## Ortner's syndrome caused by pulmonary arterial hypertension associated with mixed connective tissue disease

Sirs.

Ortner's syndrome is a clinical condition featuring hoarseness that is attributable to left recurrent laryngeal nerve palsy, caused by various cardiovascular diseases (1). Here, we describe the first case of a patient with mixed connective tissue disease (MCTD) complicated by Ortner's syndrome, and the improvement of her hoarseness through bosentan administration.

A 24-year-old Japanese woman presented with Raynaud's phenomenon. Two years later, she was diagnosed as having MCTD with fever, polyarthritis, endocarditis, sausage-like fingers, reflux oesophagitis, lymphadenopathy, hypocomplementaemia, positive anti-nuclear antibody (x5120) and positive anti-U1-RNP antibody (235 index). High-resolution computed tomography (HRCT) showed no significant enlargement of the pulmonary artery trunk (PAT), whose diameter was 31 mm (Fig. 1A). Since transthoracic echocardiography showed only mild right ventricular hypertrophy and trivial pulmonary artery regurgitation, she was maintained on low- to moderate-dose prednisolone without any cardiovascular medications for the next two years.

She was admitted to our hospital for examination of gradually developing exertional dyspnea, WHO class II, and worsening pulmonary valve regurgitation with periodic echocardiography. Although HRCT showed no sign of interstitial pneumonia, PAT diameter was enlarged to 35 mm, greater than that of the ascending aorta (Fig. 1B). Chronic thromboembolic pulmonary hypertension was denied by lung perfusion scintigraphy. Mean pulmonary arterial pressure (mPAP) was 29 mmHg and pulmonary arterial wedge pressure (PAWP) was 13 mmHg by right cardiac catheterisation. The minute ventilation/carbon dioxide production ($VE/VCO_2$) slope was 37.5 from a cardiopulmonary exercise test. Based on these results, she was diagnosed with PAH. During this admission, she also realised that she sounded hoarse. Since gastro-esophageal reflux was suspected to be associated with her hoarseness, a proton pump inhibitor was added to the therapy, in addition to beraprost sodium (120 μg/day).

Her dyspnea gradually worsened to WHO class III the following year. Right cardiac catheterisation revealed mPAP and PAWP elevated to 40 mmHg and 3 mmHg, respectively, and the $VE/VCO_2$ slope rose to 43.7. Her hoarseness worsened. Oral bosentan was started from 125 mg/day and then gradually increased to 250 mg/day without any side effects. Two months later, her dyspnea improved and the $VE/VCO_2$ slope was reduced to within the normal range (33.3). However, her voice was still hoarse. Video laryngoscopy showed paralysis of the left vocal cord without any of the following: ulcerations, oedema, necrotising vasculitis with airway obstruction, or tumour (Fig. 1C). Left recurrent laryngeal nerve paralysis associated with PAH was suspected because HRCT showed that PAT was enlarged to 40 mm in diameter, which was larger than the measurement from one year previously (Fig. 1D). Five months later, fatigue, polyarthritis and hypocomplementaemia reappeared and oral prednisolone was increased to 30 mg/day. Subsequently, mPAP was 21 mmHg and PAT had shrunk to 34 mm, as seen by magnetic resonance imaging. The left vocal cord paralysis largely disappeared, as seen by video laryngoscopy.

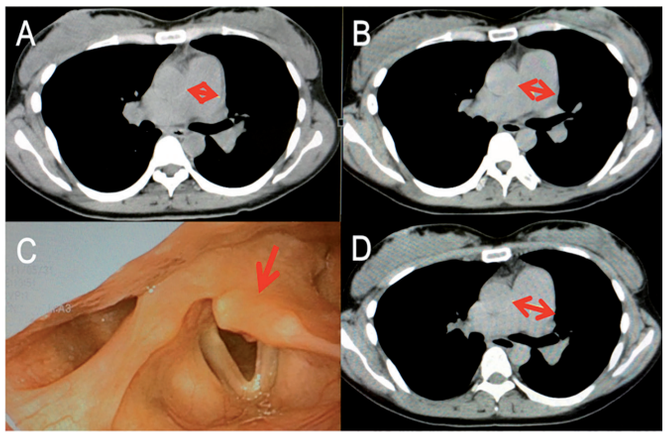


**Fig. 1.** Pulmonary artery trunk diameter in HRCT images and paralysis of the left vocal cord.
Pulmonary artery trunk diameters were 31 mm when the patient was diagnosed with MCTD (**A**), 35 mm when she was admitted with dyspnea 2 years after the diagnosis of MCTD (**B**), and 40 mm 3 years after the diagnosis of MCTD (**D**). Laryngoscopy shows the fixation of the left arytenoid (**C**).

Although laryngeal involvement is a rare complication of autoimmune rheumatic diseases, SLE-associated cases are well-recognised (2-4). Laryngeal complication can be caused by direct infiltration of immune complexes on laryngeal mucosa or muscles. Recurrent laryngeal neuropathy is also triggered by vasculitis involving the vasa nervorum, neuritis or dilated pulmonary artery (2-4).

Despite PAH being a major complication of MCTD (5), there is no report of Ortner's syndrome, although a few cases of Ortner's syndrome from SLE-associated PAH have been seen, none of them improved (6, 7). In the two Ortner's syndrome cases due to cardiovascular disease-associated PAH, several months were needed to recover from the paralysis after its improvement (8, 9). A similar time lag (five months) was found in this case, which we speculate was the time needed for the expanded arteries to contract and cease compression on the nerve.

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