Peertechz

CLINICAL GROUP

OPEN JOURNAL OF
Orthopedics and Rheumatology

ISSN: 2641-3116 DOI: https://dx.doi.org/10.17352/ojor

Case Report

Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review

Jose Octavio Gonzalez Enriquez[1], Carlos Abud Mendoza[2]* and David Alejandro Herrera Van Oostdam[1]

[1]Faculty of Medicine of the Autonomous University of San Luis Potosí, Central Hospital "Dr. Ignatius Morones Prieto" SLP. Mexico

[2]Rheumatology Research Unit, Faculty of Medicine UASLP and Central Hospital, SLP, Mexico

Received: 25 January, 2023
Accepted: 23 February, 2023
Published: 24 February, 2023

***Corresponding author:** Carlos Abud Mendoza, MD, Rheumatology Research Unit, Faculty of Medicine UASLP and Central Hospital, SLP, Av. V. Carranza 2395, San Luis Potosi, S.L.P., 78240, Mexico, Email: c_abud@hotmail.com

ORCiD: https://orcid.org/0000-0002-3749-5831

Keywords: Anti-pl-12 antibody; Anti-synthetase syndrome; Interstitial lung disease; Autoimmune hepatitis

https://www.peertechzpublications.com

Check for updates

Abstract

Antisynthetase Syndrome (ASS) is a rare chronic autoimmune disorder, associated with interstitial lung diseases (the most important feature), such as Dermatomyositis (DM) and Polymyositis (PM). The cause of ASS is unknown. The hallmark of ASS is the presence of serum autoantibodies directed against aminoacyl-tRNA synthetases (anti-ARS involved in protein synthesis). Anti -Jo1 is the most common (20% - 30%); anti-PL12 is present in 2% - 5% of SAS, associated with Interstitial Lung Disease (ILD) in 90%, mainly as Non-Specific Interstitial Pneumonia (NSIP). Autoimmune hepatitis is related to rheumatological diseases (2.7% - 20% in systemic lupus erythematosus, 6% - 47% in primary Sjögren's syndrome), however, is rare in patients with inflammatory myopathies, and there is no previous reported association with SAS. A literature search was carried out using the PubMed and EMBASE databases in English and Spanish. Our case, a 62-year-old woman who developed polyarthritis, with progressive dyspnea, facial and lower limb edema, proximal muscle weakness, and Raynaud's phenomenon; high-resolution chest CT, showing pulmonary interstitial disease, consistent with Nonspecific Interstitial Pneumonia (NSIP). She had elevated transaminases and a prolonged prothrombin time, with positive anti-nuclear and anti-smooth muscle antibodies, and was made a diagnosis with autoimmune hepatitis type 1 (HAI). According to this presentation and reports of the literature review, anti-PL12 patients are characteristically associated with a severe phenotype of lung inflammation, that does not necessarily require myositis manifestation. To our knowledge, there is not any case of the antisynthetase syndrome and autoimmune hepatitis reported previously in the literature.

Introduction

Antisynthetase syndrome (ASS) is defined as a subtype of Idiopathic Inflammatory Myopathies (IIMs) and can be classified according to clinical and/or serologic association to Muscle-Specific Antibodies (SMA), the clinical presentation has a weakness, frequent involvement pulmonary, arthritis, an exceptional pattern in muscle biopsy, fever of unknown origin, typical cutaneous lesions and Raynaud's phenomenon cover the unique spectrum with aminoacyl-tRNA-synthetases being both the hallmark and the trigger, the most frequent IgG isotype, against the synthetase enzyme, which forms Transfer RNA (tRNA), more frequently affects females (female to male ratio is estimated to be approximately 7:3). Anti-synthetase syndrome (SAS) is uncommon, 8-9 / million, the main clinical manifestations include Polymyositis (PM)/Dermatomyositis (DM), diffuse pulmonary interstitial disease, polyarthritis, Raynaud's phenomenon and "mechanical hands". Aminoacyl tRNA synthetases are cytoplasmatic enzymes, during the translation phase of protein synthesis, they catalyze the binding of specific amino acids to the matching tRNA. In each cell, 20 different synthetases are present, corresponding to a single amino acid [1]. Antisynthetase antibodies can be found in 11.1% - 39.19% of patients with IIM, antibodies have been detected against nine of them, including anti-Jo-1 (histidyl-tRNA synthetase), anti-PL-7 (threonyl), anti- PL-12 (alanyl), anti-EJ (glycyl), anti-OJ (isoleucyl), anti-KS (asparaginyl), anti-Zo (phenylalanyl), anti-Ha (tyrosyl) and most recently anti-asparaginyl (YRS); anti -Jo1 the most common (20% - 30%); anti-PL12 are present in 2% - 5% of SAS, associated with

Citation: Enriquez JOG, Mendoza CA, Van Oostdam DAH (2023) Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review. Open J Orthop Rheumatol 8(1): 008-012. DOI: https://dx.doi.org/10.17352/ojor.000047

Interstitial Lung Disease (ILD) in 90%, mainly Non-Specific Interstitial Pneumonia (NSIP), identified from 1986 [2,3].

Autoimmune hepatitis is related to rheumatological diseases (2.7% - 20% systemic lupus erythematosus, 6% - 47% primary Sjögren's syndrome), is rare in patients with inflammatory myopathies, and there is no reported association with SAS.

Clinical case

The patient is a 62-year-old woman who developed polyarthritis, with progressive dyspnea, facial and lower limb edema, and proximal muscle weakness mainly in the lower limbs with an MMT-8 score of 110. She was referred for 2 years with Raynaud's phenomenon, and in the last month, skin sclerosis from the dorsal aspect of the feet thru the lower third of the legs and generalized hyperpigmentation, without skin sclerosis. Chest examination with decreased breath sounds and basal rales. Complementary laboratory tests included normal blood count, a high Erythrocyte Sedimentation Rate (ESR) of 49 mm, high C-Reactive Protein (CRP) 11 mg/dl, hypertransaminasemia (AST 272 U/L, ALT 326 U/L), alkaline phosphatase 442 U/L, gamma-glutamyltransferase 103 U/ml, total bilirubin 0.5 mg/dl, LDH 460 U/L, albumin 2.2 mg/dl, gamma globulins 4.3 g/dL, elevated creatine kinase (247 U/ml).

Her chest X-ray with a fine bilateral interstitial pattern, which was confirmed through high-resolution chest CT, showing pulmonary interstitial disease, with glass ground areas and grid shadows could be seen under the pleura of bilateral lungs and around the bronchial vascular bundles, abnormalities consistent with Nonspecific Interstitial Pneumonia (NSIP).

There wasn't any clinical mass or nodules in the breast examination, any pelvic abnormalities in the CT scan, nor serologic tumor markers detected.

In the further work-up of the dyspnea, we found Pulmonary Hypertension (PH) of 32 mmHg, dilatation of the right ventricular cavity, and paradoxical septal motion. Cardiologists suggested that, in absence of a classic pulmonary embolism image in the CT scan, echocardiographic changes were probably due to pulmonary hypertension.

Capillaroscopy with areas of avascularity, mega capillaries, and decreased density. A skin biopsy of the left forearm was done, showing the epidermis with network hyperkeratosis and atrophy, spongiosis, flattening of ridges and pigment loss, and papillary and reticular dermis with basophilic degeneration of the collagen, compatible with dermatomyositis.

Treatment was started with prednisone at a dose of 1 mg/kg, as well as mycophenolic acid, and tacrolimus, with significant improvement in functional and skin lesions, with a progressive reduction in the dose of glucocorticoids.

Simultaneously, she had elevated transaminases and a prolonged prothrombin time, with positive anti-nuclear and anti-smooth muscle antibodies, for which was made a diagnosis of autoimmune hepatitis type 1 (HAI), with negative hepatitis viral markers. The global score for the diagnosis of HAI is + 15 points (definitive HAI in a pre-treatment state).

The main suspicion was either pure dermatomyositis or an overlap syndrome (with autoimmune hepatitis). Positive anti-nuclear antibodies at a 1:1280 dilution with a filamentary fibrillar cytoplasmic pattern, with negative anti-dsDNA, but a positive Anti-Smooth Muscle Antibody (ASMA) 1:80 and negative Anti-Mitochondrial Antibody (AMA). According to the International Consensus on ANA Patterns (ICAP), this pattern of ANA is not typically associated with inflammatory myopathies. The only clinical manifestation we could associate with the former pattern was interstitial pneumonia, in which there is an association with the positivity of anti cytokeratine 19 antibodies [4].

Three weeks later we obtain the results from the SMA panel, with positive anti-PL-12 (+ + +) and anti-Ro 52 (+ + +) antibodies. Our diagnosis was an overlap syndrome, with the antisynthetase syndrome (anti-PL12 and Ro-52 antibodies) and autoimmune hepatitis; unfortunately, our patient died suddenly before the programmed liver biopsy.

Search strategy

We searched PubMed for original articles, reviews, letters, short communications, and notes in English and Spanish language sources using the following keywords: ("antisynthetase syndrome"[Supplementary Concept] OR "antisynthetase syndrome"[All Fields] OR "antisynthetase syndrome"[All Fields]) AND (("aminoacyl trna synthetases"[MeSH Terms], we reviewed 33 articles, omitted 5 articles because of the inadequate information, and summarized 28 relevant articles. We conducted these literature searches according to the recommended search strategy for narrative reviews.

Discussion

Our patient presented skin stigmata, generalized hyperpigmentation and heliotrope erythema, arthritis, and progressive dyspnea, besides bilateral radiological interstitial pattern, characteristic of dermatomyositis / antisynthetase syndrome.

Patients with anti-PL-12 antibodies share some clinical characteristics with positive anti-Jo-1 patients. The antibody reacts to the transfer RNA for the amino acid alanine and the alanyl tRNA enzyme, inhibiting aminoacylation with alanine, being this feature is distinctive compared to other types of antisynthetase antibodies. The first clinical description included six patients with a mean age of 52 years and the presence of Raynaud's phenomenon, myositis, lung fibrosis, and one patient with sclerodactyly [3,5]. Patients testing positive for anti-PL-12 and anti-PL-7 antibodies have a higher incidence of ILD and a lower incidence of inflammatory myositis when compared with patients testing positive for anti-Jo-1.

Anti-PL12 patients are associated with a severe phenotype of lung inflammation, that does not necessarily require myositis

Citation: Enriquez JOG, Mendoza CA, Van Oostdam DAH (2023) Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review. Open J Orthop Rheumatol 8(1): 008-012. DOI: https://dx.doi.org/10.17352/ojor.000047

associated; in a recent cohort the coexistence with muscle and lung involvement was present in 9% at the onset of the disease *vs.* 65% of exclusive lung involvement; the mean FVC at the onset of the disease is lower than compared to patients with anti-Jo1 and anti PL7 with lung involvement, similar results are reported in other studies. Our patient presented with NSIP, the most frequent tomographic pattern of lung interstitial disease (ILD), followed by an overlap with Organizing Pneumonia (OP), as reported by Debray, et al. [6].

The presence of anti-Ro-52 as our patient is a common element; anti-synthetase antibodies are generally considered to be mutually exclusive, yet cases of ARS co-occurrence have been described. Antibodies against Ro (including Ro52) are considered the most common type of associated antibodies in ARS-positive patients, occurring in 30% - 65% of cases. In the specific case of anti-PL12, the presence of anti-Ro52 antibody is present in > 25% of the patients. The main association in the presence of ILD, also, in some reports there is a higher activity score of myositis, higher relapses, and a higher proportion of overlap syndrome [7,8,17-28].

Liver dysfunction occurs in 43% of patients with connective tissue disorders. The elevation of CK, DHL and transaminases in patients with inflammatory myopathies is considered to be due to the activity of the disease and rarely to the coexistence of liver injury. There are few case reports of this association, one of primary biliary cholangitis with inflammatory myopathy, and the other with autoimmune hepatitis (Table 1) and nodular regenerative hyperplasia, it is important to mention the damage induced by drugs, however, the level of transaminases and the established therapy have low rates of liver damage, it is not the typical response to it, the titers for ASMA are more characteristic and significant, although it must be recognized that they are not completely specific, viral infections were ruled out.

To our knowledge, there is not any case of the antisynthetase syndrome and autoimmune hepatitis reported previously in the literature.

Similar to anti-Jo1, the prognosis of anti-PL12 ASS seems to be determined by pulmonary involvement, especially in the case of disproportionate pulmonary hypertension, a particularly rare complication of anti-PL12 syndrome. The potential explanation of pulmonary hypertension in our patient may be due to undiagnosed interstitial lung disease and rarely explained with exceptional association with portal hypertension related to liver nodular regenerative hyperplasia. The patient was not submitted to Right Heart Catheterization (RHC).

The prevalence of PH evaluated by RHC in anti-synthetase patients is 8%, 30% (5/16) of the patients had anti-PL12 and only 2 had a positive anti-Ro52 antibody; an interesting fact was that there was an absence of association between the presence of ILD and the development of PH, nor was related with the severity of ILD; the number of patients included was low and only 45% of the patients with a possible diagnosis of PH determined by echocardiogram were submitted to RHC. But this rises the hypothesis that PH could indicate a different mechanism not related to ILD, such as nodular regenerative hyperplasia.

Informed consent: Patient signed informed consent regarding publishing their data and photographs.

Table 1: Clinical characteristics of patients with anti-PL-12 autoantibodies.

Ref.	[2]	[9]	[3]	[11]	[15]	[27]	[13]	[15]	[1]	[16]	Present case
N =	1	1	5	31	12	1	17	84	9	1	1
Age	63	80	52 (35-60)	52 (22-73)	48 (17-64)	33	60 (42-85)	50.5(42-61)	-	64	62
Sex	F	M	5F, 1M	25F,6 M	9F, 3M	F	-	F (73.8%)	-	F	M
Myositis	-	Subclinical. (biopsy: perimysial inflammatory infiltrate)	+ (66%)	+ (32%)	+ (33%)	-	+ (41%)	+ (35.7%)	+ (77.8%)	-	+
Skin	+	-	+ (33%)	-	+ (41%)	-	-	-	+ (44.4%)	-	+
Raynaud		+	+ (66%)	+ (64%)	+ (58%)	-	+ (47%)	+ (56%)	+ (11.1%)	-	+
Arthritis	+	-	+ (33%)	+ (58%)	+ (33%)	+	+ (11.6%)	+ (35.7%)	+ (66.7)	-	+
Mechanic hands	-	-	-	+ (16%)	+ (16%)	-	+ (5.8%)	+ (45%)	+ (11.1%)	-	+
Dysphagia	-	+	-	-	+ (16%)	-	+ (23.5%)	-	-	-	-
PH	-	-	-	-	-	-	+ (11.7%)	-	-	-	+
ILD	+ NSIP	+ UIP	+ (66%)	+ (70%,13 UIP, 9 NSPI)	+ (100%, 11UIP,1 PF)	+ NSIP	+ (100%, 15 NISP, 2 OP)	+ (69%)	+ (33.3 %)	+ NSIP	+ NSIP
Overlap disease	RA	-	-	5 SSc 5 UCTD 1 SLE	1 SS 5 UCTD 2 SSc	-	-	No	No	No	Yes
Autoimmune hepatitis	No	No	No	No	No	No	No	No	No	No	Yes
ANA	+ 1:320	+ 1:640	NA	+ (48%)	NA	+ 1:1280	+ 1: 80 (35%)	+ (59.4%)	-	+ 1 :160	+ 1:1280
Anti-Ro-52	+	+	-	+ (35%)	-	-	+ (29%)	+ (59.2)	-	-	+

NA: Not Applicable; ILD: Interstitial Lung Disease; PF: Pulmonary Fibrosis; UIP: Usual Interstitial Pneumonia; NSIP: Nonspecific Interstitial Pneumonia; ANA: Anti-Nuclear Antibodies; SS: Sjögren's Syndrome; UCTD: Undifferentiated Connective Tissue Disease; SSc: Systemic Sclerosis; SLE: Systemic Lupus Erythematosus; RA: Rheumatoid Arthritis; HP: Pulmonary Hypertension.

Citation: Enriquez JOG, Mendoza CA, Van Oostdam DAH (2023) Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review. Open J Orthop Rheumatol 8(1): 008-012. DOI: https://dx.doi.org/10.17352/ojor.000047

References

1. Marco JL, Collins BF. Clinical manifestations and treatment of antisynthetase syndrome. Best Pract Res Clin Rheumatol. 2020 Aug;34(4):101503. doi: 10.1016/j.berh.2020.101503. Epub 2020 Apr 11. PMID: 32284267.
2. Ishikawa Y, Yukawa N, Kawabata D, Ohmura K, Fujii T, Usui T, Mimori T. A case of antisynthetase syndrome in a rheumatoid arthritis patient with anti-PL-12 antibody following treatment with etanercept. Clin Rheumatol. 2011 Mar;30(3):429-32. doi: 10.1007/s10067-010-1666-1. Epub 2011 Jan 11. PMID: 21221686.
3. Bunn CC, Bernstein RM, Mathews MB. Autoantibodies against alanyl-tRNA synthetase and tRNAAla coexist and are associated with myositis. J Exp Med. 1986 May 1;163(5):1281-91. doi: 10.1084/jem.163.5.1281. PMID: 3701255; PMCID: PMC2188100.
4. Fujita J, Dobashi N, Ohtsuki Y, Yamadori I, Yoshinouchi T, Kamei T, Tokuda M, Hojo S, Okada H, Takahara J. Elevation of anti-cytokeratin 19 antibody in sera of the patients with idiopathic pulmonary fibrosis and pulmonary fibrosis associated with collagen vascular disorders. Lung. 1999;177(5):311-9. doi: 10.1007/pl00007649. PMID: 10467022.
5. Targoff IN, Arnett FC. Clinical manifestations in patients with antibody to PL-12 antigen (alanyl-tRNA synthetase). Am J Med. 1990 Mar;88(3):241-51. doi: 10.1016/0002-9343(90)90149-8. PMID: 2178410.
6. Debray MP, Borie R, Revel MP, Naccache JM, Khalil A, Toper C, Israel-Biet D, Estellat C, Brillet PY. Interstitial lung disease in anti-synthetase syndrome: initial and follow-up CT findings. Eur J Radiol. 2015 Mar;84(3):516-523. doi: 10.1016/j.ejrad.2014.11.026. Epub 2014 Dec 3. PMID: 25541020.
7. Yamasaki Y, Satoh M, Mizushima M, Okazaki T, Nagafuchi H, Ooka S, Shibata T, Nakano H, Ogawa H, Azuma K, Maeda A, Tonooka K, Ito H, Takakuwa Y, Inoue M, Mitomi H, Kiyokawa T, Tsuchida K, Matsushita H, Mikage H, Murakami Y, Chan JY, Ozaki S, Yamada H. Clinical subsets associated with different anti-aminoacyl transfer RNA synthetase antibodies and their association with coexisting anti-Ro52. Mod Rheumatol. 2016;26(3):403-9. doi: 10.3109/14397595.2015.1091155. Epub 2015 Oct 19. PMID: 26344678.
8. Sabbagh S, Pinal-Fernandez I, Kishi T, Targoff IN, Miller FW, Rider LG, Mammen AL; Childhood Myositis Heterogeneity Collaborative Study Group. Anti-Ro52 autoantibodies are associated with interstitial lung disease and more severe disease in patients with juvenile myositis. Ann Rheum Dis. 2019 Jul;78(7):988-995. doi: 10.1136/annrheumdis-2018-215004. Epub 2019 Apr 24. PMID: 31018961; PMCID: PMC7570952.
9. Jubber A, Tripathi M, Taylor J. Interstitial lung disease and inflammatory myopathy in antisynthetase syndrome with PL-12 antibody. BMJ Case Rep. 2018 Oct 14;2018:bcr2018226119. doi: 10.1136/bcr-2018-226119. PMID: 30323103; PMCID: PMC6194426.
10. Kalluri M, Sahn SA, Oddis CV, Gharib SL, Christopher-Stine L, Danoff SK, Casciola-Rosen L, Hong G, Dellaripa PF, Highland KB. Clinical profile of anti-PL-12 autoantibody. Cohort study and review of the literature. Chest. 2009 Jun;135(6):1550-1556. doi: 10.1378/chest.08-2233. Epub 2009 Feb 18. PMID: 19225060.
11. Schneider F, Yousem SA, Oddis CV, Aggarwal R. Pulmonary Pathologic Manifestations of Anti-Alanyl-tRNA Synthetase (Anti-PL-12)-Related Inflammatory Myopathy. Arch Pathol Lab Med. 2018 Feb;142(2):191-197. doi: 10.5858/arpa.2017-0010-OA. Epub 2017 Oct 2. PMID: 28967806.
12. Elferjani B, Liaqat A, Zaman M, Sexton M. Anti-Synthetase Syndrome-Related Interstitial Lung Disease With Anti-PL-12 Antibodies. Cureus. 2021 Jan 27;13(1):e12936. doi: 10.7759/cureus.12936. PMID: 33654616; PMCID: PMC7916638.
13. Hervier B, Wallaert B, Hachulla E, Adoue D, Lauque D, Audrain M, Camara B, Fournie B, Couret B, Hatron PY, Dubucquoi S, Hamidou M. Clinical manifestations of anti-synthetase syndrome positive for anti-alanyl-tRNA synthetase (anti-PL12) antibodies: a retrospective study of 17 cases. Rheumatology (Oxford). 2010 May;49(5):972-6. doi: 10.1093/rheumatology/kep455. Epub 2010 Feb 15. PMID: 20156976.
14. Cavagna L, Trallero-Araguás E, Meloni F, Cavazzana I, Rojas-Serrano J, Feist E, Zanframundo G, Morandi V, Meyer A, Pereira da Silva JA, Matos Costa CJ, Molberg O, Andersson H, Codullo V, Mosca M, Barsotti S, Neri R, Scirè C, Govoni M, Furini F, Lopez-Longo FJ, Martinez-Barrio J, Schneider U, Lorenz HM, Doria A, Ghirardello A, Ortego-Centeno N, Confalonieri M, Tomietto P, Pipitone N, Rodriguez Cambron AB, Blázquez Cañamero MÁ, Voll RE, Wendel S, Scarpato S, Maurier F, Limonta M, Colombelli P, Giannini M, Geny B, Arrigoni E, Bravi E, Migliorini P, Mathieu A, Piga M, Drott U, Delbrueck C, Bauhammer J, Cagnotto G, Vancheri C, Sambataro G, De Langhe E, Sainaghi PP, Monti C, Gigli Berzolari F, Romano M, Bonella F, Specker C, Schwarting A, Villa Blanco I, Selmi C, Ceribelli A, Nuno L, Mera-Varela A, Perez Gomez N, Fusaro E, Parisi S, Sinigaglia L, Del Papa N, Benucci M, Cimmino MA, Riccieri V, Conti F, Sebastiani GD, Iuliano A, Emmi G, Cammelli D, Sebastiani M, Manfredi A, Bachiller-Corral J, Sifuentes Giraldo WA, Paolazzi G, Saketkoo LA, Giorgi R, Salaffi F, Cifrian J, Caporali R, Locatelli F, Marchioni E, Pesci A, Dei G, Pozzi MR, Claudia L, Distler J, Knitza J, Schett G, Iannone F, Fornaro M, Franceschini F, Quartuccio L, Gerli R, Bartoloni E, Bellando Randone S, Zampogna G, Gonzalez Perez MI, Mejia M, Vicente E, Triantafyllias K, Lopez-Mejias R, Matucci-Cerinic M, Selva-O'Callaghan A, Castañeda S, Montecucco C, Gonzalez-Gay MA. Influence of Antisynthetase Antibodies Specificities on Antisynthetase Syndrome Clinical Spectrum Time Course. J Clin Med. 2019 Nov 18;8(11):2013. doi: 10.3390/jcm8112013. PMID: 31752231; PMCID: PMC6912490.
15. Ghysen K, Leys M. A 64-year-old woman with interstitial lung disease and positive antibodies against aminoacyl-transfer RNA synthetases in the absence of myositis: presentation of an anti-PL-12 positive antisynthetase syndrome. Acta Clin Belg. 2018 Oct;73(5):389-392. doi: 10.1080/17843286.2017.1403133. Epub 2017 Nov 27. PMID: 29173135.
16. McHugh NJ, Tansley SL. Autoantibodies in myositis. Nat Rev Rheumatol. 2018 Apr 20;14(5):290-302. doi: 10.1038/nrrheum.2018.56. PMID: 29674612.
17. Opinc AH, Makowska JS. Antisynthetase syndrome - much more than just a myopathy. Semin Arthritis Rheum. 2021 Feb;51(1):72-83. doi: 10.1016/j.semarthrit.2020.09.020. Epub 2020 Dec 22. PMID: 33360231.
18. Cojocaru M, Cojocaru IM, Chicos B. New Insights into Antisynthetase Syndrome. Maedica (Bucur). 2016 Jun;11(2):130-135. PMID: 28461832; PMCID: PMC5394574.
19. Jariwala S, Tomann T, Burger A. Sa.89. Primary Biliary Cirrhosis Associated with Inflammatory Myopathy in a 57 Year Old Male. Clin Immunol - CLIN IMMUNOL. 31 de diciembre de 2008; 127.
20. de Souza FH, Barros TB, de Moraes MT, Missumi LS, Lima FR, Levy-Neto M, Shinjo SK. Hepatite autoimune e dermatomiosite: uma rara associação [Autoimmune hepatitis and dermatomyositis: a rare association]. Acta Reumatol Port. 2012 Jul-Sep;37(3):264-7. Portuguese. PMID: 23348116.
21. Solomon J, Swigris JJ, Brown KK. Myositis-related interstitial lung disease and antisynthetase syndrome. J Bras Pneumol. 2011 Jan-Feb;37(1):100-9. doi: 10.1590/s1806-37132011000100015. PMID: 21390438; PMCID: PMC3676869.
22. Pinal-Fernandez I, Casal-Dominguez M, Huapaya JA, Albayda J, Paik JJ, Johnson C, Silhan L, Christopher-Stine L, Mammen AL, Danoff SK. A longitudinal cohort study of the anti-synthetase syndrome: increased severity of interstitial lung disease in black patients and patients with anti-PL7 and anti-PL12 autoantibodies. Rheumatology (Oxford). 2017 Jun 1;56(6):999-1007. doi: 10.1093/rheumatology/kex021. PMID: 28339994; PMCID: PMC5850781.
23. Zhan X, Yan W, Wang Y, Li Q, Shi X, Gao Y, Ye Q. Clinical features of anti-synthetase syndrome associated interstitial lung disease: a retrospective cohort in China. BMC Pulm Med. 2021 Feb 12;21(1):57. doi: 10.1186/s12890-021-01399-5. PMID: 33579248; PMCID: PMC7881640.
24. Podgórska J, Werel P, Klapaczyński J, Orzechowska D, Wudarski M, Gietka A. Liver involvement in rheumatic diseases. Reumatologia.

Citation: Enriquez JOG, Mendoza CA, Van Oostdam DAH (2023) Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review. Open J Orthop Rheumatol 8(1): 008-012. DOI: https://dx.doi.org/10.17352/ojor.000047

2020;58(5):289-296. doi: 10.5114/reum.2020.99782. Epub 2020 Oct 13. PMID: 33227094; PMCID: PMC7667950.

25. Jain P, Patel S, Simpson HN, Silver RM, Lewin DN, Campbell RC, Guimaraes M, Silver KC. Nodular Regenerative Hyperplasia of the Liver in Rheumatic Disease: Cases and Review of the Literature. J Investig Med High Impact Case Rep. 2021 Jan-Dec;9:23247096211044617. doi: 10.1177/23247096211044617. PMID: 34514900; PMCID: PMC8436301.

26. Perez Ruiz F, Orte Martinez FJ, Zea Mendoza AC, Ruiz del Arbol L, Moreno Caparros A. Nodular regenerative hyperplasia of the liver in rheumatic diseases: report of seven cases and review of the literature. Semin Arthritis Rheum. 1991 Aug;21(1):47-54. doi: 10.1016/0049-0172(91)90056-6. PMID: 1948101.

27. Hervier B, Meyer A, Dieval C, Uzunhan Y, Devilliers H, Launay D, Canuet M, Têtu L, Agard C, Sibilia J, Hamidou M, Amoura Z, Nunes H, Benveniste O, Grenier P, Montani D, Hachulla E. Pulmonary hypertension in antisynthetase syndrome: prevalence, aetiology and survival. Eur Respir J. 2013 Nov;42(5):1271-82. doi: 10.1183/09031936.00156312. Epub 2013 Feb 8. PMID: 23397301.

28. Handa T, Nagai S, Kawabata D, Nagao T, Takemura M, Kitaichi M, Izumi T, Mimori T, Mishima M. Long-term clinical course of a patient with anti PL-12 antibody accompanied by interstitial pneumonia and severe pulmonary hypertension. Intern Med. 2005 Apr;44(4):319-25. doi: 10.2169/internalmedicine.44.319. PMID: 15897644.

Citation: Enriquez JOG, Mendoza CA, Van Oostdam DAH (2023) Anti-synthetase syndrome with positive anti-PL-12 antibodies associated with autoimmune hepatitis: case report and literature review. Open J Orthop Rheumatol 8(1): 008-012. DOI: https://dx.doi.org/10.17352/ojor.000047