REVIEW ARTICLE

Systemic lupus erythematosus and myasthenia gravis

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KEY WORDS

coexistence, myasthenia gravis, systemic lupus erythematosus

ABSTRACT

This review summarizes current knowledge on systemic lupus erythematosus (SLE) coexisting with myasthenia gravis (MG). SLE can precede or follow the development of MG. SLE can also be observed in patients with MG following thymectomy. Overlapping signs and symptoms of a few different autoimmune diseases in a given patient are presented. Coexistance of SLE and MG is a rare phenomenon. It has already been observed; however, only sporadic clinical cases have been described.

Systemic lupus erythematosus (SLE) is an autoimmune disease with no predilection to involve specific organs, and is characterized by the presence of anti-native DNA and anti-SM antibodies, which may contribute to the occurrence of sustained proinflammatory state in the body.[1,2] Immune disorders associated with polyclonal activation of B lymphocytes are believed to play a central role in the pathogenesis of SLE.

Signs and symptoms of various autoimmune diseases may coexist with the previously diagnosed SLE.[3-5] Such pathological links are observed in 30% of SLE patients. However, the incidence of other autoimmune diseases varies among patients. A follow-up of 215 SLE patients, who were studied in the context of comorbidities, showed that the most common concomitant diseases include Sjögren's syndrome (13% of cases), followed by rheumatoid arthritis and thrombocytopenia (both 6% of cases), and finally, antiphospholipid syndrome and hypothyroidism (both 4% of cases).[3] However, occasionally SLE is diagnosed later in a given patient, i.e. after another autoimmune disease has been documented.

Myasthenia gravis (MG) is one of the autoimmune diseases closely associated with SLE. MG may develop prior to or after the onset of clinically overt SLE. Also, SLE may develop in patients with MG who have undergone thymectomy.[3,6-12]

Unlike SLE, MG is an organ-specific autoimmune disease predominantly associated with activation of T lymphocytes and the presence of specific autoantibodies directed against the acetylcholine receptor[11,13], specific tyrosine kinase receptors (MuSK), and the muscle proteins[14]. There is evidence that these antibodies could be a direct cause of the disease by impairing myoneural junction function, which in turn reduces muscular strength, thus leading to fatigue. Because the thymus is the site of T lymphocyte production, any pathological changes in the organ (hyperplasia, thymoma) inevitably result in cell dysfunction. An increased number and activation of autoreactive $CD4^+$ T lymphocytes are considered to be major pathogenic factors of MG.[15] Their interaction with B lymphocytes leads to autoantibody production, which form immune complexes resulting in immune response that cause organ damage.[16] Under physiological conditions, regulatory T lymphocytes inhibit the activity of $CD4^+$ T lymphocytes, which stops the autoimmune process. It has been suggested that deficiency or dysfunction of regulatory $CD4^+$ $CD25^+$ T lymphocytes are the pathogenic factors in connective tissue diseases[17] and create favorable environment predisposing to the development of MG[15] and SLE[1,16].

It has been highlighted recently that α chemokine subfamily (CXC) is involved in the pathogenesis of both disorders.[12,18] These chemokines participate in the chemoattraction of numerous immunoreactive cells. Some chemokines act as activators of monocytes, dendritic cells, T, B and NK cells, eosinophils and basophils. They also participate in angiogenesis[19], which is particularly important in connective tissue diseases[20,21]. CXCL13

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chemokine probably plays a major role in autoimmune response in MG. Studies on animal models proved that its interaction with B lymphocytes may result in subsequent SLE development.[12]

SLE rarely occurs concomitantly with MG; there are only a few reports of single cases or small groups of patients, and the issue merits further research.[22] There have been attempts to provide evidence for the associations between the two autoimmune diseases, which despite differences in pathogenesis show certain similarities. Both conditions demonstrate higher prevalence in the population of young women, both are characterized by periods of exacerbation and remission in the clinical course, and by the presence of anti-nuclear antibodies.[6] Moreover, it is assumed that both diseases are provoked by genetic, environmental, hormonal, and immunological factors.[8,23-30] There are more abundant published data on SLA than on MG. Common causative factors include bacterial and viral infections, smoking, pesticides, estrogens, various medications, and exposure to ultraviolet light.[31]

Thymectomy is an established treatment option for patients with thymoma-associated MG and selective erythroid aplasia.[32] However, it is noteworthy that pure erythroid aplasia may also develop following thymectomy.[32] Thymectomy is likely to result not only in SLE but also a number of other autoimmune diseases including idiopathic portal hypertension, Hashimoto's disease, cutaneous vessel vasculitis, and antiphospholipid syndrome. SLE after thymectomy manifests mainly polyartithis[6]; however, other symptoms including skin lesions, cytopenia, pleuritis, and an increased body temperature have also been observed[5].

It should be emphasized that the role of thymectomy as a factor underlying the onset of SLE in patients with MG still remains obscure. Thymectomy likely initiates the excessive production of autoantibodies in patients predisposed to SLE.[33] However, little is known about the pathologic mechanism behind this phenomenon. In MG patients thymectomy has been observed to slightly reduce the number of T lymphocytes and attenuate immune tolerance, and to cause B lymphocyte hyperactivity and hypergammaglobulinemia. A variety of autoantibodies, including anti-dsDNA and anticardiolipin, are usually detected.[6,32]

In conclusion, it should be stressed that the issues of SLE coexisting with MG discussed here are complex and remain unclear. Further research is needed, particularly to evaluate the exact role of prolactin, whose potential regulatory function in patients with MG has recently been reported.[15] It is well known that suppression of prolactin secretion may be a novel ancillary treatment mode for patients with moderate SLE.[15,24,34,35]

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Toczeń rumieniowaty układowy a męczliwość mięśni prążkowanych

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męczliwość mięśni prążkowanych, toczeń rumieniowaty układowy, współwystępowanie

STRESZCZENIE

Podjęto próbę podsumowania aktualnego stanu wiedzy na temat powiązań między toczniem rumieniowatym układowym (*systemic lupus erythematosus* – SLE) a męczliwością mięśni prążkowanych (*myasthenia gravis* – MG). Zwrócono uwagę na możliwość ujawnienia się SLE w okresie poprzedzającym rozpoznanie MG, po rozpoznaniu MG lub też w grupie chorych z MG po wykonanej tymektomii. Nawiązano do problematyki nakładania się u tego samego chorego objawów różnych chorób autoimmunologicznych. Skojarzenie SLE i MG nie jest zjawiskiem częstym. Problem ten jest zauważany, lecz jak dotąd opisywany tylko na podstawie obserwacji pojedynczych przypadków chorobowych.

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