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Pulmonary thromboembolism in congenital heart defects with severe pulmonary arterial hypertension

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ABSTRACT

Introduction: Congenital heart defect (CHD) with shunt can lead to severe, even irreversible pulmonary arterial hypertension (PAH); in extreme form to Eisenmenger syndrome (ES). Despite relatively good long-term survival, these patients often suffer from cyanosis and multisystemic dysfunction, where pulmonary artery thrombosis can be a potentially fatal complication. Together with bleeding these are the most frequent causes of non-cardiac death in patients with severe PAH due to CHD.

Patients and methods: Prospective study of 40 patients with severe PAH due to CHD (28 female/12 male, median age 41.5 years) was performed, with the aim to analyze the presence of pulmonary artery thrombosis and correlating anatomical and laboratory risk factors.

Results: Previous thrombosis and/or thromboembolic event was found in 7 patients (17.5%). Significant differences in cyanotic vs non-cyanotic patients were in red blood count parameters: median hemoglobin level 195 vs 141 ($p<0.0001$), median erythrocytes count 6.62 vs 4.88×10^{12}/l ($p<0.0001$), median hematocrit 0.58 vs 0.44 ($p<0.0001$). Laboratory findings causing increased risk for thrombosis were increased thrombocytes aggregation in 15 patients (37.5%), hypercoagulation in 5 patients (12.5%) and endothelial dysfunction in 8 patients (20%). Anatomical risk factor—severe pulmonary artery dilatation (>40 mm in female and >45 mm in male) was found in 19 patients (51.4%).

Conclusions: Patients with severe PAH due to CHD represent a high-risk group for pulmonary artery thrombosis with morphological and flow pathology combined with secondary erythrocytosis and coagulation abnormalities. A relatively high incidence of platelet hyperaggregability shown in our study would propose that aspirin therapy might be considered in some highly selected patients with severe PAH due to CHD. Further studies though are needed to support this data.

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1. Introduction

The presence of a hemodynamically significant congenital heart defect (CHD) with shunt can lead to increased pulmonary arterial flow and pressure. The onset and severity of pulmonary arterial hypertension (PAH) are quite variable according to the type of CHD, and in an extreme form can lead to Eisenmenger syndrome (ES) with irreversible PAH [1,2], contraindicated to any further correction.

Pulmonary arterial chances in PAH are closely studied but still not completely understood. Endothelial dysfunction and histomorphological changes in small pulmonary arterial vessels are the releasing factors of PAH [1]. Due to the increased pulmonary arterial pressure and resistance a secondary dilatation of proximal pulmonary artery is seen, with in situ thrombosis also described [1]. Even pulmonary artery dissection or rupture is sometimes reported [3,4].

ES represents a unique group among patients with PAH. The long-term survival of these patients is traditionally described as much better compared to those with other types of severe PAH [1,2,5]; despite the presence of extreme pulmonary arterial pressure, which can be systemic or even suprasystemic. This is usually contributed to the well preserved right ventricular (RV) function [5–8]. The presence of the defect is supposed to serve as a "pop-off valve", enabling the severely overloaded RV decompression and so preventing its decompensation and failure. This is why patients with a late CHD closure usually do much worse than before surgery or compared to patients with persistent cardiac shunting.

On the other hand, this RV "protection" in ES is paid with the cost of right-to-left shunting through the defect that leads to mixing of desaturated blood to systemic circulation resulting in patient's cyanosis. Cyanosis and systemic hypoxemia lead again to compensatory secondary erythrocytosis, changes in hemocoagulation and also changes in most of the body organs [5,9,10].

So, in ES, patients have complications resulting not only from the CHD and PAH but also from cyanosis and multisystemic dysfunction [9,10]. Therefore there are combined several risk factors for possible pulmonary arterial thrombosis (Fig. 1).

On the other hand these patients often suffer from severe bleeding complications as well. Both these complications are the most common cause of "non-cardiac" death in ES, as frequently as in 20% [11].

The necessity or the appropriateness of anticoagulation therapy is often discussed and until now it is not solved. In patients with PAH it is usually recommended [1] but in ES subgroup of patients the use of anticoagulation is a controversy [2,11–14], with no real benefit proven; also in the guidelines there is no expert consensus on this point. On the contrary, often secondary fatal bleeding complications with or without anticoagulation therapy are described.

2. Aims of the study

The aim of the study was to analyze patients with severe PAH due to CHD for the presence of pulmonary artery thrombosis and risk factors, like pulmonary arterial dilatation, and establishing possible correlations with cyanosis, secondary erythrocytosis and coagulation abnomalities. The aim was to define high-risk patients where anticoagulation therapy would be most profitable.

3. Patients

The patients analyzed were 40 patients with severe PAH due to CHD, 28 female (70%) and 12 male (30%), with median age 41.5 years (23–78 years). Age groups were as follows: there were 16 patients with ≤40 years of age (40%), 17 patients between 40 and 60 years (42.5%) and 7 patients ≥60 years (17.5%).

23 patients (57.5%) had a simple shunt lesion (atrial septal defect, ventricular septal defect or persistent arterial duct) and 7 patients (17.5%) had a combined shunt and 10 patients (25%) a complex heart defect. Nine (22.5%) patients had a previous defect closure without a residual shunt. All patients had an invasively confirmed severe PAH (mean pulmonary artery pressure >45 mmHg; and systolic pulmonary pressure >2/3 of systemic systolic arterial pressure).

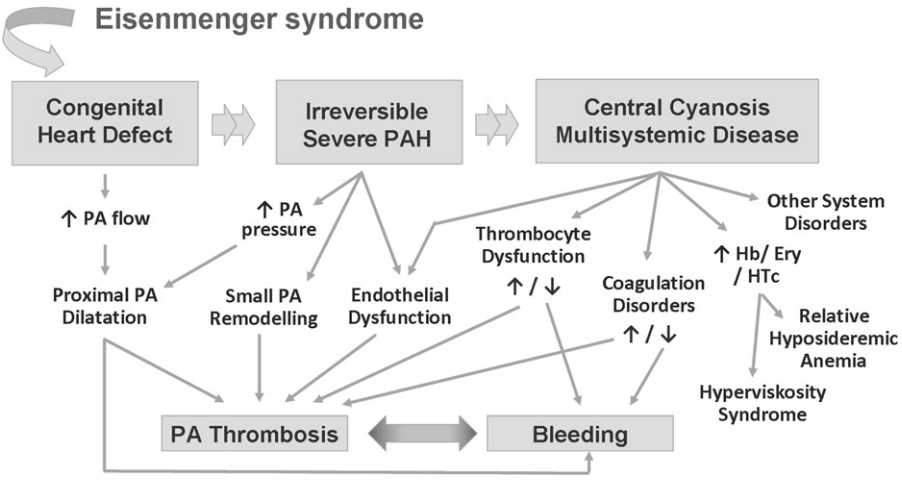

Fig. 1 – Complex pathological situations than can lead to pulmonary artery thrombosis and/or bleeding in patients with Eisenmenger syndrome.