CM&R *Rapid Release*. Published online ahead of print August 28, 2019 as doi:10.3121/cmr.2019.1469

Tattoo Koebnerization and Severe Pulmonary Hypertension

Matthew Patel and Karim Ladak, MD

Running footer: Tattoo Koebnerization and Pulmonary Hypertension

Total Number of Tables: 1.
Total Number of Figures: 2.

Word Count of the Text: 541.

Corresponding Author:
Matthew Patel
34 Southlea Avenue
Toronto, Ontario M4G 3L9 Canada
Email: matthewpatel@rcsi.com

Received: October 22, 2018
Revised: May 25, 2019
Accepted: June 24, 2019

doi:10.3121/cmr.2019.1469

Keywords: sarcoidosis, pulmonary hypertension, Koebnerization, tattoo reaction.

Case:

A 35-year-old African-American male was admitted to hospital with progressively worsening dyspnea of 1.5 years duration. Pre-morbid function was excellent. History and examination were unremarkable for other features of respiratory, cardiac and connective tissue disease. He had 10-year-old tattoos, but denied travel, substance use, exposures and sick contacts. Family history was non-contributory. Past medical history included hypertension, idiopathic uveitis, and a recent JAK2-negative polycythemia. His only medications were steroid eye-drops.

Admission pulse oximetry was 87%. He was afebrile and normotensive. Chest X-ray revealed enlarged pulmonary arteries but otherwise normal lung fields. An outpatient chest CT done four months prior showed similar findings. Echo demonstrated right heart enlargement, but normal left heart (figure 1). Right heart catheterization showed severe pulmonary arterial hypertension with pressures of 108/55mmHg, yet normal wedge pressures. Workup for secondary causes of pulmonary hypertension yielded a positive ANA (1:640) without other features of autoimmune disease (Table 1).

During hospitalization, a sliver of one of his tattoos became raised and urticarial. Skin biopsy was performed, demonstrating an extensive epithelioid, non-caseating granulomatous infiltrate associated with exogenous black carbon pigment, surrounded by small lymphocytes (figure 2). Special stains were negative. This tattoo Koebnerization was consistent with sarcoidosis. Repeat CT chest was performed and displayed new findings of subtle, central right upper lobe fibrosis with peribronchiolar honeycombing and tiny scattered perivascular lymphadenopathy, without hilar lymphadenopathy.

The patient started vasodilators and glucocorticoids with rapid improvement, and was discharged on ambrisentan, tadalafil, and methylprednisolone. Adalimumab was started as a steroid-sparing agent.

Discussion:

Sarcoidosis is a multisystem disease of unknown etiology, characterized by epithelioid non-caseating granulomas with usual onset between 20 – 40 years of age, and more commonly seen in African Americans (as in this patient) relative to Caucasians.[1] Antigenic triggers are unknown, but tattoos have been proposed as potential antigenic stimuli for granuloma formation.[2,3] Sarcoidal skin reactions in tattoos are rare but reports date back to 1952.[4] These Koebnerization responses primarily affect red (cinnabar), black (ferric oxide), and blue-black tattoos, and often precede other systemic disease manifestations.[5] In the diagnosis of sarcoidosis, tattoos serve as a safe and convenient site for biopsy.

Sarcoidosis-associated pulmonary hypertension (SAPH) is an increasingly recognized cause of morbidity and mortality whose prevalence ranges from 5-20%.[6] It is categorized as WHO class 5, pulmonary hypertension, occurring through various mechanisms including intrinsic vasculopathy, mechanical obstruction of vasculature by lymphadenopathy, fibrotic destruction of vascular beds and hypoxic vasoconstriction.[7] SAPH usually occurs in radiographically advanced cases, but vasculopathic SAPH does rarely present in radiologic stage 0, as in our patients.[6] SAPH should be suspected when dyspnea exceeds the degree of radiographic abnormalities, and if respiratory symptoms are resistant to anti-inflammatory therapy. Echocardiography and 6-

minute walk test are reasonable screening tools, however RHC is the gold standard for diagnosis.[6] Unfortunately, the prognosis is grave with a 5-year mortality of 45%.[8]

While the patient's ethnicity, uveitis, interstitial lung disease, and skin biopsy findings support the diagnosis of SAPH, the degree of CT chest findings are not as extensive as one may expect, and the positive ANA is unusual. While a firm diagnosis of pulmonary sarcoidosis cannot be made without a lung/lymph node biopsy, extensive clinical and serologic evaluation for connective tissue disease was negative, and a lack of pulmonary interstitial findings does not exclude the exclude SAPH.[5]

References:

1. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med. 1997;336(17):1224-1234. doi:10.1056/NEJM199704243361706. Medline

2. Agostini C, Adami F, Semenzato G. New pathogenetic insights into the sarcoid granuloma. Curr Opin Rheumatol. 2000;12(1):71-76. doi:10.1097/00002281-200001000-00012. Medline

3. Papageorgiou PP, Hongcharu W, Chu AC. Systemic sarcoidosis presenting with multiple tattoo granulomas and an extra-tattoo cutaneous granuloma. J Eur Acad Dermatol Venereol. 1999;12(1):51-53. doi:10.1111/j.1468-3083.1999.tb00809.x. Medline

4. Lubeck G, Epstein E. Complications of tattooing. Calif Med. 1952;76(2):83-85 Medline.

5. O'Beirne SL, O'Dwyer DN, Walsh SM, Dodd JD, Crotty TB, Donnelly SC. The lady with the dragon tattoo. Irish Journal of Medical Science (1971 -). 2017;186(1):157-160. doi:10.1007/s11845-016-1439-1. Medline

6. Shlobin O, Baughman R. Sarcoidosis-Associated Pulmonary Hypertension. Semin Respir Crit Care Med. 2017;38(04):450-462. doi:10.1055/s-0037-1603767. Medline

7. Diaz-Guzman E, Farver C, Parambil J, Culver DA. Pulmonary hypertension caused by sarcoidosis. Clin Chest Med. 2008;29(3):549-563, x. doi:10.1016/j.ccm.2008.03.010. Medline

8. Boucly A, Cottin V, Nunes H, et al. Management and long-term outcomes of sarcoidosis-associated pulmonary hypertension. Eur Respir J. 2017;50(4):1700465. doi:10.1183/13993003.00465-2017. Medline

Author Affiliations

Matthew Patel*, and Karim Ladak, MD†

*Medical Student, Royal College of Surgeons in Ireland, Dublin, Ireland

†Department of Rheumatology, Hospital for Special Surgery, Cornell University, New York City, USA

Table:

Table 1. Workup for the pulmonary hypertension in this patient.

Investigation	**Result**
Inflammatory markers *	Normal
Complements	Normal
dsDNA	Normal
ANCA	Normal
Scleroderma	Normal
Serologies ¶	Normal
Angiotensin converting enzyme (ACE)	Normal
1, 25-OH-vitamin D	Normal
Peripheral flow	Normal
V/Q scan	Normal

*Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Anti-RNP, Anti-Sm, Anti-SSa (Ro), Anti-SSb (La), Anti-Jo-1

Figures:

Figure 1. Echo in four-chamber view. Grossly enlarged right ventricle (top left) and right atrium (bottom left), with bowing of the interventricular septum into the left ventricle.

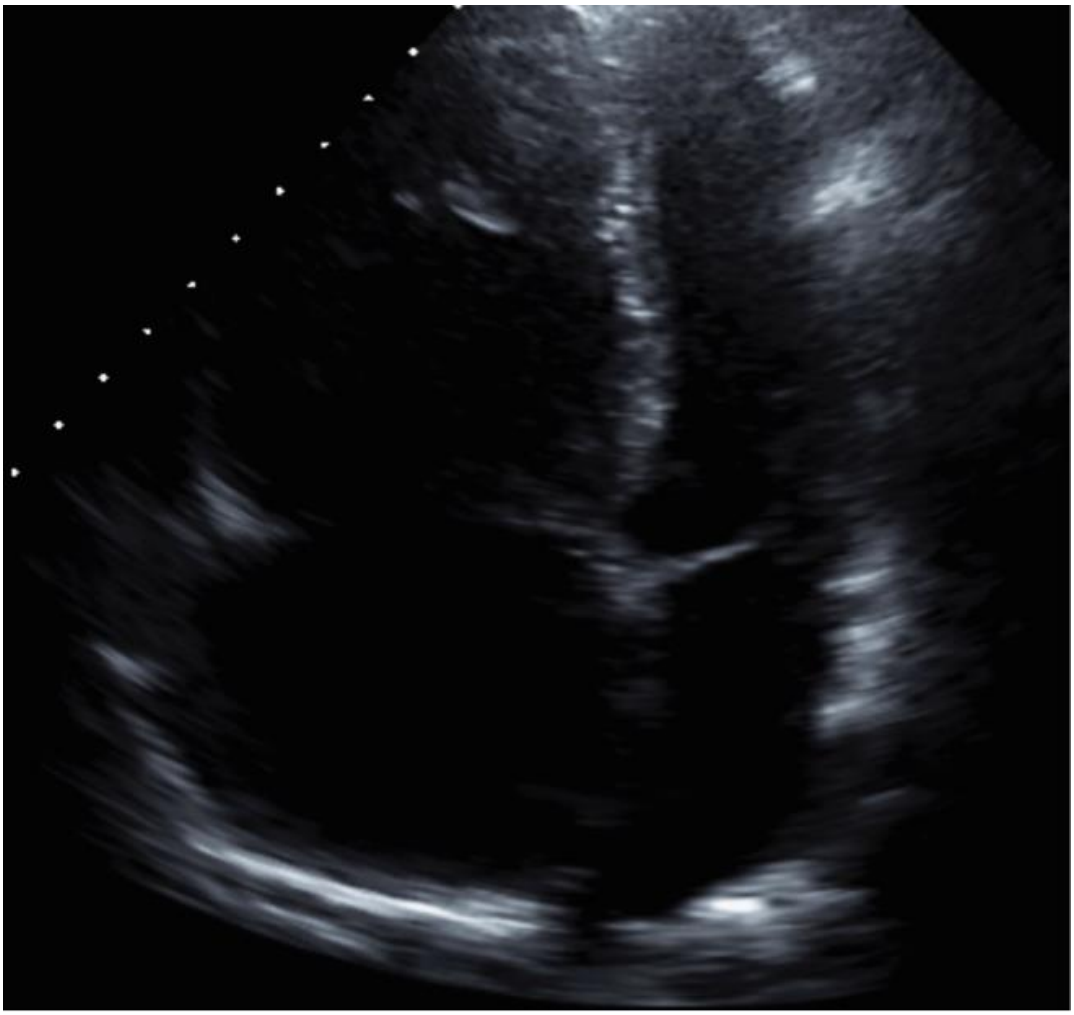

Figure 2. Extensive epithelioid, non-caseating granulomatous infiltrate associated with exogenous black carbon pigment, surrounded by small lymphocytes.