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Original article

Progression of pulmonary artery dilatation in patients with pulmonary hypertension coexisting with a pulmonary artery aneurysm

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ABSTRACT

Background: Pulmonary artery (PA) dilatation is usually observed in patients with pulmonary hypertension (PH), but a PA aneurysm (PA diameter > 40 mm) is rare. The difference between characteristics of patients with and those without progression of PA diameter remains poorly understood. We assessed the changes in PA diameter in patients with PH coexisting with and without a PA aneurysm.

Methods: We investigated the changes in PA diameter by multi-detector computed tomography performed twice with an interval of more than one year in 44 patients with PH. Seventeen patients had a PA aneurysm and 27 patients did not have a PA aneurysm at baseline.

Results: The median follow-up period was 3.6 years. All patients received medical or invasive treatment for PH. At baseline, main PA diameters were 52 ± 15 mm in patients with a PA aneurysm and 33 ± 3 mm in patients without a PA aneurysm. Mean PA pressure was higher in patients with a PA aneurysm than in those without a PA aneurysm (61 ± 15 mmHg vs. 51 ± 16 mmHg, $p = 0.04$). At follow-up, mean PA pressure significantly decreased in both patients with a PA aneurysm (44 ± 11 mmHg) and patients without a PA aneurysm (41 ± 18 mmHg). Main PA diameter significantly increased in patients with a PA aneurysm (65 ± 28 mm, change ratio: 23.3%), while it did not increase in patients without a PA aneurysm (32 ± 3 mm, change ratio: −3.1%).

Conclusions: PA dilatation progressed in patients with a PA aneurysm despite treatment of PH. The progression of PA dilatation is independent of reduction of PA pressure by PH treatment.

Introduction

Pulmonary artery (PA) aneurysm was found in approximately 1 in 14,000 autopsies [1]. PA aneurysm is defined as main PA diameter of more than 40 mm [2]. PA aneurysm occurred at a younger age than aortic aneurysm with an equal sex incidence [3]. Eighty-nine percent of PA aneurysms were in main PA and 11% were in PA branches [4]. Congenital causes (heart defects and connective tissue abnormalities such as Marfan syndrome), acquired causes [infection, vasculitis, pulmonary hypertension (PH), pulmonary embolism, neoplasm, and iatrogenic causes] and idiopathic have been recognized as the reason for PA aneurysm [5]. There is no consensus on the treatment of PA aneurysm. The efficacy of medical therapy and surgical treatment remains uncertain.

PA dilatation is usually observed in patients with PH, but the formation of a PA aneurysm is rare in patients with PH. When a PA aneurysm has expanded, it can be an independent risk factor for unexpected death in patients with PH [6]. PA dissection is a cause of death in patients with a PA aneurysm [7]. However, the difference between characteristics of patients with and those without progression of PA dilatation is not well understood. It is important to know the characteristics for treatment of PH and a PA aneurysm and prediction of prognosis. Thus, we conducted a retrospective study to assess the changes in PA diameter in PH patients with and those without a PA aneurysm.

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Materials and methods

Study population

We investigated 44 patients who received multi-detector computed tomography (MDCT) two times with an interval of more than one year in Okayama University Hospital. Initial MDCT measurement of PA diameter was defined as the baseline value. Seventeen patients had a PA aneurysm and 27 patients did not have a PA aneurysm at baseline. We obtained clinical characteristics from medical records. Hemodynamic parameters were obtained from right heart catheterization performed within 3 months of the MDCT study. Cardiac output was measured by the Fick method. This retrospective study was approved by the Ethics Committee of Okayama University Hospital, and written informed consent was given by all patients.

Definition of PA aneurysm

We performed MDCT using a Somatom Definition Flash scanner (Siemens Medical Solutions, Munich, Germany) and Aquilion scanner (Toshiba Medical Systems, Otawara, Japan). The main, right and left PAs and ascending aorta diameters were measured at the level of the PA bifurcation (ideally when the right and left PAs appear to be similar sizes) using electronic calipers (Supplemental Fig. 1). PA aneurysm was defined as main PA diameter of more than 40 mm [2]. Behcet diseases, arteritis, and Marfan syndrome were excluded as the cause of PA aneurysm depending on symptoms, physicality, and imaging findings.

Outcome

Change ratio of PA diameter between baseline and follow-up were primary outcome of this study.

Statistical analysis

All statistical analyses were performed with SPSS software version 21.0 (SPSS Inc., Chicago, IL, USA). All data are expressed as mean values ± standard deviation or median (interquartile range). Continuous variables in two groups were compared by the unpaired *t*-test or Mann–Whitney *U* test, and categorical variables were compared by the chi-square test. PA diameter and mean PA pressure obtained at baseline and at follow-up were analyzed using a paired *t*-test. Change ratios of PA diameter between baseline and follow-up were compared using analysis of covariance (ANCOVA) models with the baseline PA diameter as the covariate. Cut-off values of increase in PA diameter were determined on the basis of receiver-operating characteristic (ROC) curve analysis. Univariate regression analysis was performed for various parameters that might affect PA aneurysm. Univariate regression analysis was performed to evaluate the risk factors for PA aneurysm and progression of PA aneurysm. Kaplan–Meier analysis was used to estimate survival status, and the log-rank test was used for survival distribution comparison in patients. Patients were censored if they died or underwent lung transplantation or PA dissection. Cox proportional hazards analysis was performed to evaluate the factors associated with survival. Values of p less than 0.05 were considered significant.

Results

Cases of PA aneurysm progression

Clinical characteristics of the 17 patients with a PA aneurysm are shown in Table 1. We show representative images of cases with and without PA aneurysm in Fig. 1. A 60-year-old woman was diagnosed with idiopathic pulmonary arterial hypertension (PAH) (Case 1, supplemental Fig. 2). Initial contrast MDCT demonstrated a PA aneurysm with a main PA diameter of 66 mm. Initial mean PA pressure was 75 mmHg. We started to treat the patient with a prostacyclin analogue, ambrisentan, anticoagulation, and oxygen. Seven years later, mean PA pressure was significantly decreased to 44 mmHg, but repeated MDCT showed expansion of the PA aneurysm with a main PA diameter of 129 mm. The patient received artificial PA artery replacement surgery. In histological analysis, severe elastic fiber degradation was observed in the area of the PA aneurysm.

A 40-year-old woman was diagnosed with PH associated with peripheral pulmonary stenosis (Case 2, supplemental Fig. 3). Initial MDCT demonstrated a PA aneurysm with a main PA diameter of 63 mm. Initial mean PA pressure was 63 mmHg. We treated the patient with a prostacyclin analogue, ambrisentan and diuretics. She also received balloon pulmonary angioplasty several times. Two years later, mean PA pressure was significantly decreased to 41 mmHg, but repeated MDCT showed expansion of the PA aneurysm with a main PA diameter of 112 mm. She died suddenly one month after repeated MDCT.

A 56-year-old woman was diagnosed with PH associated with congenital heart disease (Case 3, supplemental Fig. 4). Initial MDCT demonstrated a PA aneurysm with a main PA diameter of 91 mm. Initial mean PA pressure was 54 mmHg. We started to treat the patient with intravenous prostacyclin and oxygen. Three years later, mean PA pressure was significantly decreased to 45 mmHg, but repeated MDCT showed expansion of the PA aneurysm with a main PA diameter of 93 mm. She died of right heart failure.

Baseline characteristics of patients with and those without a PA aneurysm

Baseline characteristics of the patients are shown in Table 2. The patients were predominantly female. Idiopathic/heritable PAH and PAH associated with congenital heart disease accounted for most of the cases. Thirty patients (68.2%) were not treated with PH-specific drugs. In the other patients, a prostacyclin analogue, endothelin receptor antagonists, and phosphodiesterase 5 inhibitors were used alone or in combination.

Seventeen patients had a PA aneurysm and 27 patients did not have a PA aneurysm at baseline. There were no significant differences in clinical diagnosis between the two groups. Main, right, and left PA diameters were significantly larger in patients with a PA aneurysm than in those without a PA aneurysm (main PA diameter: 52 ± 15 mm vs. 33 ± 3 mm, $p < 0.01$; right PA diameter: 29 ± 8 mm vs. 21 ± 5 mm, $p < 0.01$; left PA diameter: 29 ± 7 mm vs. 21 ± 4 mm, $p < 0.01$). The ratio of main PA diameter to ascending aorta diameter was significantly higher in patients with a PA aneurysm than in those without a PA aneurysm (2.3 ± 0.7 vs. 1.3 ± 0.2, $p < 0.01$).

Follow-up

Follow-up characteristics of the patients are shown in Table 3. The median follow-up period was 3.6 years (interquartile range: 2.1–7.8 years). There was no significant difference between the median follow-up periods in the two groups. All of the patients were treated with PH-specific drugs alone or in combination or with occlusion of a cardiac shunt or balloon pulmonary angioplasty. Mean PA pressure significantly decreased in both patients with a PA aneurysm (from 61 ± 15 mmHg to 44 ± 11 mmHg, $p < 0.01$) (Fig. 2A) and patients without a PA aneurysm (from 51 ± 16 mmHg to 41 ± 18 mmHg, $p < 0.01$) (Fig. 2B). Main PA diameter was significantly increased at follow-up in patients with a PA aneurysm

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