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Difficulties in the diagnosis of antisynthetase syndrome

ABSTRACT

Antisynthetase syndrome is a rare subtype of idiopathic inflammatory myopathies, characterised by co-ocurrence of myositis, arthritis, interstitial lung disease, Raynaud phenomenon, fever and mechanic's hands. Symptoms frequently appear asynchronously. The presence of antisynthetase antibodies in a patient's serum is considered an immunological hallmark of the disease. Arriving at a proper diagnosis of antisynthetase syndrome remains a considerable challenge, and the diagnosis is often delayed. The manuscript discusses possible obstacles in the diagnostic process of antisynthetase syndrome.

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KEY WORDS: antisyntetase syndrome; idiopathic inflammatory myopathies; interstitial lung disease; arthritis; diagnosis

INTRODUCTION

Antisynthetase syndrome is a subtype of idiopathic inflammatory myopathies with a unique clinical picture. The condition is classified as a rare disease, with a prevalence estimate of 1/25,000–33,000 according to the Orphanet registry [1], but the actual prevalence is probably significantly underestimated. Data on the prevalence of the disease in the Polish population are not known. According to the EuroMyositis International Registry, antisynthetase syndrome occurs less frequently than dermatomyositis and polymyositis, but more frequently than sporadic inclusion myositis and necrotizing autoimmune myopathy [2]. Antisynthetase syndrome is more common in women (a W:M ratio of approximately 7:3) and the mean age of onset is 48 ± 15 years [2].

Antisynthetase syndrome is distinguished from other idiopathic inflammatory myopathies based on its unique clinical picture, which involves the co-occurrence of symptoms such as myositis, arthritis, interstitial lung disease, mechanic's hands, Raynaud's phenomenon and fever [3]. Despite the classification of the disease as an idiopathic inflammatory myopathy, muscle involvement may be mild or subclinical and non-muscular symptoms may often predominate in the clinical picture [3]. The serological markers of anti-synthetase syndrome are autoantibodies against amino-acyl-tRNA synthetases (antisynthetase antibodies). Antisynthetase antibodies include anti-Jo-1, anti-PL-7, anti-PL-12, anti-EJ, anti-OJ, anti-KS, anti-Zo and anti-Ha [4]. Of these, anti-Jo-1 antibodies are by far the most frequently detected — in up to 30% of patients with idiopathic inflammatory myopathies, while other individual types of antisynthetase antibodies are found in no more than 5% of patients [4]. Antisynthetase autoantibodies usually occur in isolation, although cases of co-occurrence have also been reported [5].

The unique clinical picture, low prevalence and non-specific diagnostic criteria contribute to delays in the accurate diagnosis of the disease. The aim of this paper is to discuss the most common difficulties in the diagnostic process of antisynthetase syndrome.

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DIAGNOSTIC CRITERIA

The diagnosis of antisynthetase syndrome in patients is based on finding the typical clinical picture and identifying antisynthetase antibodies in a patient's serum. So far, several classification and diagnostic criteria have been proposed. The current standard for diagnosing idiopathic inflammatory myopathies continues to be the classification criteria jointly developed by EULAR and ACR in 2017 [6]. The algorithm proposed by EULAR/ACR replaced the previously used Bohan and Peter criteria [7, 8]. Criteria of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) take into account the following components: age of onset of symptoms, proximal muscle weakness in the upper and lower limbs and neck muscle weakness, pathognomonic skin lesions (heliotrope erythema, Gottron's sign/papules), dysphagia, elevated muscle enzymes, presence of anti-Jo-1 antibodies and optionally histopathological examination of a skeletal muscle specimen [6]. The main limitations of the new diagnostic criteria are the omission of muscle-specific antibodies other than anti-Jo-1 antibodies, with the risk of failing to diagnose patients with less common antisynthetase antibodies. Furthermore, among non-muscular symptoms, the EULAR/ACR criteria include only pathognomonic skin lesions and dysphagia, which carries the risk of overlooking the disease in patients with a predominance of other non-muscular symptoms. The criteria do not take into account articular complaints and interstitial lung lesions, both of which may be predominant in the antisynthetase subtype. In an analysis by Greco et al., only 59.5% of patients in whom antisynthetase syndrome was suspected from the clinical picture met the EULAR/ACR criteria for the diagnosis of idiopathic inflammatory myopathy [9]. They included all patients with anti-Jo-1 antibodies and only 20% of patients with other antisynthetase autoantibodies [9]. The authors of the analysis proposed modifying the criteria so that each antisynthetase antibody would be assigned a weight equal to the anti-Jo-1 antibody. After an analysis using these modified criteria, 95% consistency with clinical diagnoses was obtained [9].

Due to the distinctive nature of antisynthetase syndrome, criteria dedicated to this subtype of the disease have also been developed. Solomon's diagnostic criteria, published in 2011, involve dividing clinical symptoms into major and minor criteria [10]. Major criteria include inflammatory myopathy (diagnosed using the Bohan and Peter criteria) and interstitial lung disease [10]. Polyarthritis, Raynaud's phenomenon and mechanic's hands were considered minor criteria [10]. The diagnosis of antisynthetase syndrome requires demonstrating the presence of antisynthetase antibodies in a patient's serum and the co-occurrence of both major criteria or one of the major criteria with the presence of at least two minor criteria [10]. Other criteria dedicated to antisynthetase syndrome have been proposed by Connors and colleagues [11]. According to the mentioned criteria, the diagnosis of the disease requires the presence of antisynthetase antibodies and at least one symptom from the spectrum of antisynthetase syndrome [11]. These criteria are considerably broader than those proposed by Solomon, and for this reason, they are considered by some authors to be preliminary criteria, allowing the suspicion of antisynthetase syndrome, rather than its formal diagnosis. It should be emphasised that, regardless of the criteria used, muscle involvement is not necessary for the diagnosis of antisynthetase syndrome.

Considering the limitations of the criteria proposed so far, experts have called for the development of new diagnostic schemes that better reflect the spectrum of symptoms involved in antisynthetase syndrome and their variability over time [12, 13]. New classification criteria are currently being developed as part of a collaborative effort between EULAR and the ACR on the EULAR-ACR Classification Criteria for Antisynthetase Syndrome (CLASS) project.

DIAGNOSTIC DIFFICULTIES

Despite the fairly unique clinical picture, accurate diagnosis of antisynthetase syndrome remains a considerable challenge. In patients with anti-Jo-1 antibodies, the mean time to correct diagnosis is 6 months, while in patients with less common autoantibodies the mean diagnostic delay is up to one year [14, 15]. In some cases, the disease remains undiagnosed for many years or other disease entities are initially diagnosed, such as undifferentiated connective tissue disease, rheumatoid arthritis, other systemic connective tissue diseases, idiopathic interstitial lung disease or interstitial pneumonia with autoimmune features [16].

Table 1. Comparison of available criteria for the diagnosis of antisynthetase syndrome

	EULAR/ACR	Solomon et al.	Connors et al.
Target group	IIM	Antisynthetase syndrome	Antisynthetase syndrome
Antibodies	Only anti-Jo-1	All antisynthetase antibodies	All antisynthetase antibodies
Muscular involvement	Physical examination, and optionally a biopsy	According to the Bohan and Peter criteria; major criterion	According to the Bohan and Peter criteria
Interstitial lung disease	No	Yes, major criterion	Yes
Arthritis	No	Yes, minor criterion	Yes
Mechanic's hands	No	Yes, minor criterion	Yes
Raynaud's phenomenon	No	Yes, minor criterion	Yes
Fever	No	No	Yes

EULAR/ACR — European League Against Rheumatism/American College of Rheumatology; IIM — idiopathic inflammatory myopathies

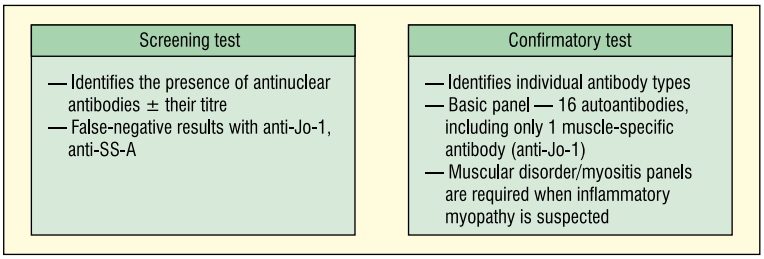

Figure 1. Immunorheumatology diagnosis in antisynthetase syndrome

IMMUNORHEUMATOLOGY DIAGNOSTICS

Antisynthetase antibodies, an immunological marker of antisynthetase syndrome, belong to a large group of antinuclear antibodies. According to the current guidelines, evaluation for antinuclear antibodies should be performed in patients with clinical suspicion of systemic disease and should be based on a two-step scheme [17]. In the first stage of the diagnosis, a screening test with the use of the indirect immunofluorescence method with the HEp-2 cell line is recommended; and if a positive result is obtained, the diagnosis should be extended to include confirmatory tests detecting individual autoantibodies [17]. A wide range of diagnostic panels are now available on the market for use in screening and extended diagnosis, based on immunofluorescence, immunoblotting, immunodiffusion or immunoenzymatic techniques. In clinical practice, the assessment of autoantibodies against the 16 most common nuclear and cytoplasmic antigens using the immunoblot method (antibodies against: dsDNA, nucleosomes, histones, ribosomal protein P, DSF 70, nRNP/Sm, Sm, SS-A, Ro-52, SS-B, Scl-70, PM-Scl, Jo-1, Centromere B, PCNA and AMA-M2) is most commonly used as a confirmatory test. It is worth noting that only one of the muscle-specific antibodies, the antibody against Jo-1, was included in the panel described above. The detection of other muscle-specific antibodies, including other antisynthetase antibodies, requires an extension of the diagnostic procedure to include specific panels for myositis (so-called myositis/muscular disorder panels). Omitting the assessment of less common muscle-specific antibodies may lead to underdiagnosis and incorrect diagnostic conclusions. Therefore, the authors consider it reasonable to use specific panels in routine clinical practice in patients with a clinical suspicion of antisynthetase syndrome. With a negative screening test result, confirmatory testing is generally not recommended but may be indicated when antisynthetase syndrome is suspected. Low expression of Jo-1 and SS-A antigens on HEp-2 cells can lead to false-negative screening test results, despite the presence of anti-Jo-1 and anti-SS-A antibodies [17]. The scheme of immunorheumatology diagnosis in antisynthetase syndrome is shown in Figure 1.

THE DIFFERENT TIMING OF ONSET OF SYMPTOMS

Diagnosis of the disease is complicated by the fact that not all symptoms are necessarily present in every patient, and complaints may

appear at different times [14, 18, 19]. A trend towards the progression of the clinical picture over time was noted in an observational study on a group of 828 patients with antisynthetase antibodies from the AENEAS (American and European NEtwork of Antisynthetase Syndrome) registry [14]. At the beginning of the disease, a significant proportion of patients presented only with isolated symptoms — arthritis, myositis or interstitial lung disease. Isolated articular symptoms occurred in 22% of patients with anti-Jo-1 antibodies, isolated myositis in 33% of patients with anti-OJ antibodies, while in 36–43% of patients with anti-PL-7, anti-PL-12 and anti-EJ antibodies the disease started with isolated interstitial lung lesions. The classic triad of coexisting myositis, arthritis and interstitial lung disease was observed in only 18% of patients with anti-Jo-1 and less than 10% of patients with other antisynthetase autoantibodies. Over time, however, most patients developed further symptoms, and by the end of the follow-up, the vast majority of patients had either the classic triad of symptoms or at least two symptoms coexisting [14]. The different timing of symptom onset was also demonstrated in a retrospective study analysing 55 patients with antisynthetase syndrome hospitalised in a Brazilian centre [18]. In the described cohort, the most common first symptom of the disease was joint complaints, observed in 43.6% of patients. In addition, there was a high prevalence of fever as an isolated symptom (41.8%). In 38.2% of patients, the antisynthetase syndrome initially manifested itself only with muscle symptoms, while in 36.4% of patients only interstitial lung lesions were initially observed. Raynaud's phenomenon and mechanic's hands as isolated symptoms were relatively rare, occurring in less than 20% of patients. Only 2 of 55 patients had a simultaneous involvement of joints, muscles and lungs. Subsequent clinical symptoms appeared at different time points in individual patients. In the cohort described above, the median time between the onset of first symptoms and the development of fully-symptomatic antisynthetase syndrome was 19.9 months, reaching 60.2 months in the case with the maximum time to fully symptomatic disease [18]. A multicentre study of Spanish patients with antisynthetase syndrome analysed the course of the disease in 148 individuals [19]. In 32.4% of patients, the antisynthetase syndrome started with isolated interstitial lesions, in 26.9% only myositis was initially observed and in 17.9% the disease started with polyarthritis. At the end of follow-up, the most common clinical presentation was the co-occurrence of myositis and interstitial lung disease (67.6%) [19].

Although the majority of patients show a gradual progression to other symptoms from the spectrum of antisynthetase syndrome, some patients are oligosymptomatic. In the AENEAS study, up to 36% of patients with anti-PL-12 antibodies did not develop articular or muscular symptoms in addition to interstitial lung disease at the end of follow-up. Similarly, 28% of patients with anti-OJ antibodies had myositis without concomitant arthritis or interstitial lung disease at the end of the study [14].

ARTICULAR SYMPTOMS MIMICKING RHEUMATOID ARTHRITIS

In a significant proportion of patients with antisynthetase syndrome, joint involvement can be observed in the form of arthralgia or arthritis. Arthritis appears to be more frequent in the group of patients with anti-Jo-1 antibodies compared with patients with other serological profiles [14]. Symmetric inflammation of small joints of the hand, primarily of the interphalangeal, metacarpophalangeal and wrist joints, is most commonly observed and may need to be differentiated from rheumatoid arthritis [3]. Involvement of large joints (knee, elbow, shoulder, ankle, hip), distal interphalangeal joints and foot joints is less common [20]. It has been observed that when arthritis is present from the early stages of the disease, it is more likely to resemble RA — typically with symmetric involvement of multiple joints, with the presence of RF and destructive changes in the joints, whereas late-onset arthritis tends to resemble arthritis in the course of systemic connective tissue diseases [21].

The accurate diagnosis is rendered difficult by the fact that antibodies against citrullinated peptides (anti-CCP) may be present not only in the course of RA but also in patients with antisynthetase syndrome [22–24]. Further studies are required to assess whether anti-CCP antibodies prognose an overlap syndrome with RA or whether they may be present in an isolated antisynthetase syndrome. In patients with antisynthetase syndrome and anti-CCP antibodies, arthritis is associated with a more severe clinical course and more often leads to radiographic damage compared with seronegative patients [24].

Table 2. Diagnostic criteria for IPAF and its signs shared with antisynthetase syndrome

IPAF criterion	Obligatory for IPAF diagnosis	Consistency with antisynthetase syndrome
Presence of interstitial lung lesions on HRCT/surgical biopsy	Yes	Yes
Exclusion of another cause of ILD	Yes	Yes
Unmet diagnostic criteria for any systemic connective tissue disease	Yes	No
The domain of clinical symptoms: — mechanic's hands — fingertip ulcers — arthritis or morning stiffness in multiple joints lasting > 60 minutes — telangiectasias on the hands — Raynaud's phenomenon — unascertained swelling of the fingers — Gottron's sign	Required fulfilment of ≥ 1 criterion in ≥ 2 domains	Yes, partly: mechanic's hands arthritis Raynaud's phenomenon
The serological domain: — ANA titre ≥ 1:320, fluorescence pattern: diffuse, speckled, homogeneous — ANA in any titer with nucleolar or centromere fluorescence pattern — RF > 2× upper limit of normal — anti-CCP — anti-dsDNA, anti-Ro (SS-A), anti-La (SS-B), anti-RNP, anti-Sm, anti-Scl70, antisynthetase antibodies, anti-PM-Scl, anti-MDA5	Required fulfilment of ≥ 1 criterion in ≥ 2 domains	Yes, partly: antisynthetase antibodies
The morphological domain: — radiological pattern in HRCT: NSIP, OP, superimposition of NSIP and OP, LIP — findings of histopathology/surgical biopsy of lung: NSIP, OP, overlap of NSIP and OP, LIP, interstitial lymphoid nodules with foci of proliferation, diffuse lymphoplasmacytic infiltration — multisite involvement (other than ILD) with no other cause: • pleural effusion or pleural thickening • pericardial effusion or pericardial thickening • small airway disease with airflow obstruction, bronchiolitis or bronchial dilatation • pulmonary vasculopathy	Required fulfilment of ≥ 1 criterion in ≥ 2 domains	Yes, partly: interstitial lung lesions on HRCT/histopathology

IPAF — interstitial pneumonia with autoimmune features; HRCT — high-resolution computed tomography; ILD — interstitial lung disease; RF — rheumatoid factor; NSIP — non-specific interstitial pneumonia; OP — organising pneumonia; LIP — lymphocytic interstitial pneumonia

The subgroup of patients with arthritis as the first symptom of antisynthetase syndrome seems to be at a particularly high risk of misdiagnosis or long delay in time to correct diagnosis which exceeded 2 years in a multicentre observational study [20]. A significant proportion of patients are initially diagnosed with seronegative rheumatoid arthritis or other forms of inflammatory arthropathies. Lefevre et al. report that in their study, 60% of patients were initially treated with at least one disease-modifying drug based on a diagnosis of seronegative polyarthritis before a correct diagnosis of antisynthetase syndrome was made [20].

Experts recommend increased vigilance and active observation of patients with isolated arthritis for the possible development of other components of antisynthetase syndrome [20, 22].

SIMILARITIES AND DISSIMILARITIES WITH IPAF

The criteria for antisynthetase syndrome partly overlap with those of a newly distinguished disease entity, interstitial pneumonia with autoimmune features (IPAF), distinguished in 2015 by the European Respiratory Society and American Thoracic Society [25]. This diagnosis is used for patients with interstitial lung disease who do not meet the diagnostic criteria for any systemic connective tissue diseases, but present with certain clinical symptoms and abnormalities in additional tests corresponding to the spectrum of systemic connective tissue diseases [25]. The diagnosis of IPAF requires that at least one criterion in each of at least 2 of the 3 domains — clinical, serological and/or morphological domain — have to be met [25]. The diagnostic criteria for IPAF and its signs shared with antisynthetase syndrome are shown in Table 2.

An analysis of the IPAF criteria clearly shows that there is some overlap with the picture of antisynthetase syndrome. In terms of clinical symptoms, patients with IPAF, like those with antisynthetase syndrome, may present with mechanic's hands, arthritis or Raynaud's phenomenon, among others, and the immunological

criteria include the presence of antisynthetase antibodies. One can easily imagine a situation where a patient with interstitial lung disease and symptoms in the spectrum of antisynthetase syndrome does not meet the current EULAR/ACR criteria for the diagnosis of idiopathic inflammatory myopathy. The question remains: should such a patient be diagnosed with IPAF or should they be diagnosed with antisynthetase syndrome according to, for example, the Connors criteria? In the absence of uniform diagnostic criteria for antisynthetase syndrome, it is difficult to clearly differentiate between the two disease entities. It therefore seems reasonable to approach the issue as a kind of spectrum and continuum rather than separate disease entities [26].

INTERDISCIPLINARY COOPERATION — KEY TO A CORRECT DIAGNOSIS?

In recent years, the role of interdisciplinary cooperation between doctors of different specialities has been emphasised. Such cooperation may also be crucial in the diagnosis and care of patients with antisynthetase syndrome. Levi et al. demonstrated the validity of including a rheumatologist in the multispecialty team diagnosing patients with interstitial lung disease [27]. In the study cited above, 60 patients with interstitial lung disease were assessed twice — the first assessment was performed by a multispecialty team consisting of a pulmonologist, radiologist and pathomorphologist, and the second assessment was performed independently by a rheumatologist. The typical multispecialty team correctly identified systemic connective tissue disease in 13 patients (including 1 with antisynthetase syndrome), and adding a rheumatology assessment allowed a correct diagnosis of systemic connective tissue disease to be made in a further 9 patients, among whom there were as many as 3 with antisynthetase syndrome [27].

CONCLUSIONS

The accurate diagnosis of antisynthetase syndrome remains a considerable challenge. The diversity of symptoms and their tendency to progress over time make it difficult to establish the diagnosis early. Because of the possibility of false-negative results of the screening test for antinuclear antibodies, in the presence of clinical symptoms from the spectrum of antisynthetase syndrome, it is reasonable to extend the diagnosis by including confirmatory tests. The detection of antisynthetase antibodies requires the use of specific muscular disorder panels that detect less common muscle-specific antibodies. Cooperation between a pulmonologist and a rheumatologist may improve the accuracy of diagnoses of interstitial lung disease in the course of systemic connective tissue diseases, including antisynthetase syndrome. New diagnostic criteria for antisynthetase syndrome, taking into account frequent non-muscular symptoms, are underway.

References

1. Anquetil C, Benveniste O. Antisynthetase syndrome. Orphanet. https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=81 (6 February 2022).
2. Lilleker JB, Vencovsky J, Wang G, et al. all EuroMyositis contributors. The EuroMyositis registry: an international collaborative tool to facilitate myositis research. Ann Rheum Dis. 2018; 77(1): 30–39, doi: 10.1136/annrheumdis-2017-211868, indexed in Pubmed: 28855174.
3. Opinc AH, Makowska JS. Antisynthetase syndrome - much more than just a myopathy. Semin Arthritis Rheum. 2021; 51(1): 72–83, doi: 10.1016/j.semarthrit.2020.09.020, indexed in Pubmed: 33360231.
4. Ghirardello A, Doria A. New insights in myositis-specific autoantibodies. Curr Opin Rheumatol. 2018; 30(6): 614–622, doi: 10.1097/BOR.0000000000000548, indexed in Pubmed: 30234722.
5. Gelpí C, Kanterewicz E, Gratacos J, et al. Coexistence of two antisynthetases in a patient with the antisynthetase syndrome. Arthritis Rheum. 1996; 39(4): 692–697, doi: 10.1002/art.1780390424, indexed in Pubmed: 8630123.
6. Bottai M, Tjärnlund A, Santoni G, et al. International Myositis Classification Criteria Project consortium, the Euromyositis register and the Juvenile Dermatomyositis Cohort Biomarker Study and Repository (JDRG) (UK and Ireland). EULAR/ACR classification criteria for adult and juvenile idiopathic inflammatory myopathies and their major subgroups: a methodology report. RMD Open. 2017; 3(2): e000507, doi: 10.1136/rmdopen-2017-000507, indexed in Pubmed: 29177080.
7. Bohan A, Peter JB. Polymyositis and dermatomyositis (first of two parts). N Engl J Med. 1975; 292(7): 344–347, doi: 10.1056/NEJM197502132920706, indexed in Pubmed: 1090839.
8. Bohan A, Peter JB. Polymyositis and dermatomyositis (second of two parts). N Engl J Med. 1975; 292(8): 403–407, doi: 10.1056/NEJM197502202920807, indexed in Pubmed: 1089199.
9. Greco M, García de Yébenes MJ, Alarcón I, et al. Idiopathic inflammatory myopathies and antisynthetase syndrome: contribution of antisynthetase antibodies to improve current classification criteria. Ann Rheum Dis. 2019; 78(9): 1291–1292, doi: 10.1136/annrheumdis-2019-215031, indexed in Pubmed: 30910990.
10. Solomon J, Swigris JJ, Brown KK. Myositis-related interstitial lung disease and antisynthetase syndrome. J Bras

Pneumol. 2011; 37(1): 100–109, doi: 10.1590/s1806-37132011000100015, indexed in Pubmed: 21390438.
11. Connors G, Christopher-Stine L, Oddis C, et al. Interstitial Lung Disease Associated With the Idiopathic Inflammatory Myopathies. Chest. 2010; 138(6): 1464–1474, doi: 10.1378/chest.10-0180.
12. Cavagna L, Castañeda S, Sciré C, et al. AENEAS Collaborative Group Members. Antisynthetase syndrome or what else? Different perspectives indicate the need for new classification criteria. Ann Rheum Dis. 2018; 77(8): e50, doi: 10.1136/annrheumdis-2017-212368, indexed in Pubmed: 28970214.
13. Castañeda S, Cavagna L, González-Gay MA. New Criteria Needed for Antisynthetase Syndrome. JAMA Neurol. 2018; 75(2): 258–259, doi: 10.1001/jamaneurol.2017.3872, indexed in Pubmed: 29255888.
14. Cavagna L, Trallero-Araguás E, Meloni F, et al. Influence of Antisynthetase Antibodies Specificities on Antisynthetase Syndrome Clinical Spectrum Time Course. J Clin Med. 2019; 8(11), doi: 10.3390/jcm8112013, indexed in Pubmed: 31752231.
15. Cavagna L, Nuño L, Scirè CA, et al. AENEAS (American, European NEtwork of Antisynthetase Syndrome) collaborative group. Clinical Spectrum Time Course in Anti Jo-1 Positive Antisynthetase Syndrome: Results From an International Retrospective Multicenter Study. Medicine (Baltimore). 2015; 94(32): e1144, doi: 10.1097/MD.0000000000001144, indexed in Pubmed: 26266346.
16. Masiak A, Marzec M, Kulczycka J, et al. The clinical phenotype associated with antisynthetase autoantibodies. Reumatologia. 2020; 58(1): 4–8, doi: 10.5114/reum.2020.93505, indexed in Pubmed: 32322117.
17. Fischer K. Autoprzeciwciała w codzienne praktyce klinicznej. Rheumatology Forum. 2016; 2(1): 39–50.
18. Baccaro AC, Behrens Pinto GL, Carboni RCS, et al. The clinical manifestations at the onset of antisynthetase syndrome: A chameleon with multiple faces. Reumatismo. 2020; 72(2): 86–92, doi: 10.4081/reumatismo.2020.1275, indexed in Pubmed: 32700874.
19. Trallero-Araguás E, Grau-Junyent JM, Labirua-Iturburu A, et al. IIM Study Group and Autoimmune Diseases Study Group (GEAS) of the Spanish Society of Internal Medicine (SEMI). Clinical manifestations and long-term outcome of anti-Jo1 antisynthetase patients in a large cohort of Spanish patients from the GEAS-IIM group. Semin Arthritis Rheum. 2016; 46(2): 225–231, doi: 10.1016/j.semarthrit.2016.03.011, indexed in Pubmed: 27139168.
20. Lefèvre G, Meyer A, Launay D, et al. Club Rhumatismes, Inflammation. Seronegative polyarthritis revealing antisynthetase syndrome: a multicentre study of 40 patients. Rheumatology (Oxford). 2015; 54(5): 927–932, doi: 10.1093/rheumatology/keu404, indexed in Pubmed: 25349440.
21. González-Gay MA, Montecucco C, Selva-O'Callaghan A, et al. AENEAS (American and European NEtwork of Antisynthetase Syndrome) collaborative group. Timing of onset affects arthritis presentation pattern in antisyntethase syndrome. Clin Exp Rheumatol. 2018; 36(1): 44–49, indexed in Pubmed: 28770709.
22. Cavagna L, Nuño L, Scirè CA, et al. AENEAS (American and European NEtwork of Antisynthetase Syndrome) Collaborative Group. Serum Jo-1 Autoantibody and Isolated Arthritis in the Antisynthetase Syndrome: Review of the Literature and Report of the Experience of AENEAS Collaborative Group. Clin Rev Allergy Immunol. 2017; 52(1): 71–80, doi: 10.1007/s12016-016-8528-9, indexed in Pubmed: 26782036.
23. Ide V, Bossuyt X, Blockmans D, et al. Prevalence and clinical correlates of rheumatoid factor and anticitrullinated protein antibodies in patients with idiopathic inflammatory myopathy. RMD Open. 2018; 4(2): e000661, doi: 10.1136/rmdopen-2018-000661, indexed in Pubmed: 30116555.
24. Meyer A, Lefevre G, Bierry G, et al. Club Rhumatismes et Inflammation. In antisynthetase syndrome, ACPA are associated with severe and erosive arthritis: an overlapping rheumatoid arthritis and antisynthetase syndrome. Medicine (Baltimore). 2015; 94(20): e523, doi: 10.1097/MD.0000000000000523, indexed in Pubmed: 25997035.
25. Fischer A, Antoniou KM, Brown KK, et al. "ERS/ATS Task Force on Undifferentiated Forms of CTD-ILD". An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. Eur Respir J. 2015; 46(4): 976–987, doi: 10.1183/13993003.00150-2015, indexed in Pubmed: 26160873.
26. Graney BA, Fischer A. Interstitial Pneumonia with Autoimmune Features. Ann Am Thorac Soc. 2019; 16(5): 525–533, doi: 10.1513/AnnalsATS.201808-565CME, indexed in Pubmed: 30695649.
27. Levi Y, Israeli-Shani L, Kuchuk M, et al. Rheumatological Assessment Is Important for Interstitial Lung Disease Diagnosis. J Rheumatol. 2018; 45(11): 1509–1514, doi: 10.3899/jrheum.171314, indexed in Pubmed: 30111640.