Management of Sarcoidosis-associated Pulmonary Hypertension

Editor – We read with interest Patel and Ladak's report¹ of a patient presenting with tattoo koebnerization and severe pulmonary hypertension (PH) in the setting of a new diagnosis of sarcoidosis. As the authors note, sarcoidosis-associated pulmonary hypertension (SAPH) is classified as World Health Organization group 5 PH, a "miscellaneous" form of PH that develops through various mechanistic pathways.² The case patient was treated with vasodilators as an inpatient, improved, and then was discharged on a regimen that included ambrisentan and tadalafil for the treatment of SAPH.

Ambrisentan and tadalafil are not indicated for the treatment of SAPH. Endothelin receptor antagonists and phosphodiesterase-5 inhibitors are approved by the U.S. Food and Drug Administration (FDA) for the treatment of group 1 PH only. No therapeutics have been approved by the FDA for the treatment of SAPH. The use of ambrisentan and tadalafil to treat SAPH represents off-label use of these drugs, which may be appropriate for selected patients, as it apparently was for the case patient.

PH attributable to sarcoidosis appears to occur in a heterogeneous group of patients and is caused by a diversity of mechanisms.³ Both pre-capillary and post-capillary vascular pathology may result in the development of PH in patients with sarcoidosis. Both benefits and harms have been reported in patients with SAPH after initiation of pulmonary vasodilators.⁴ Among sarcoidosis patients with advanced fibrocavitary disease, PH-directed therapies may worsen oxygenation by inhibiting hypoxic pulmonary vasoconstriction, leading to increased shunting.⁵ Among SAPH patients with pulmonary venous disease, PH-directed treatment may result in pulmonary edema.⁶ Some studies have shown benefit from PH-directed therapy for SAPH, supporting its use in well-selected patients.⁷

Management of SAPH in the outpatient setting with PH-directed medication requires close follow-up to assess for possible harms resulting from the drugs. Under most circumstances, it is advisable to treat SAPH by treating the underlying sarcoidosis that resulted in PH, in addition to considering PH-directed treatment. The cornerstone treatment for sarcoidosis is corticosteroids, but other anti-inflammatory and immunomodulatory therapies may be included. If PH-directed therapy is being considered for a patient with SAPH, the patient should be informed that there are no FDA-approved medications for SAPH and counseled about the potential harms that might result from PH-directed treatment. Additional research is needed to define the precise role of anti-inflammatory and immunomodulatory therapeutics in the treatment of SAPH.

Keywords: Pulmonary hypertension; Sarcoidosis; Treatment; Management

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Author Response: Pulmonary Vasodilators in Sarcoidosis-associated Pulmonary Hypertension

Editor – We thank Ho and Kuschner¹ for their knowledgeable comments on our case, specifically around the need to individualize therapy for each patient, multimodal therapeutic interventions including immunosuppression, and close follow-up.

Sarcoidosis-associated pulmonary hypertension (SAPH) is often classified as WHO group 5.^{2,3} However, the pathophysiology of pulmonary hypertension in sarcoidosis is multifactorial and it can also be classified as WHO group 1 (pulmonary arterial hypertension), group 2 (pulmonary hypertension from left heart disease), group 3 (pulmonary