Successful management of pulmonary hypertension with baricitinib in a dermatomyositis patient

Sirs,

Pulmonary arterial hypertension (PAH) rarely complicates the course of idiopathic inflammatory myopathies (IIM) with a prevalence ranging between 7% and 14%. Data derives from anti-synthetase syndrome cohorts, with few data available for other IIM. Usually, PAH is associated with interstitial lung disease (ILD), being classified as group 3 PAH (1, 2). However, the occurrence of PAH in absence of ILD, classified as group 1, has been reported in IIM as a late event characterised by severe prognosis. Current treatment for group 1 PAH in IIM relies on the administration of vasoactive agents combined with standard IIM treatment (3).

An adult patient with anti-Ku dermatomyositis (DM), refractory to multiple treatments, presented with worsening disease. Initially, the clinical picture was dominated by severe skin and muscle involvement, characterised by ulcerative lesions of hands, armpits and eyelids, Gottron papules, Raynaud's phenomenon (RP), heliotrope rash and increased muscle enzymes. No signs of ILD nor cardiac involvement were detected; while alteration of the microcirculation was evidenced at the nailfold videocapillaroscopy. Glucocorticoids (GC) along with immunosuppressant, including methotrexate, azathioprine, mofetil mycophenolate, intravenous immunoglobulins (IVIg) and rituximab were consequently administered to achieve disease control with final good response of muscle involvement in presence of recalcitrant skin disease. For RP nifedipine was started since the beginning.

In 2023, the patient presented with chest discomfort, severe dyspnoea and asthenia. High resolution CT documented ILD in < 10% of lung parenchyma with normal lung function tests. Echocardiography revealed the presence of PAH signs and the patient was referred to the cardiology unit to undergo right heart catheterisation (RHC) that evidenced precapillary PAH (Table I). Macitentan was administered but the patient experienced severe diarrhoea after one week of treatment with severe relapse of skin disease. Multiple calcifications in lower extremities and in the sacral area appeared, the latter colliquated with consequent skin ulceration. High dose GC were administered with baricitinib 4 mg per day. Baricitinib choice relied on effectiveness demonstrated on skin involvement and the possible role in halting vascular remodelling (4). At the follow up visit no respiratory symptoms were present and active skin alterations resolved. Echocardiography documented the absence of PAH signs with no need of new RHC. Laboratory parameters were all within the normal range and GC were progressively tapered up to 5 mg per day.

Table I. Echocardiography and RHC parameters pre and after baricitinib treatment.

	Echocardiography			RHC
Parameters	T0	T1	Parameters	T0
EF (%)	66.8	61.8	PAPm (mmHg)	26
RA area (cm^2)	16.2	15.7	PAWP (mmHg)	9
RV diameter (mm)	38	36	PVR (UW)	2.5
TR Vmax (cm/s)	275	194.9	Cardiac output (L/min)	7.9
PAPs (mmHg)	35	20	CI (min/m^2)	4.1
TAPSE (mm)	20.9	24	RA (mmHg)	4
			RV (mmHg)	36/0

TAPSE: tricuspid annular plane systolic excursion; RA: right atrium; RAA: right atrial area; RHC: right heart catheterisation; RAP: right atrial pressure; RV: right ventricle; PAPm: mean pulmonary artery pressure; PAWP: pulmonary arterial wedge pressure; CI: cardiac index; PVR: pulmonary vascular resistance; TR Vmax: tricuspid regurgitation velocity peak.

The reported case represents the first patient with anti-Ku DM, complicated by PAH in the absence of extensive ILD, treated with the Janus kinase inhibitor (JAKi) baricitinib with excellent clinical and instrumental response and achievement of remission of pulmonary vascular disease. It is precisely the microvascular disease phenotype that constitutes the possible rationale for the efficacy of baricitinib. Indeed, several studies have been conducted documenting how PAH-specific vascular remodelling depends on activation of the JAK2/STAT3 axis through stimulation of various cytokines and growth factors, such as IL-6, IL-11, PDGF, VEGF, and via the alternative non-SMAD signalling pathway of TGFβ (4). In two pioneering studies, conducted *in vitro* and in animal models, baricitinib was tested, because of its inhibition of JAK2, with evidence of marked reduction of all vascular remodelling-associated processes underlying PAH: transition of endothelial cells to myofibroblasts (endothelial-mesenchymal transition), survival and migration of myofibroblasts, and vasoconstriction (5, 6).

In absence of therapies capable of reversing the damage to pulmonary vasculature, and considering the pathogenetic basis of PAH, JAKi could represent a viable therapeutic strategy in the management of these patients, especially in the context of DM (7). However, more in-depth studies on preclinical models of PAH and data on larger cohorts of patients are required to define the possible role of JAKi, and in particular anti-JAK2, in the management of PAH.

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