Letters to the editor

OVERVIEW

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Mitral stenosis-related pulmonary embolism as a potential cause of vocal cord paralysis

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Editor – In their lesson of the week article, Raja Shariff *et al* listed a differential diagnosis of Ortner's syndrome which should have included not just compression of the left recurrent laryngeal nerve (LRLN) by left atrial enlargement but also compression of the recurrent laryngeal nerve by a 'large thrombotic formation that completely occlude(s) the outflow tract of the pulmonary artery', as in the case of pulmonary embolism (PE) reported by Polverino *et al*.[1,2] Accordingly, for the sake of completeness, they should have evaluated their patient not only for left atrial enlargement but also for stigmata of PE.

The rationale for evaluation for PE even when left atrial enlargement has been documented by echocardiography is that mitral stenosis is a risk factor for PE (and, hence, for Ortner's syndrome) in its own right, and also a risk factor for mitral stenosis-related mortality.[3–5] The occurrence of mitral stenosis-related PE was exemplified by a 43-year-old man who presented with severe mitral stenosis, atrial fibrillation (AF) and haemoptysis. Contrast enhanced computed tomography demonstrated the presence of a left pulmonary embolism. Left atrial thrombus was also present, as shown by cardiac magnetic resonance imaging and by transthoracic echocardiography. Deep vein thrombosis was excluded by ultrasonography.[3] In the clinicopathological study of 51 cases of mitral stenosis published by Jordan *et al*, pulmonary emboli or infarcts were present at necropsy in 27 cases. In that study, 16 of the instances of PE and/or pulmonary infarct were associated with the presence of mural thrombi in the right atrium. Furthermore, peripheral venous thrombi were found in eight cases.[4] Pulmonary embolism was listed as a cause of death in six of the 59 patients with mitral stenosis-related mortality reported by Donzelot *et al*.[5]

PE-related Ortner's syndrome has not been reported in the context of mitral stenosis. Nevertheless, in view of the above observations and in order to maximise the impact of 'lesson of the week' as a 'teachable moment', evaluation for PE should be included in the evaluation of mitral stenosis patients with vocal cord paralysis even when left atrial enlargement is present.[2–5] The purpose of that exercise would be to rule out (or rule in) the possibility that LRLN compression might be attributable to mitral stenosis-related PE, given the fact that the latter can have a fatal outcome. At the very least, evaluation for PE should include an evaluation for peripheral venous thrombi (as a risk factor for PE) and a transoesophageal evaluation specifically to look for stigmata of PE. ■

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JAK-inhibition as a therapeutic strategy for refractory primary systemic vasculitides

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Editor – I read with interest the vasculitis update by Mooikhin Hng and colleagues who mention tociluzumab (anti-IL-6) as a therapeutic option in refractory giant cell arteritis (GCA), and wish to add that tocilizumab has been used successfully in refractory polyarteritis nodosa (PAN).[1,2] More importantly, patients with GCA who do not respond to biologics have few treatment options other than high doses of systemic corticosteroids.

These patients provide crucial learning experiences and the pressing need to understand pathogenesis of vasculitides in more detail. Inflammatory cytokines from effector T-cell subtypes allows self-sustained signalling in vasculitis and Janus-associated kinase inhibitors (JAKinibs; small molecules that inhibit JAK1, JAK2, JAK3 and Tyk2) have proven quite useful in controlling tissue inflammation in some refractory systemic vasculitis (supplementary material S1).[5–9] Immunophenotyping data in large vessel vasculitides show distinct characteristics between GCA and Takayasu's arteritis (TAK), but also have similarities such as Th1, Th-17 and Tfh cells involved in both disease relapses and such knowledge may help with personalised therapies.[3] The IL6/JAK/STAT3 axis in systemic sclerosis was one of the initial models where the efficacy of tofacitinib as a potential anti-fibrotic agent was recognised, and was then shown to reverse graft-versus-host

disease indicating multiple effects in lowering inflammation. Even with JAKinibs, it is clear that deep understanding in redundancy of pathways is necessary before considering a particular inhibitor for a trial/experimental therapy.

Successful clinical trials of small molecules in vasculitides will shed new light into pathogenesis, but biologic use requires careful consideration of added risks (infection or malignancy) while effectiveness also means the duration of treatment may be indefinite. Working with SHARE (Single-Hub Access for Pediatric Rheumatology in Europe) or vasculitis foundations will help physicians understand these difficult diseases and in improving patients' lives. ■

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Supplementary material

Additional supplementary material may be found in the online version of this article at www.rcpjournals.org/clinmedicine:
S1 – Use of JAKinibs in vasculitides.

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A further explanation for chest pain without visible coronary artery disease

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Editor – we read with interest the review and recommendations by Rogers *et al* on how to identify and manage functional cardiac symptoms.[1] The messages resonate with our experiences both on the acute take and in the clinic. The authors refer to 'syndrome x' as an alternative name for non-cardiac chest pain (NCCP) whereby patients have chest pain without evidence of epicardial coronary artery disease. While many cases of chest pain without epicardial coronary disease are non-cardiac in nature, it is increasingly recognised that up to 50% of patients with anginal symptoms, investigated in the catheter laboratory, have symptoms caused by coronary microvascular dysfunction (CMD). This has become known as ischaemia with non-obstructed coronary arteries (INOCA).[2] INOCA can be challenging to diagnose because it is not seen at angiography. It is, therefore, frequently overlooked. This is unfortunate because it is associated with increased risk of cardiac events yet responds to stratified medical therapy.[2,3]

Rogers *et al* describe how medically unexplained symptoms are associated with younger age and female sex, two factors which are also associated with CMD and INOCA.[2,4] Guidelines on investigation and management of INOCA have recently been published by the European Society of Cardiology.[5] We recognise the difficulty faced by clinicians in identifying functional syndromes and that they are highly prevalent. Given the prognostic implications of CMD and the fact that it is a potentially treatable condition, it is important that clinicians consider the diagnosis of INOCA before labelling symptoms as non-cardiac in origin. ■

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Functional disorders and chronic pain

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Editor – I read the article by Eccles and Davies with great interest.[1] I think they have highlighted well the overlapping issues of chronic pain and fatigue symptoms and the diagnostic overlap between patients with fibromyalgia and myalgic encephalomyelitis / chronic fatigue syndrome (ME/CFS).

I was, however, disappointed to note that there are a number of deficiencies within the article. While they are correct to note that there are multiple referral pathways for patients with chronic pain,