Congenital rubella syndrome and left pulmonary artery sling

To the Editors:

The classic rubella syndrome is characterised by the combination of cardiac, ocular and hearing defects, although infection and damage can occur in every organ system. Since the advent of effective vaccination, the number of new cases of congenital rubella has plummeted.

The cardiac abnormality most frequently found in rubella syndrome is a combination of branch pulmonary artery stenosis and patent ductus arteriosus, though isolated branch pulmonary artery stenosis is twice as common as isolated patent ductus arteriosus [1]. However, a wide variety of cardiac malformations may be produced, such as ventricular and atrial septal defects, stenosis of the pulmonary and aortic valves, Fallot's tetralogy, coarctation of the aorta, tricuspid atresia and transposition of the great vessels. Localised pulmonary arterial stenosis may appear in one of three main forms. First, there may be isolated or multiple stenoses of the pulmonary arteries themselves. Secondly, there may be involvement of the bifurcation of the pulmonary trunk, the so-called coarctation of the pulmonary artery. Thirdly, stenosis may be due to a membrane situated immediately above the pulmonary valve [2]. Why rubella virus has such a predilection for the structure of the embryological sixth dorsal arch is not known, but it is certainly true that finding of patent ductus arteriosus and pulmonary artery stenosis far exceed those of valvular and septal defects in this infection [3].

We present the case of 17-yr-old girl with congenital rubella syndrome, recurrent pneumonia in childhood and a New York Heart Association functional class I–II/IV. Physical examination included a low-frequency systolic ejection murmur in the left infraclavicular region. The 12-lead ECG was normal and the transthoracic echocardiogram showed normal pulmonary artery pressure with absence of a normal origin of the left pulmonary artery. ^{99m}Tc-MAA (macroaggregates of albumin) lung scintigraphy demonstrated moderate hypoperfusion of the left lung and the computed tomography angiography showed an anomalous left pulmonary artery arising from the posterior portion of the right pulmonary artery and running between the trachea and the oesophagus to reach the left hilum (fig. 1). Also, mild compression of the main stem and the left bronchi were seen. No associated anomalies of the tracheobronchial tree were found.

An anomalous origin of the left pulmonary artery, *i.e.* which arises from the right pulmonary artery and courses to the left, passing between the trachea and oesophagus, is also known as pulmonary artery sling, and is a rare congenital condition probably due to involution of the proximal left sixth arch [4]. Its incidence is 3–6% of all aortic arch anomalies, though it has never been described in the congenital rubella syndrome. Patients affected by pulmonary artery sling may be classified generally into two groups: one with a normal bronchial pattern and the other with one or more malformations of the bronchotracheal tree, such as stenosis of a long segment of the trachea or absence of the pars membranacea, as well as cardiovascular abnormalities

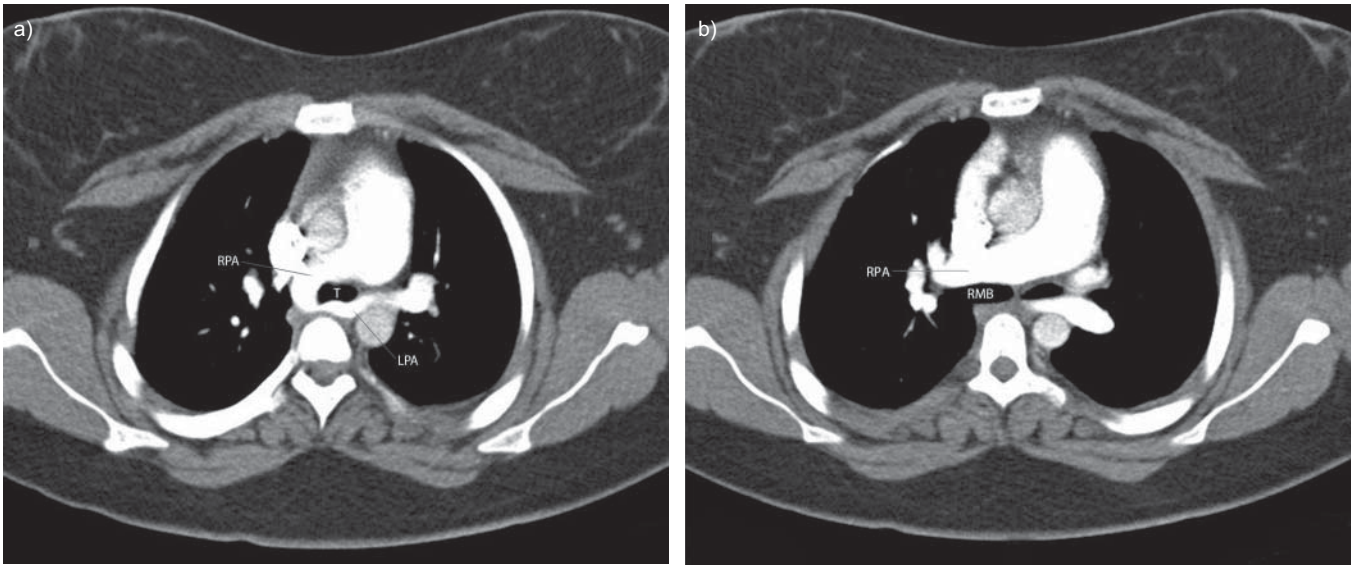

FIGURE 1. Computed tomography angiography images, at the level of a) the distal trachea (T) and b) the right main bronchus (RMB). The anomalous left pulmonary artery (LPA) originates from the posterior wall of the right pulmonary artery (RPA), passes over the right main bronchus and runs posterior to the trachea, encircling it, and goes leftwards between the trachea and oesophagus to reach the left pulmonary hilum. The left pulmonary artery is narrowed at the origin and midpoint from the impression of the right and left bronchi.

[5]. In the latter group, mortality and morbidity are high during infancy because compression of the trachea and right main stem bronchus produces severe respiratory distress within the first year of life. However, asymptomatic pulmonary artery slings are typically diagnosed incidentally in adolescence or adulthood.

Pulmonary artery sling can be repaired in infancy with low operative mortality and excellent long-term patency of the left pulmonary artery, by dividing the left pulmonary artery and implanting it into the main pulmonary artery anterior to the trachea [6]. In contrast to symptomatic patients, the prognosis for asymptomatic patients is excellent and surgical intervention is not indicated.

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Effects of fasudil in patients with high-altitude pulmonary hypertension

To the Editors:

High-altitude pulmonary arterial hypertension (HAPH) is characterised by increased pulmonary vascular resistance (PVR) secondary to hypoxia-induced pulmonary vasoconstriction and vascular remodelling of pulmonary arterioles [1]. Among the potential therapeutic targets is the RhoA/Rho kinases (ROCK) signalling pathway. The GTPase RhoA is a member of the Rho protein family, which regulates cellular functions such as contraction, motility, proliferation and apoptosis, and ROCKs are the best characterised downstream targets for RhoA [2, 3]. Activation of the small GTP-binding protein RhoA and its downstream target ROCK play a significant role in the pathogenesis of pulmonary hypertension (PH). The effectiveness of Rho/ROCK inhibition has been shown in several murine models of PH [4–7]. Fasudil, a ROCK inhibitor, is a potent vasodilatator approved in Japan for the treatment of brain vessel vasospasm induced by subarachnoid haemorrhage. It has been shown to reduce PVR in patients with severe idiopathic pulmonary arterial hypertension (PAH) [8, 9]. The aim of our study was to investigate the potential therapeutic effects of fasudil on pulmonary artery pressure (P_{pa}) in Kyrgyz highlanders with HAPH.

19 patients with HAPH, all permanent residents of the Tien-Shan Mountains (altitude 3,200–3,600 m) were studied. The study was approved by the ethics committee of the National Center of Cardiology and Internal Medicine (Bishkek, Kyrgyzstan) and all subjects gave informed consent. All subjects underwent health screening by history, physical examination, ECG, spirometry, blood pressure measurement and biochemical analysis for liver and kidney functions in order to exclude any pathology that might have potential influence on HAPH.

The effects of fasudil hydrochloride hydrate (Eril; Asahi Kasei Pharma Corp., Tokyo, Japan) and placebo (saline vehicle) on pulmonary haemodynamics were compared in a randomised, double-blind study. Each patient attended our high-altitude hospital at 3,600 m on two occasions, 1 day apart. On each occasion, echocardiographic studies were performed at baseline and after 30 min rest. Following this, fasudil or placebo were administered intravenously in a dose of 1 mg·min^{-1} for the following 30 min (total dose of fasudil 30 mg). Echocardiography was started 5 min before the fasudil or placebo infusion finished. Cardiac frequency (f_C), systemic arterial pressure and arterial oxygen saturation (S_{a,O_2}) were monitored continuously during the study (PROPAQ 102; Protocol Systems Inc., Dallas, TX, USA).

Doppler echocardiography was performed using a portable ultrasound system equipped with a 2.5-MHz probe (SpectraMax; SonoSite, Bothell, WA, USA). Systolic P_{pa} was estimated from the systolic pressure gradient between the right ventricle and the right atrium by the peak continuous-wave Doppler velocity of the tricuspid regurgitation jet velocity (TRV) using the modified Bernoulli equation plus right atrial pressure estimated from the inferior vena cava size and collapsibility with respiration. A pulsed Doppler pulmonary blood flow velocity signal was