Scleroderma MANITOBA

PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS

Dr. Sabrina Hoa, MD MSC,
Rheumatologist, clinical researcher at the CHUM Research Centre

Dr. Tamara Grodzicky, MD FRCPC
Rheumatologist, clinical researcher at the CHUM Research Centre

Pulmonary arterial hypertension (PAH) means "high pressure in the arteries of the lungs". PAH is different from systemic arterial hypertension, which is usually referred to as "high blood pressure" and measured at the upper arm with a blood pressure monitor.

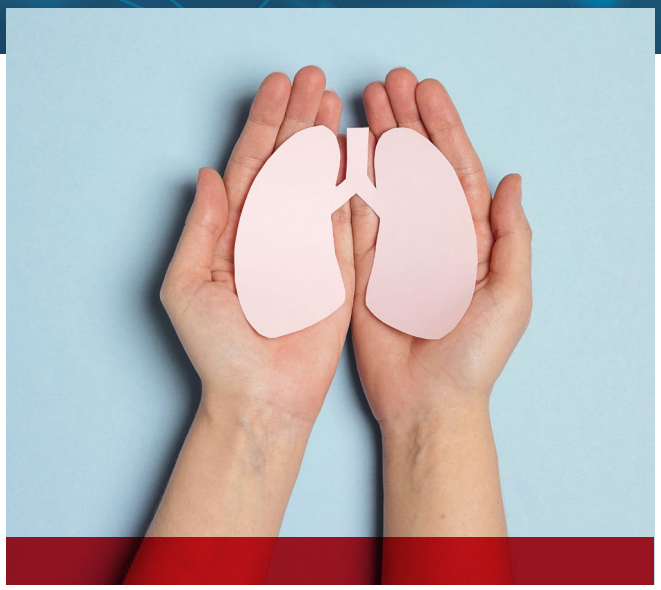
UNDERSTANDING PAH IN SYSTEMIC SCLEROSIS

PAH in systemic sclerosis is due to an exaggerated and progressive narrowing of the small blood vessels in the lungs. This is caused, on the one hand, by the increased presence of molecules (chemical signals) that promote the contraction and obliteration of the pulmonary arteries, and on the other hand, by a relatively insufficient quantity of molecules that promote their dilation. The factor that triggers this imbalance is unknown.

When the blood vessels in the lungs are narrowed, it is harder for the blood to circulate and get oxygenated. As a result, the level of oxygen in the blood becomes reduced, leading to suboptimal oxygenation of the body's organs and tissues.

The danger of having persistently very high pressure in the arteries of the lungs is also due to the fact that it makes it harder for the right side of the heart to pump blood through the lungs. Over time (several years), this eventually causes the right side of the heart to fail (right-side heart failure).

WHO IS AT RISK OF DEVELOPING PAH?



PAH occurs in 10 to 15% of patients with systemic sclerosis. PAH is most often associated with the limited form of systemic sclerosis and with more than 5 years of disease. The presence of certain autoantibodies, including anti-centromere, anti-U1-RNP, anti-Th-To and anti-U3-RNP (fibrillarin), are also risk factors for PAH.

WHAT ARE THE SYMPTOMS OF PAH?

PAH is often silent at first, but over time it can cause a variety of symptoms: shortness of breath and fatigue during physical exertion, chest pain, impending loss of consciousness or even unconsciousness (syncope) in more advanced cases.

Physical examination by the doctor is often not very revealing in the early stages, but it will show signs of heart dysfunction in more severely affected people. In these latter cases, the examination will show, for example, abnormal auscultation of the heart with the stethoscope and, in the event of heart failure, abnormal distension of the neck veins and swelling (edema) of the feet and legs.

HOW TO SCREEN FOR PAH?

Given the absence of specific symptoms at the onset of PAH, rheumatologists routinely screen all systemic sclerosis patients using pulmonary function tests (PFTs) and echocardiograms. A blood test for NT-proBNP, a specific marker for the heart, can also be used for screening. These tests are done annually in patients at higher risk of developing PAH, such as patients with the limited form of systemic sclerosis and long disease duration, or those with autoantibodies specified earlier.

When PAH is suspected, a more invasive type of investigation, i.e., catheterization of the right (and often also the left) side of the heart, is necessary to confirm the diagnosis. This is performed by a cardiologist. The pressure in the pulmonary arteries is then measured directly using a catheter inserted through a vein in the crease of the elbow or the groin.

Other tests may also be performed at this time to rule out other potential causes of pulmonary hypertension, such as heart disease, small clots in the lungs, lung fibrosis or emphysema, or sleep apnea.

PULMONARY ARTERIAL HYPERTENSION IN SYSTEMIC SCLEROSIS

TREATMENT FOR PAH IN SYSTEMIC SCLEROSIS

Given the complexity of the diagnosis, initial assessment, administration of certain medications and follow-up, patients suspected of having PAH are referred to specialized centres for management, with concomitant follow-up by the treating rheumatologist.

Indications for starting treatment for PAH include confirmation of the diagnosis by cardiac catheterization and the presence of symptoms (shortness of breath on physical exertion) with moderate to severe functional impairment. Treatments for PAH act by dilating vessels that are too narrowed, thus reducing the high pressure in the pulmonary arteries. Medications for PAH work through different mechanisms:

- Endothelin-1 receptor antagonists: bosentan (Tracleer®), ambrisentan (Volibris®) and macitentan (Opsumit®);
- Phosphodiesterase-5 inhibitors: sildenafil (Revatio®) and tadalafil (Adcirca®); Soluble guanylate cyclase stimulator: riociguat (Adempas®);
- Prostacyclins: epoprostenol (Flolan®), treprostinil (Remodulin®) and selexipag (Uptravi®).

In patients with moderate functional impairment, medications from the first two categories above are used alone or in combination. These medications are given by mouth and require periodic blood tests to monitor for side effects. If the disease is progressive or severe with symptoms at the slightest exertion, then inhaled, subcutaneous or intravenous prostacyclins may be added.

Concomitant treatment with medications such as diuretics (e.g., furosemide/Lasix®) and inotropic agents (improve the contractility of the heart muscle) are also useful for treating heart failure. Home oxygen therapy is reserved for patients with very severe disease. As a last resort, there is the option of lung or heart-lung transplantation, after a detailed medical and multidisciplinary assessment.

The follow-up of patients with PAH is done through a medical questionnaire, physical examination, and periodic investigations: blood samples, echocardiogram, pulmonary function test and in some cases, a repeat cardiac catheterization. The 6-minute walking distance can also be used to evaluate the effectiveness of treatment, typically associated with decreased shortness of breath and improved tolerance to physical exertion, which translates to the ability to walk further in 6 minutes.

IN SUMMARY

PAH is a serious complication of systemic sclerosis. However, over the past two decades, several new medications have been studied and approved for the treatment of PAH and can improve the quality of life and life expectancy of systemic sclerosis patients with PAH. Because PAH is often a silent disease in its early stages, it is essential to screen at-risk patients in order to make an early diagnosis and begin treatment if indicated.