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CASUISTIC PAPER

A patient with overlap syndrome: systemic lupus erythematosus, dermatomyositis, and Sjögren's syndrome – a rare overlapping diseases case report

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ABSTRACT

Introduction and aim. Autoimmune rheumatic diseases are a group of disorders with similar clinical, laboratory and immunological manifestations. Connective tissue diseases include systemic scleroderma, dermatomyositis or polymyositis, Sjögren's syndrome, rheumatoid arthritis, and systemic lupus erythematosus. If the patient meets the diagnostic criteria for at least two of these diseases and has specific serologic markers, a diagnosis of overlap syndrome is possible.

Description of the case. This case describes a 27-year-old man who had a history of paroxysmal fever, night sweats, erythema-like skin lesions on the forearms and lower legs, a feeling of progressive muscle weakness especially in the proximal muscles, and dry mouth. The patient was diagnosed with an overlap syndrome: systemic lupus erythematosus, dermatomyositis, and Sjögren's syndrome.

Conclusion. Overlap syndrome is difficult to treat due to its multisystem nature, requiring a symptomatic therapeutic approach and careful control of medication doses to reduce side effects while controlling disease activity.

Keywords. autoimmune diseases, overlap syndrome, self-reactive

Introduction

Overlap syndrome is an inflammatory rheumatic disease in which the patient has clinical features of various autoimmune rheumatic diseases.[1-3] Mixed connective tissue disease is a rare autoimmune disease characterized by the presence of anti-RNP antibodies.[4,5] The most common diseases included in overlap syndrome are rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, dermatomyositis, polymyositis, and Sjögren's syndrome.[6-8] Overlap syndrome can be diagnosed if the patient meets at least both diagnostic criteria and has specific serologic markers.[1,3] The pathogenesis is based on the development of an excessive, antigen-driven, self-reactive immune response that is a consequence of genetic predisposition and environmental factors.[2]

Systemic lupus erythematosus (SLE) is a complex, chronic autoimmune disease with variable clinical manifestations associated with the presence of multiple autoantibodies, such as anti-dsDNA and anti-Sm, which cause the deposition of immune complexes.[9-11]

Sjögren's syndrome is a chronic inflammatory autoimmune disease of unknown etiology with ANA> 1:80 and anti-Ro and anti-La antibodies. The disease specif-

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ically affects the lacrimal and salivary glands with lymphocyte infiltration resulting in impaired function.[12,13]

Dermatomyositis is a rare idiopathic inflammatory myopathy accompanied by dermatitis. Autoimmune mechanisms play a major role in the pathogenesis of dermatomyositis, among which anti-Jo-1, anti-SRP and anti-Mi-2 autoantibodies play an important role.[14,15]

Aim

The aim of this study was to present this unique disease entity with typical clinical features, detected in a 27-year-old man.

Description of the case

A 27-year-old Caucasian man, he reported paroxysmal fever, night sweats, erythema-like skin lesions on the forearms and lower legs, a feeling of progressive muscle weakness, especially proximal muscles, and dry mouth, which was confirmed by a physical examination. The appearance of these ailments was associated with the consumption of large amounts of alcohol during sertalinum treatment.

During the patient's stay in August 2020 on the ward, the alanine aminotransferase level was monitored, which was initially 138 U/L (norm: 10–49) and eventually decreased to 76 U/L (norm: 10–49), the creatine kinase level was initially 822 U/L (norm: 46–171) and then decreased to 84 U/L (norm: 46–171), gamma glutamyltranspeptidase value was 209 U/L (norm: <73), immunoglobulin G 20.33 g/L (norm: 6.59–16.00), interleukin-67 (IL-67) 16 pg/mL (norm: <3.4), lactate dehydrogenase 521 U/L (norm: 120–246). Laboratory investigations revealed antibody titer of 1: 5120, granular and nuclear staining of 1: 10240, ANA 3 present in high titer of RNP, Sm, SSA and SSB as well as dsDNA, decreased levels of complement components C3 and C4, leukopenia and lymphopenia, mild anemia, thrombocytopenia, liver damage and hypergammaglobulinemia. The parotid glands are heterogeneous, with reduced echogenicity, with the presence of small hypoechogenic areas up to 2-3 mm in diameter. Under general anesthesia, a section of the mucosa of the lower lip along with the salivary gland was taken for histopathological examination.

The patient was diagnosed with overlap syndrome: systemic lupus erythematosus, dermatomyositis and Sjögren's syndrome in August 2020. Intravenous methylprednisolone was administered, followed by oral steroids, and cyclosporine when the transaminase levels decreased. The treatment resulted in improvement of the patient's general condition and improvement of the myopathy symptoms. The treatment included pulses of methylprednisolone, followed by continued systemic intravenous steroid therapy, and cyclosporine was added after transaminase levels decreased. After the treatment, the patient felt better and the symptoms of myopathy resolved. On follow-up, leukopenia and thrombocytopenia persisted, responding poorly to the previous treatment. After hematological consultation trepanobiopsy was suggested, but the patient did not agree. After improvement of the patient's condition, he was discharged home with recommendations to follow a liver diet, follow-up examinations were ordered and the patient was declared unfit for work. In treatment, he received 6 pulses of methylprednisolone at 500 mg, then oral prednisone at a dose of 60 mg/d and cyclosporine at a dose of 200 mg/d (body weight 88.7 kg).

On September 25, 2020, he was re-admitted to assess the tolerance and effectiveness of treatment, the concentration of cyclosporine was determined (58.6 ng/ml) and due to non-therapeutic levels (> 80), the dose of cyclosporine was increased to 250 mg/day, the dose of prednisolone was reduced to 40 mg/day.

In March 2021, the patient was hospitalized due to the intensification of skin lesions such as erythema of the neckline, face, arms and hands. Additionally, significant leukopenia was found – WBC $2*10^3$/μl (norm: $4*10^3$–$10*10^3$), and vitamin B12 deficiency was found – 189 pg/ml (norm: 211–911). The patient was given 5 infusions of methylprednisolone, 125 mg each, and injections of vit. B12 (3 x 1000j each). The level of white blood cells was normalized: WBC $7.14*10^3/mm^3$ and skin changes disappeared. Still in treatment: prednisolone 20 mg/d with slow reduction and cyclosporine 250 mg/d.

The patient was hospitalized in 2022 for parenchymal liver injury. The patient developed hypertension as a result of taking steroid medication. On admission, the patient reported no significant complaints, no signs of muscle weakness, and skin lesions on the hands were still present on physical examination. Chronic myopathic changes were found in the right quadriceps muscle. Recordings from the rectus muscle of the right anterior and tibial right thigh demonstrating electrical silence at rest in the muscles. There is no abnormality in the conduction parameters of the examined nerves. Laboratory tests of alanine aminotransferase were initially 263 U/L, and after two weeks the level dropped to 136 U/L, creatine kinase value was 96 U/L, rheumatolophrenic factor in IgM caliber was 29.4 IU/ml (norm: ≥ 20), gamma glutamyltranspeptidase was initially 204 U/L, and after two weeks decreased to 105 U/L.

Laboratory tests performed showed leukopenia, no thrombocytopenia, hypertransaminasemia with slightly elevated cholestasis parameters. Autoimmune tests revealed the presence of anti-nuclear granular fluorescence antibodies 1: 320 and cytoplasmic fluorescence antibodies 1: 640, in ANA 3 highly positive RNP, SS-A, Sm, Ro-52, ribosomal protein P, complement components normal. After gastrointestinal consultation, it was

recommended to consider liver biopsy due to the triple digit transaminase values found in 2020.

In 2022, leukopenia with lymphopenia appeared again (WBC 2.5*10^3/µl, Lymph 17%), which disappeared after infusions of methylprednisolone (from 1 to 3 a 250 mg) and immunoglobulins – 80 g/month – 2 infusions of 40 g, every 4 weeks 6 times, starting from March 2022, a total of 480 g.

In April 2022 there was an attempt to include Mycophenolate Mofetil, but it ended with a 3-fold increase in transaminases (administration stopped). Regular monthly supplementation of vitamin B12 (a 1000 units) was ordered.

With such a therapeutic regimen, the patient's development to date was characterized by marked clinical improvement, which allowed him to significantly improve his functional capacity. The patient was classified as unfit for work. The patient was discharged home with recommendations to follow a liver diet, photoprotection, and to take medications such as prednisone, vitamin B12, proton pump inhibitor, and bisoprolol. A visit to the rheumatology department was scheduled to evaluate disease activity and to continue immunoglobulin treatment.

Table 1. Comparison of patient outcomes in disease exacerbation and in remission after intravenous administration of methylprednisolone

	Exacerbation of disease 2021	Remission of disease 2021 after infusions of methylprednisolone
WBC (4–10*10^3/µl)	2.0	7.14
	Exacerbation of disease 2022	**Remission of disease 2022 after infusions of methylprednisolone**
WBC (4–10*10^3/µl)	2.5	3.7

Discussion

Overlap syndromes are very rare and affect people with systemic lupus erythematosus who also have features of another rheumatologic condition, including rheumatoid arthritis, Sjögren's syndrome, vasculitis, and/or myositis.[1-3] Identifying patients with overlapping syndromes is important as these patients may require different monitoring and treatment regimens.[1,2] Clinically, as seen in this case, the most characteristic symptomatology is the presence of erythema-like skin lesions on the forearms and lower legs, a feeling of progressive muscle weakness, especially proximal muscle weakness, dry mouth and night sweats. Due to the overlap of the abovementioned diseases, the patient was treated with steroids and immunoglobulin infusions.

The treatment of the overlap syndrome depends on the symptoms predominant in the clinical picture and involves the treatment of the diseases that are part of it. The results of the study by Balbir-Gurman et al. indicate a relatively high incidence of scleroderma overlap syndrome with Sjgogren's syndrome or myositis, and the overlap of scleroderma with SLE is quite rare, the frequent use of steroids, cyclophosphamide and DMARDs, as well as IVIG in patients with overlapping scleroderma is observed.[3] Ramya et al. described a case of a patient with overlapping symptoms of SLE, systemic scleroderma, and secondary Sjögren's syndrome who received immunosuppressive and corticosteroid therapy.[16] Recently, biologic medications have been used in refractory cases of overlap syndrome, but the ill effect of such medications is the high likelihood of disease exacerbation in these patients.[16-20] Itikyala et al. described a syndrome of overlap between systemic lupus erythematosus and vasculitis associated with a cytoplasmic anti-neutrophil antibody; the patient is doing well after treatment with rituximab, but this entity should be recognized and requires appropriate treatment.[10] On the other hand, we describe a rare case of overlap between three diseases: SLE, dermatomyositis and Sjögren's syndrome, which are currently well controlled by treatment with corticosteroids and immunoglobulin infusions, while controlling the patient's general condition.

Conclusion

Due to the multisystem nature of the overlap syndrome, it is difficult to treat. Clarification of each patient's condition can lead to improved patient care.

Declarations

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Author contributions

Conceptualization, A.S., M.I., and P.D.; Methodology, P.D.; Validation, A.S., and M.I.; Formal Analysis, A.S., M.I., and P.D.; Investigation, A.S., and M.I.; Writing – Original Draft Preparation, A.S.; Writing – Review & Editing, A.S., and M.I.; Visualization, A.S.; Supervision, P.D.; Project Administration, P.D. All authors have read and agreed to the published version of the manuscript.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

The data sets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

Ethics approval

Consent for publication was obtained from participant.

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