

Clinicopathologic Session

Case 2/2001 – An 18-year-old male with dyspnea and pulmonary arterial hypertension (Hospital e Maternidade Celso Pierro/Grupo de Estudo em Correlação Anatomoclínica (GECAC) - Pontifícia Universidade Católica - Campinas, SP)

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We report the case of an 18-year-old white male complaining of sporadic episodes of dyspnea. The patient reported that one week earlier, edema in the lower limbs appeared and progressively extended to the abdomen and upper limbs. The patient also reported that on the day before he had experienced dyspnea. He then sought medical assistance and was hospitalized. The patient denied any pathologic antecedent and the use of tobacco, alcohol, and drugs.

On physical examination, the patient was cyanotic (++)/4. His respiration rate was 27 breaths per minute, his heart rate was 98bpm, and his blood pressure was 110/60mmHg. His central venous pressure remained between 27 and 29cm of water. His pulmonary examination was considered within the normal range. On cardiac auscultation, his heart rhythm was regular with increased intensity of the second cardiac sound in the pulmonary area and a systolic murmur of +/4 in the tricuspid area. His abdomen examination revealed mild and painless hepatomegaly. Edema was observed in the lower and upper limbs and in the abdominal wall, as well.

A chest X-ray in the anteroposterior projection showed moderate enlargement of the cardiac silhouette due to the right atrium and bulging of the left pulmonary trunk segment (fig. 1).

The electrocardiography showed sinus rhythm, heart rate of 100bpm, QRS axis of +120°, morphology of right bundle-branch block in V1 with a QRS duration of 0.08s, and

a deep S wave in V5 and V6, suggesting right ventricular hypertrophy (figs. 2A and B).

The catheterization of the pulmonary artery through venous via revealed pulmonary artery pressure of 48mmHg (normal = 25mmHg) and pulmonary vascular resistance of 724 dines/s/cm⁵ (normal = 225 – 315 dines/s/cm⁵). The pulmonary capillary pressure remained normal. The hemogram, assessment of the renal function, coagulation tests, and urinary sediment examination were all normal.

A few hours after hospitalization, the patient suddenly experienced shallow breathing, bradycardia, total atrioventricular block, and evolved with electromechanical dissociation. The patient did not respond to the resuscitation maneuvers and died.

Diagnostic hypotheses – 1) Heart failure due to rheumatic valvular disease – mitral stenosis; 2) Primary pulmonary hypertension.

(Medical student Marcos Bianchini Cardoso)

Discussion

Clinical features – Pulmonary hypertension is defined as a pressure in the pulmonary arterial system higher than 25mmHg at rest and higher than 30mmHg during exercise¹.

Primary pulmonary hypertension is a rare condition that is clinically defined after exclusion of all cardiac and pulmonary diseases that may cause elevation of the pressure in the pulmonary artery and elevation of vascular resistance. Its major symptoms are dyspnea, thoracic pain, and syncope, and, on examination, signs of different grades of cor pulmonale may be present. Among the causes of secondary pulmonary hypertension we emphasize pulmonary

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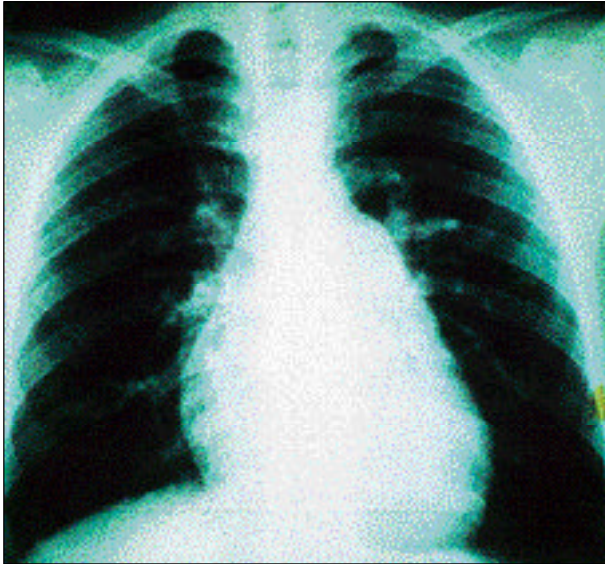


Fig. 1 – Chest X-ray in the anteroposterior projection.

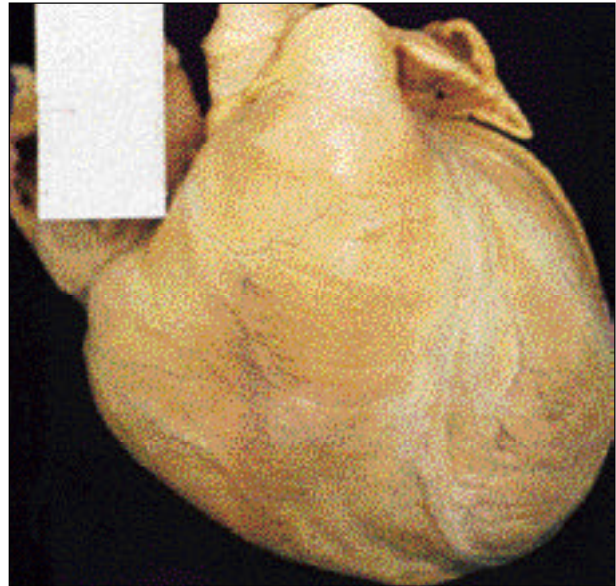


Fig. 3 – External view of the anterior surface of the heart showing marked bulging of the right ventricular outflow tract.

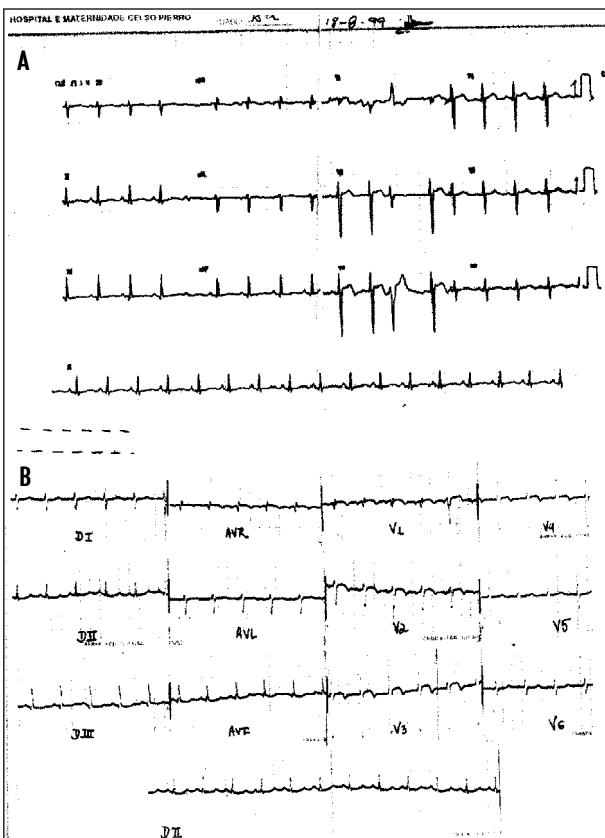


Fig. 2A and 2B – Electrocardiograms.

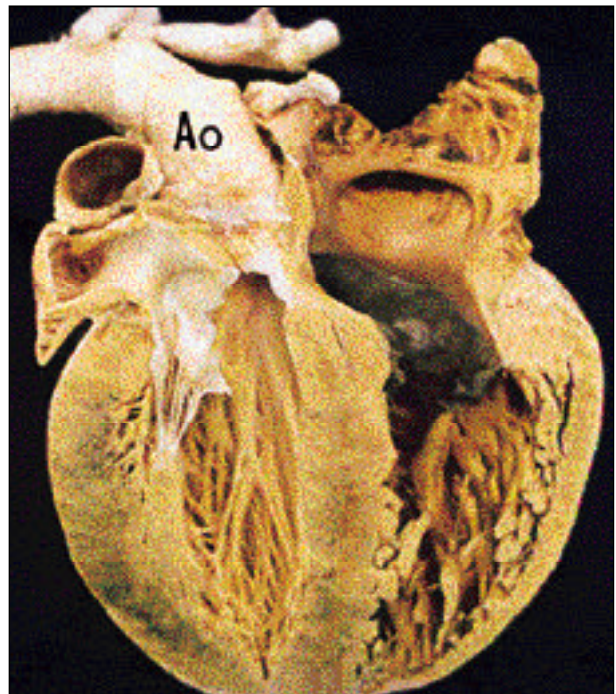


Fig. 4 – Section of the heart (4-chamber section) showing right ventricular dilation and hypertrophy. Ao- aorta.

disorders (chronic obstructive pulmonary disease, congenital anomalies), heart diseases (congenital malformations, left heart failure), thromboembolic disorders, exogenous substances (cocaine, anorectics), portal hypertension, and HIV infection¹.

According to clinical data, we can exclude pulmonary hypertension secondary to mitral stenosis because of the

normal capillary pressure, allowing the suggestion of the diagnosis of primary pulmonary hypertension, because electrocardiographic data and the radiography did not differentiate them. The cardiac murmur of tricuspid insufficiency may be justified by a probable enlargement of the right ventricle.

(Dr. Maria Aparecida Barone Teixeira and medical student Sandrigo Mangini)

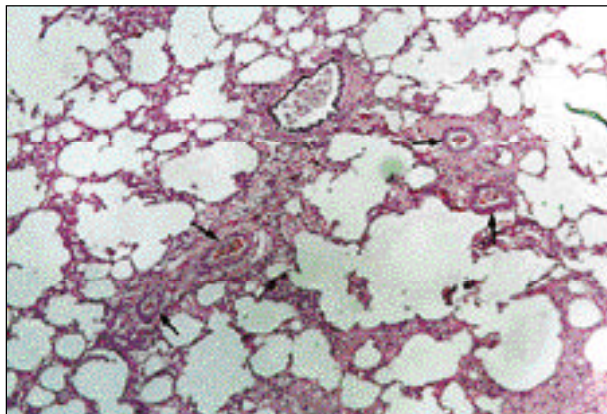


Fig. 5 – Microphotograph of the pulmonary parenchyma, where preacinar vessels with hypertrophy of the tunica media can be seen (arrows). Hematoxylin and eosin stain, original magnification 40 X.

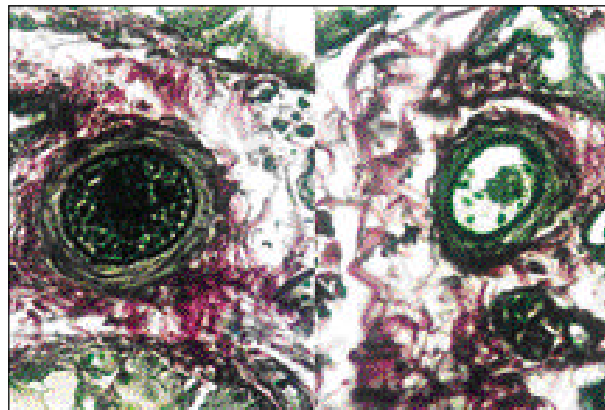


Fig. 6 – Microphotograph of intraacinar pulmonary arterial branches showing isolated hypertrophy of the tunica media. Müller stain, original magnification 400 X.

Table 1 – Mean percentage of medial thickness in regard to the external diameter of the peripheral pulmonary arteries.

External diameter (µm)	Mean external diameter (µm)	% of thickness of the tunica media – normal values*	% of thickness of the tunica media – results
0-50*	27.25	9.6	35.2
51-100**	77.84	7.4	13.5
101-200***	135.35	7.2	19.3

* 20 arterioles measured; ** 10 arterioles measured; *** 8 arteries measured; * normal values according to Haworth and Hislop⁵.

Autopsy

The heart weighed 600g and was enlarged due to diffuse thickening of the walls. The right ventricular outflow tract was very dilated (fig. 3). The ventricular cavities were slightly enlarged, and the atria were moderately dilated (fig. 4). No rheumatic valvular disease was found, and the tricuspid valve did not show insufficiency when the reflux test was performed. The microscopic study of the myocardium revealed hypertrophy of the fibers.

The lungs were slightly congested, and the major and peripheral branches of the pulmonary artery showed no thrombosis, embolism, or even lipoidosis (fig. 5). The liver had characteristics of passive congestion, which was confirmed on the microscopic examination. The histopathologic study of the lungs showed a normal parenchyma and arteries with no occlusive lesions of the tunica intima, on the hematoxylin and eosin stain (Fig. 6). The Müller stain for elastic fibers was performed, and the thicknesses of the medial layer of the arterioles with external diameters varying from 0 to 50µm, from 51 to 100µm, and from 101 to 200µm were measured and recorded as percentages. These measurements showed a 4-fold, 2-fold, and 3-fold increase, respectively, confirming the arteriopathy characterized by isolated medial hypertrophy. Measurements were performed with the aid of the Quantimet-500 Leica system of image analysis.

(Drs. Maria Aparecida Barone Teixeira and Vera Demarchi Aiello)

Comments

The anatomical and radiological findings are in accordance, and this was confirmed by the specimen that matched the cardiac silhouette on chest X-ray, mainly the prominence of the right ventricular outflow tract, ie, the pulmonary artery. Right ventricular hypertrophy, both grossly and microscopically, is the reliable anatomical substrate of the electrocardiographic changes, ie, QRS axis shifted to the right, and morphology of right bundle-branch block. The electrocardiogram did not show hypertrophy of the left chambers, therefore, not matching the autopsy findings.

In regard to histopathology, no plexogenic pulmonary arteriopathy was observed in our case.

Even though in primary pulmonary hypertension no pathognomonic histologic lesion exists, most cases reported show proliferative lesions of the tunica intima and dilated lesions, such as plexiform and angiomatoid lesions²⁻⁴; only few cases show isolated hypertrophy of the tunica media, as our patient did.

The patient's symptoms, dyspnea, cyanosis, and edema, are the clinical equivalents of the development of arteriopathy and consequent cor pulmonale. However, the lack of correlation between the severity of the histologic lesions (only hypertrophy of the tunica media, with no intimal occlusive lesions) and the patient's symptoms is worthy of note^{1,2}. Even though a greater pulmonary resistance is observed in patients with plexiform lesions, a lot of heterogeneity exists between the hemodynamic measures and

the histologic pattern². In our case, we could not correlate the grade of arteriopathy (isolated hypertrophy of the tunica media) with the pressure levels of the pulmonary artery. Pietra et al², in a study of 58 patients with primary pulmonary hypertension, showed that those with plexiform arteriopathy had greater pressure levels in the pulmonary artery as compared with the ones with thrombotic arteriopathy or veno-occlusive disease; in their only case with isolated medial hypertrophy, no report exists about the pressure level in the pulmonary artery. Palevsky et al⁶, studying 19 patients with primary pulmonary hypertension, 3 of whom with isolated medial hypertrophy, showed no significant difference between the pressure levels in the pulmonary artery and the grade of arteriopathy.

The sudden onset of clinical findings and death of our patient when compared with the exclusive anatomicopatholo-

gical findings of hypertrophy of the tunica media is a fact to be discussed, because the 3 patients of the study by Palevsky et al⁶ with this type of arteriopathy did not evolve in the same way. In the study by Pietra et al² no report exists about the evolution of the patient with the same type of lesion.

According to table I, a greater grade of medial hypertrophy of the arterioles of smaller diameter (0-50µm) exists, and this could be related to the rapid evolution of the patient to death, because these arterioles account for the higher vascular resistance. However, we could not find any reference or report about this in the literature reviewed. It is worth noting that we could not find any other cause to explain the decompensation of the hemodynamic status and consequent death of the patient.

(Dr. Maria Aparecida Barone Teixeira)

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