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Editorial

Pulmonary hypertension in Takayasu's arteritis: Should be monitored closely

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Takayasu's arteritis (TAK) is a chronic, granulomatous large-vessel vasculitis, characterized by stenosis, occlusion, and aneurysm of the aorta and its main branches, especially of the subclavian, common and internal carotid arteries [1]. TAK occurs more commonly in young females, generally starting before forty years of age and is present more often in Far Eastern and Asian countries. Although, large-vessel associated symptoms and signs such as claudication of an extremity, decreased brachial artery pulse, systolic BP difference or a subclavian bruit are common diagnostic features, cardiopulmonary symptoms such as shortness of breath, chest pain and cough are also frequently present in TAK [1,2].

Pulmonary hypertension (PH), defined by a mean pulmonary artery pressure ≥ 25 mm Hg at rest measured during right heart catheterization, may develop due to pre-capillary causes such as lung diseases, chronic hypoxia and chronic thromboembolic diseases or post-capillary etiology associated with left-heart disease, aortic regurgitation or pulmonary arteritis. In different case series, the frequency of PH in TAK has been reported to range between 0% to 17.8% and pulmonary arterial involvement (PAI) 5.7% to 18.8% [2–10]. Clinically silent findings of PH and PAI may slowly progress, leading to the gradual development of congestive heart failure (CHF). PH is now routinely screened with transthoracic echocardiography as a non-invasive detection method in TAK. However, the definition of PH based on noninvasive echocardiographic assessment only estimates rather than direct measurement of hemodynamic pressures performed with right heart catheterization and therefore leading to the over or underestimation of real pressures.

In this issue of International Journal of Cardiology, Huang K et al. in a cross-sectional study, investigates Takayasu's arteritis patients with pulmonary arterial involvement in China. Patients with pulmonary symptoms (n = 86) were first assessed with pulmonary CT-angiography and 57 patients who were determined to have PAI were categorized as PH positive or negative groups after right-heart catheterization. PAI with PH group had a longer disease duration, higher rate of dyspnea, shorter 6 MWD and lower PaO_2. This group also had higher presence of aneurysms, bilateral thrombotic occlusions and mortality. This data suggests that TAK patients with pulmonary artery involvement and pulmonary hypertension possibly have a worse prognosis compared to the rest of the TAK population.

First major issue in understanding the clinical importance of PH in TAK is the prevalence of cardiologic disorders vs PAI among PH patients. The first review of literature bringing together PH in case presentations/series with TAK is done by Toledano et al. reporting cases between 1975 and 2009 [8]. Although, PH associated with PAI is reported to have a higher mortality in this review, the authors observed that low rate of systemic symptoms and non-specificity of pulmonary manifestations may lead to a late diagnosis of PAI or PH in TAK patients. In one of the recent series from China, PAI was also present in 75% of PH patients [9].

In contrast to these pre-selected series of pulmonary involvement, in two large series from Turkey and Korea, PH was present in 12% and 15%, these series gave the rate of PAI 6.9% and 13.3% [3,4]. In a recent series from Mayo Clinic, USA, among 45 patients with a cardiopulmonary abnormality (36% of TAK group) only 9 had pulmonary vasculitis on angiography and 7 had PH, whereas the rest had ventricular/atrial enlargements, valve regurgitations or CHF [2]. Two recent Turkish series also evaluated PH associated with PAI separately from isolated PH and secondary cardiovascular causes. In one Turkish series 7 of 64 (10.9%) patients had PH. Among these patients 3 had PAI (42.9%) compared to 9 patients without PH (15.7%) [7]. In the other series, when 7 patients with chronic pulmonary thrombo-embolic and left-sided heart disease were excluded from the analysis, none of the other patients with TAK (n = 70), including 4 cases with pulmonary arteritis, had PH [10]. Pulmonary hypertension prevalence in Turkey seems to be lower than the Asian series, which may suggest an institutional bias (pulmonary vs rheumatology clinics) or a true genetic and other unknown environmental factors.

PH in TAK seems to have an association with disease activity, therapeutic approaches and mortality. Prognosis seems to worsen with the presence of PH, especially when present with PAI. In Korean series, clinically active patients had a higher presence of PAI (18.1% vs 3.3%) and PH (44% vs 11.1%). In a Turkish series, cyclophosphamide or biological agents were more frequently used for treating TAK patients with PH as compared to patients without PH [7]. In USA series, although composite cardiopulmonary involvement was not predictive, patients with PH observed within 6 months of diagnosis had a near 13-fold increased risk of surgery during the follow-up period, with all seven

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PH patients having a surgical procedure [2]. In contrast, when 12 deceased TAK patients among 810 were investigated in China, PH was the possible cause of death in only 1 patient [6]. However, when selected cases with PAI and PH from the literature were assessed, the prognosis got worse with 20.5% mortality in PAI and 33.3% in PAH patients [8]. In the series by Huang et al., the 3-year mortality rate of PAI patients within a mean follow-up period of 34 months was 9% for PAI-with-PH patients compared to 0% in patients without PH. Pulmonary arterial aneurysm formation, observed only in patients with PH might also be a predictor of poor prognosis of these patients.

As a conclusion, beyond a standard recommendation for obtaining baseline large arterial imaging, consensus guidelines on the diagnosis and management of vasculitides provide little guidance on the evaluation of PH in TAK patients [2]. Nevertheless, transthoracic echocardiography has been shown as a reliable non-invasive method of detecting PH and should be the initial screening and subsequent monitoring modality for patients with concern for PH. Although the prevalence and the underlying etiological causes seem to differ, as Huang et al. and recent other studies have shown, pulmonary hypertension, especially when associated with PAI, is an important cause of morbidity and mortality in TAK patients.

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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