Pulmonary Artery Hypertension in SLE

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Pulmonary hypertension (PH) is characterized by pulmonary artery mean pressure more than 20 mm Hg. It is caused by diverse diseases. It is classified into five categories, based on etiology, pathophysiology, natural history, and response to treatment. Group 1 PH, also called pulmonary artery hypertension (PAH), includes many different diseases including PH due to connective tissue disease (CTD). The most common CTD to cause PAH is systemic sclerosis. PAH is also commonly seen in mixed connective tissue disease (MCTD), systemic lupus erythematosus (SLE), and rheumatoid arthritis. There is no uniform pathophysiologic mechanism for PH. Molecular pathogenesis of PAH is not completely known, and thus the therapeutic targets in the management of PAH are limited. This makes the prognosis and treatment of PAH due to CTD more difficult.

In this context, the paper published by Baisya et al, which provides insights into the molecular mechanism of PAH in SLE, is a step in the right direction, and I congratulate them for that. Baisya et al conducted a cluster analysis of auto antibodies in 71 patients with SLE-associated PAH. They concluded that the cluster with no definite antibody association had the highest mean right ventricular systolic pressure (RVSP) or severe PAH.[1]

One of the limitations of their study, as rightly acknowledged by the authors, is that the diagnosis of PAH is based on echocardiography alone while the gold standard is right heart catheterization. It is quite understandable that patients' acceptance of cardiac catheterization would be quite low in the Indian context. Instead of diagnosing PH solely on the basis of tricuspid regurgitation (TR) jet velocity, they could have made the diagnosis of PH, based on the guidelines provided by the American Society of Echocardiography.[2] However, it is likely that the diagnosis of PAH is valid in this cohort of patients, considering the criteria they used.

Cluster analysis is useful in identifying the risk factors and mechanisms of the disease and developing therapeutic targets. Reported incidence of PAH in SLE and autoantibody associations with SLE PAH are somewhat divergent and appear to be based on geographic location and ethnicity.[3,4] Incidence of PAH in SLE is relatively less in Taiwanese and Caucasians, while it is more in Pakistanis and African Americans.[5-7] There are significant interethnic differences observed in the REVEAL registry done in the US.[8] Similarly, different antibodies are associated with SLE PAH, as reported in different studies. In a UK study, association with lupus anticoagulant was reported, while the French reported association with anti-Ro and anti-La antibodies and the Chinese reported association with anti-RNP and anticardiolipin antibodies.[9-12] This kind of data strongly suggests the possible role played by the underlying genetic factors, and this study has to be seen as part of a bigger picture. Often there is overlap between different autoimmune rheumatological diseases, their phenotypes and prevalent antibodies.[13] Keeping in mind wide variations and smaller size of each cohort, one may consider a pooled analysis of PAH associated with different autoimmune diseases.

Antibodies interact closely with cytokines in pathogenesis of diseases. In an interesting study, researchers from the Stanford University and University of Sheffield carried out cluster analysis of circulating cytokines and chemokines in patients with PAH.[14] They identified four clusters and established an association with prognosis, although there were no difference in phenotypes. Larger studies that include patients with PAH associated with different CTD, and analyze antibody clusters as well as cytokine profiles, may throw more light on pathogenesis and prognosis and help identify therapeutic targets. A truly personalized precision medicine may not be far off.

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