Sildenafil Treatment of Unilateral Pulmonary Edema and Pulmonary Hypertension in Pulmonary Artery Agenesis

To the Editor,

Congenital pulmonary artery agenesis is a rare cardiovascular malformation, frequently oligosymptomatic,1,2 that can be complicated with unilateral pulmonary edema3 or pulmonary hypertension.1,2,4 We report the case of a patient with congenital pulmonary artery agenesis and pulmonary hypertension who developed unilateral pulmonary edema and discuss the role of sildenafil in pulmonary hypertension.

A 47-year-old woman, smoker of 20 cigarettes/day, with recurrent pulmonary infections, consulted for a hypertensive crisis. The physical examination was normal. The hemogram, biochemistry, coagulation tests, and electrocardiogram showed no alterations; there was mild hypoxemia in the arterial blood gas study. The chest x-ray revealed right pulmonary hyperlucency and a prominent left pulmonary artery. The echocardiogram showed concentric left ventricular hypertrophy.
with normal systolic function and dilation of the right ventricle with tricuspid regurgitation of 4.55 m/s. Pulmonary scintigraphy (ventilation-perfusion) disclosed the absence of right pulmonary perfusion. Computed tomography of the chest ruled out pulmonary thromboembolism, extrinsic compression of the pulmonary artery, and unilateral emphysema. The left pulmonary parenchyma showed a mosaic pattern and the right was hyperaerated (Figure 1). The respiratory functional tests showed mild obstruction with a moderate reduction of diffusion. Other causes of pulmonary hypertension were ruled out, and the patient was discharged. Two weeks later, the patient was readmitted for frank left ventricular failure. Blood pressure was 190/80 mm Hg, the ambient air saturation was 47%, and left crepitant rales were detected in the pulmonary auscultation. The ECG showed sinus tachycardia. A chest x-ray (Figure 2) revealed a left alveolar infiltrate, and the patient was started on oxygen therapy, nitroglycerin, furosemide, and antibiotics. She was clinically stabilized within 24 h, and the infiltrate disappeared. The hemodynamic study showed the following: pulmonary arterial pressure 87/25 mm Hg (mean, 49), right ventricular pressure 91/10 mm Hg, pulmonary capillary pressure 7 mm Hg, and blood pressure of 119/61 mm Hg (mean, 85). Oxygen saturation in venous blood was 56.5%, with no evidence of shunting. The pulmonary arteriography showed dilation of the main artery and of the left pulmonary artery and branch with absence of the right pulmonary artery. From the descending thoracic aorta and the right coronary, collateral “bronchial” arteries arose toward the right lung. The coronary arteries showed no lesions. She was discharged with oxygen, nifedipine, furosemide, enalapril, and coumarin derivatives, agreeing to an indication of cardiopulmonary transplantation at a referral hospital. Twenty months later, the patient worsened (New York Heart Association class III dyspnea); the 6-min walk test was 362 m and tricuspid regurgitation, estimated by echocardiography, was 3.5 m/s. Treatment with sildenafil (50 mg/24 h) was started with evident clinical improvement, remaining at 12 months in functional class II with a 6-min test of 428 m. Systolic pulmonary pressure estimated by echocardiographic study was 30 mm Hg.

Unilateral pulmonary edema is seen in various clinical scenarios. It is classified as ipsilateral or contralateral, with the latter occurring in the opposite lung to the perfusion defect. Patients with congenital pulmonary artery agenesis can present contralateral unilateral pulmonary edema during heart failure.

It is estimated that 19%-25% of patients with congenital pulmonary artery agenesis present pulmonary hypertension in adulthood, which implies a poor prognosis. Production of nitric oxide, which has a vasodilator and antiproliferative effect on the pulmonary artery, is poor in pulmonary hypertension. Sildenafil inhibits the enzyme that degrades nitric oxide (PDF-5) and results in long-term hemodynamic and functional improvement in patients with pulmonary hypertension due to various conditions, without deteriorating the ventilation/perfusion ratio and even improving it (supraselective or exclusive vasodilation effect in ventilated pulmonary areas). In our case, sildenafil treatment improved the patient’s functional capacity and normalized the hemodynamic parameters, probably because of a selective and supraselective vasodilator effect.

In conclusion, unilateral pulmonary edema can complicate the clinical progress in adults with congenital pulmonary artery agenesis. Add-on therapy of pulmonary hypertension with sildenafil should be considered in this clinical context.

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REFERENCES

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To the Editor,

The relationship between diabetes mellitus (DM) and cardiovascular disease is well recognized.1,2 The oral glucose tolerance test (OGTT) (World Health Organization [WHO] 1985 and 1999)3,4 and fasting plasma glucose (FBG) (American Diabetes Association [ADA] 1997 and 2003)5 are both methods for diagnosing DM. The agreement between these methods has been questioned in several epidemiological studies,6 and it is not clear whether they both detect the same pathophysiologic alteration. In this regard, the OGTT appears to be more able to determine the cardiovascular risk.7 The Burriana study 8 allowed us to compare the diagnostic efficacy of these methods.

This randomized, cross-sectional study was conducted among 317 persons (46.1% men) between 30 and 80 years of age and stratified by decade of age. After ruling out diabetics, 293 of the participants underwent protocolled OGTT (WHO)9 with 75 g and blood draw at fasting and at 120 min.

The criteria used to define impaired carbohydrate metabolism were those of the WHO 1985 (diabetes: blood glucose after 2 h of OGTT ≥ 200 mg/dL; impaired glucose tolerance [IGT]: blood glucose after OGTT 140-199 mg/dL; normal: blood glucose <140 mg/dL) and the ADA 1997 diagnostic criteria (diabetes: fasting plasma glucose [FPG] ≥ 126 mg/dL; impaired fasting glucose [IFG]: 110-125 mg/dL; normal: <110 mg/dL).

Lastly, the ADA 2003 modification5 was considered, in which the concept of impaired fasting glucose was expanded to include plasma glucose between 100 and 125 mg/dL.

Groups were established according to the FPG values obtained (<100, 100-109, 110-125 and 126-139 mg/dL) and according to age group by decade. For each FPG and age group, the prevalence of impaired carbohydrate metabolism (DM-IGT) was determined according to the WHO 1999 standards.

The degree of consistency between the two diagnostic standards was calculated by Cohen’s kappa. The probability of being diagnosed with diabetes by the OGTT, whether according to age group or FPG group (Table 1), is the direct result of the multiple logistic regression equation (diabetes ƒ [FPG, age]).

In the 40-49 year age group, no cases of DM were diagnosed. The clinical sensitivity and specificity of IFG 1997 (110-125 mg/dL) to diagnose DM (OGTT) were calculated, and the data were compared to the equivalents for IGT 2003 (100-125 mg/dL).

The number of persons included in each of the fasting plasma glucose groups was 197, 54, 28, and 14; among these, 15 new diabetics (1, 4, 4, and 6 in each group, respectively) were diagnosed following OGTT. The consistency for DM diagnosis between the two models (ADA 1997 and WHO 1998) was fair (K=0.53) although significant (P <.001) (Table 2). The IFG 1997 showed a sensitivity of 67% and a specificity of 88%. In the case of IFG 2003, the sensitivity improved to 93%, but the specificity dropped to 70%.

Table 1 shows that when the OGTT is done according to WHO criteria, FPG levels considered normal until 2003 (100-109 mg/dL) may hide DM at a percentage that, in at least one age group (50-59 years), exceeded 10%. Likewise, it was observed that IFG (ADA 1997) already indicates DM for 20% to 40% of cases according to age, when the WHO criteria are applied. In this regard, the EuroHeart Survey data revealed that up to 66% more individuals with impaired carbohydrate metabolism were diagnosed by OGTT than by simple FPG determination.2

The ADA’s attempt in 2003 to improve the detection of carbohydrate intolerance (DM + IFG) by lowering the cut-off levels for IFG had mixed results.4