La 149 IU/mL. Proteinuria with maximum values of 0.350 g/24h was registered in urine. The radiography of the thorax showed a homogeneous, unclearly circumscribed circular shadow on the right lung, with enlarged mediastinal shadow

(Figure 1). Therefore the multislice computed tomography (MSCT) of the thorax was made, revealing a change in the mediastinum (Figure 2). The histopathology finding, after the bronchoscopy with transbronchial biopsy

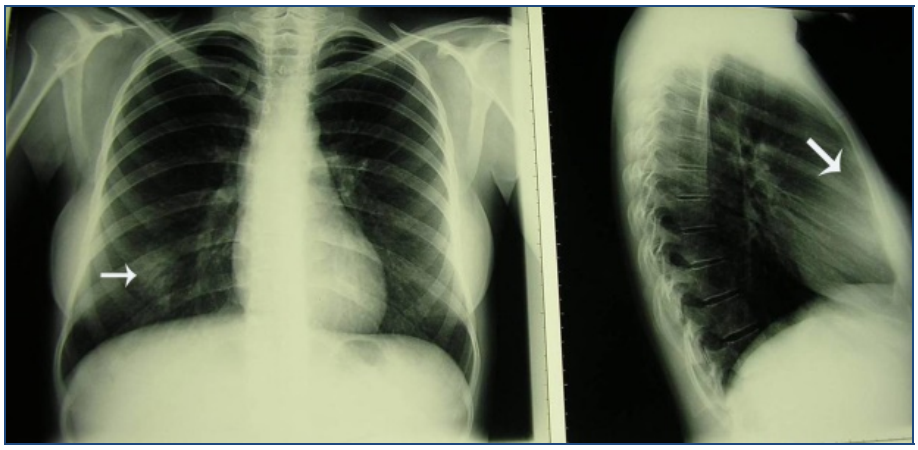

Fig. 1 - The radiography of thorax: Oval soft tissue change on the basal right lung (arrow, shown at left). Soft tissue change retrosternally (arrow, shown at right).

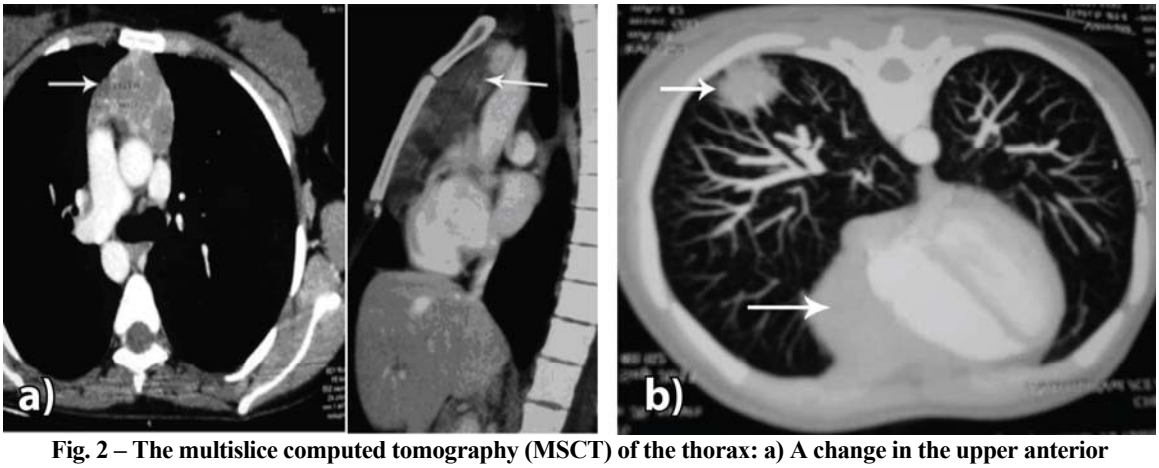

Fig. 2 – The multislice computed tomography (MSCT) of the thorax: a) A change in the upper anterior mediastinum (arrows); b) Oval change on the right lung and change in the upper anterior mediastinum (arrows).

(TBB), looked like chronic pneumonitis, while findings of percutaneous needle biopsy of the change in mediastinum did not confirm thymoma. Consilium decided to do mediastinoscopy and an open biopsy of described changes in the lung and changes in the mediastinum. Obtained histopathologic findings (*ex tempore*) of the change in the lungs were consistent with chronic lymphocytic infiltrate without the elements for the malignant disease, and histopathological findings of the change in the mediastinum were consistent with *thymus persistens*. The thymectomy was done. During hospitalization, the patient was treated with increasing doses of corticosteroids (up to 1 mg/kg body weight). Having in mind the entire course of the disease, and that pneumonitis within the SLE was radiographically and histopathologically confirmed, as well as histopathologically verified *thymus persistens*, it was decided to continue with the treatment using Cyclophosphamide pulse therapy (15 mg/kg body weight), corticosteroids and an antimalarial drug (chloroquine). The patient received six monthly and six quarterly pulsed doses of cyclophosphamide and a satisfactory therapeutic effect was achieved.

Discussion

The reviews of patients with SLE and thymoma are rare in medical literature. According to the available medical data, 2 cases of thymoma and SLE were published by Cayla et al. [6] in 1975), and 11 more cases were described in the literature from 1922 to 1975**.** Searching MEDLINE for the period from 1975 to 1998, we identified another 18 cases of thymoma and SLE. The incidence of SLE patients with thymoma is 1.5% to 2% in clinical trials and 6% to 10% with retrospectively biopsy proven thymoma [7]. The importance of these deviations is even higher having in mind a primary role of the thymus in the immune system. It is possible that the increased activity of the thymus is associated with an immune disorder, as a predisposing factor which leads to transformation into tumor [8, 9]. Documentation about the circulating thymus hormone which level in immunodeficient patients (including those with SLE) is decreased, also indicates an association between autoimmune conditions and abnormality of the thymus [10]. The presence of thymoma is found in 30% of patients with clinically manifested SLE while in 30% of cases it was discovered by accident, radiographically, as it was a case with our patient. The clinical picture of SLE is clearly visible, including all immunoserological activity indicators [5, 6, 10–13]. For the final diagnosis, given the example of our patient, we found that an additional diagnostics was necessary, such as bronchoscopy with TBB and needle biopsy of changes in the mediastinum. The definitive diagnosis was obtained after mediastinoscopy by histopathological biopsy analysis of changes in the mediastinum and lungs. The thymectomy was also performed. The condition of the lungs was the reason for increasing the dose of corticosteroids to 1 mg/kg. This corresponded to the literature data that the effectiveness of the corticosteroid immunosuppressive therapy was satisfactory in these disorders. The presented course of the disease in our patient when pneumonitis within SLE was radiographically and histopathologically confirmed and *thymus persistens* verified, was an indication to start the therapy with cyclophosphamide pulse therapy at a dose of 15 mg/kg. Thymectomy is recommended in the treatment of thymoma, but we cannot say with certainty how significant it is in the treatment of SLE. According to available literature data, the effect of thymectomy is not clear. Obviously, it does not have an effect on the immunoserological activity in SLE. This indicates that thymus is not the only cause of immunology disorders in SLE. But, a disorder of thymic function, associated with an immune disorder, as a predisposing factor, can lead to the tumor transformation [4, 7, 8]. Based on cases published in the medical literature, SLE is not an indication for thymectomy, but the clinical results showed disease remission after thymectomy in 27.8% of cases [11]. This was the case with our patient, too. However, the connection between the disorder of thymic function and SLE deserves attention and additional studies, especially when the therapeutic effects of thymectomy are considered [5, 8, 10, 13].

Conclusion

The example of our patient shows that disorder of thymic function should be considered in the etiology of autoimmune diseases, including SLE. The effect of thymectomy is difficult to assess. But, the reduction of the impaired immunological activity can be expected, considering the primary role of the thymus in the immune system. Therefore, such patients should be monitored carefully in order to identify potential factors that could affect the course of SLE.

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