EDITORIAL

Polyautoimmunity: a significant issue in connective tissue diseases

Marzena Olesińska, Katarzyna Romanowska-Próchnicka

Department of Connective Tissue Diseases, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

A recent publication by Wielosz et al[1] has brought attention to a common and significant issue related to connective tissue diseases, namely, polyautoimmunity. The term describes the presence of more than one autoimmune diseases in a single patient.[2] The objective of the study was to explore the prevalence and clinical correlations of organ-specific antibodies in 86 patients with systemic sclerosis (SSc). The results showed coexistence of autoimmune thyroid disease (ATD) in 30% and primary biliary cirrhosis (PBC) in 12% of SSc patients and higher frequency of antimitochondrial antibodies (AMAs) in limited cutaneous SSc (lcSSc) than in diffuse cutaneous SSc (dcSSc). A tendency to coexistence of AMAs and anticentromere antibodies (ACAs) was also noticed.[1]

SSc is a chronic autoimmune rheumatic disease of unknown etiology. It is characterized by microvascular abnormalities as well as cutaneous and visceral fibrosis, all accompanied by signature immune abnormalities. Patients with dcSSc show widespread and rapidly progressive skin thickening, and earlier and more severe internal organ involvement. In the lcSSc subtype, skin thickening is restricted to the distal extremities and face, and accompanied by less severe and later-onset internal organ involvement.[3] It is suggested that SSc shares the same genetic background with other autoimmune diseases. Patients with this predisposition may develop one specific disease or another, depending on the presence of either genetic factors or specific environmental triggers.[4-6]

A meta-analysis by Elhai et al[7] identified polyautoimmunity in 25.7% of 6102 patients with SSc.The most prevalent SSc-associated autoimmune diseases were autoimmune thyroid disease (AITD) (10.4%), followed by Sjögren syndrome (7.7%), dermatomyositis/polymyositis (5.6%), and PBC (3%). The authors suggested that polyautoimmunity in SSc could influence both the disease phenotype and severity. Patients with polyautoimmunity seem to have a milder disease (higher frequencies of women, of limited cutaneous subtype and of ACA positivity). Similarly in PBC, patients with SSc-PBC overlap seem to have a milder disease.[8] The authors hypothesized that some immunological interactions in the presence of an additional autoimmune disease (AID) may favor a better outcome of the disease. Therefore, further studies are needed to better determine the effect of an additional AID on the SSc phenotype.[7]

AITD, the most common SSc-associated AID, is an organ-specific disease characterized by the presence of antibodies against thyroid-specific components such as thyrotropin receptor antigen, thyroglobulin, or thyroid peroxidase. The prevalence of AITD in the general population of countries without iodine deficiency is 3% to 4%. The prevalence of antithyroid antibodies is much higher than that of AITD and increases with age.[9]

In the study by Wielosz et al,[1] 31% of SSc patients had positive antithyroid antibody titers (antithyroid peroxidase antibodies [anti-TPO] and/or antithyroglobulin antibodies [aTG]) and 30% of SSc patients were diagnosed with AITD.[5] In other studies, the coexistence of AITD and SSc varied from 1.4% to 23.1%.[7] The authors reported that patients with positive aTPO titers had significantly higher frequency of the HLA DR15 haplotype than those who are aTPO-negative. Therefore, HLA DR15 may represent the immunogenic marker of aTPO production in patients with scleroderma.[1] Furthermore, the authors emphasized that the incidence of ACAs was higher in SSc-PBC overlap than in lcSSc alone. Positive ACAs in patients with PBC indicated the risk of future lcSSc.[1]

PBC is a chronic cholestatic liver condition with autoimmune etiology frequently associated with other AIDs, especially SSc. AMAs are serological markers of PBC and occur in up to 90% to 95% of patients.[10] In the meta-analysis by Elhai et al,[7] patients with SSc/PBC were more frequently women with lcSSc and ACA positivity.[7]

Correspondence to:
Marzena Olesińska, MD, PhD, Klinika i Poliklinika Układowych Chorób Tkanki Łącznej, Narodowy Instytut Geriatrii, Reumatologii i Rehabilitacji, ul. Spartańska 1, 02-637 Warszawa, Poland, phone: +48 22 844 57 26, e-mail: marzena.olesinska@vp.pl
Received: November 15, 2016.
Accepted: November 15, 2016.
Published online: November 28, 2016.
Conflict of interest: none declared.
Pol Arch Med Wewn. 2016; 126 (11): 837-838
doi:10.20452/pamw.3660

The presence of PBC/SSc overlap potentially implies routine testing for ACAs in patients with PBC and AMAs in patients with SSc. Such testing should be also routinely done in the long-term monitoring of signs and symptoms of chronic cholestatic liver disease in these cohorts. Moreover, some studies have linked genetic associations between PBS and SSc in genes *HLADRB1*, *DQB1*, *IRF5*, and *STAT-4*.[10,11] Finally, Sakkas et al[12] have shown that the diseases are associated with the same infectious agents, such as *Helicobacter pylori* or *Chlamydia pneumoniae*.

In conclusion, polyautoimmunity is a common feature in patients with SSc. Therefore, physicians should be aware of this phenomenon when establishing a diagnosis and developing a plan to monitor and treat these patients.

REFERENCES

1 Wielosz E, Majdan M, Koszarny A, et al. Presence of organ-specific antibodies in patients with systemic sclerosis. Pol Arch Med Wewn. 2016; 126: 862-869.

2 Rojas-Villarraga A, Amaya-Amaya J, Rodriguez-Rodriguez A, et al. Introducing polyautoimmunity. Secondary autoimmune diseases no longer exist. Autoimmun Dis. 2012; 2012: 254319.

3 LeRoy EC, Black C, Fleischmajer R, et al. Scleroderma (systemicsclerosis): classification,subsetsandpathogenesis. J Rheumatol.1988; 15: 202-205.

4 Allanore Y, Avouac J, Kahan A. Systemic sclerosis: an update in 2008. Joint Bone Spine. 2008; 75: 650-655.

5 Villalta D, Imbastaro T, Di Giovanni S, et al. Diagnostic accuracy and predictive value of extended autoantibody profile in systemic sclerosis. Autoimmun Rev. 2012; 12: 114-120.

6 Mehra S, Walker J, Patterson K, Fritzler MJ. Autoantibodies in systemic sclerosis. Autoimmun Rev. 2013; 12: 340-354.

7 Elhai M1, Avouac J, Kahan A, Allanore Y. Systemic sclerosis at the crossroad of polyautoimmunity. Autoimmun Rev. 2013; 12: 1052-1057.

8 Rigamonti C, Shand LM, Feudjo M, et al. Clinical features and prognosis of primary biliary cirrhosis associated with systemic sclerosis. Gut. 2006; 55: 388-394.

9 Lazúrová I, Benhatchi K. Autoimmune thyroid diseases and nonorgan--specific autoimmunity. Pol Arch Med Wewn. 2012; 122 (Suppl 1): 55-59.

10 Rothfield N, Whitaker D, Bordwell B, et al. Detection of anticentromere antibodies using cloned autoantigen CENP-B. Arthritis Rheum. 1987; 30: 1416-1419.

11 Tan EM, Smolen JS, McDougal JS, et al. A critical evaluation of enzyme immunoassays fordetection of antinuclear autoantibodies of defined specificities. I. Precision, sensitivity, and specificity. Arthritis Rheum. 1999; 42: 455-464.

12 Sakkas LI, Chikanza IC, Platsoucas CD. Mechanisms of disease: the role of immune cells in the pathogenesis of systemic sclerosis. Nat Clin Pract Rheumatol. 2006; 2: 679-685.