Case Report

Syncope and Complete Atrioventricular Block Related to Pulmonary Thromboembolism

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The patient was a 68-year-old male with hypertension and diabetes who sought the emergency service after sudden chest pain associated with syncope. On physical examination, the patient was in shock, with a blood pressure of 70/40 mmHg and a heart rate of 34 bpm. The electrocardiogram showed complete atrioventricular block with idioventricular escape. The patient underwent provisory artificial pacemaker implantation, which, in association with general measures, allowed stabilization of the clinical parameters. The echocardiogram showed a segmentary alteration in the inferoseptoapical wall and significant dysfunction of the left ventricle associated with pulmonary hypertension. Cine coronary angiography showed no coronary lesions that could justify the clinical findings, and pulmonary arteriography revealed massive bilateral pulmonary thromboembolism. Systemic thrombolytic therapy was instituted, and the patient developed ventricular failure, refractory hypoxemia, and died. The possible pathophysiological mechanisms related to the occurrence of atrioventricular block in massive pulmonary thromboembolism are discussed, as are the clinical implications and the diagnostic and therapeutic approaches.

Pulmonary thromboembolism is a potentially lethal, highly prevalent entity in clinical practice, which can often generate diagnostic difficulties [1-3]. When pulmonary thromboembolism occurs and is properly treated, the estimated mortality is 8%, a value that may reach up to 40% when the diagnosis is delayed [3]. In some autopsy series, the antemortem diagnosis of pulmonary thromboembolism was established in only 30% of the cases [3]. This is due to the lack of specificity of the signs and symptoms, as well as to the low diagnostic sensitivity of the physical examination and basic complementary tests, such as chest radiography, arterial gas analysis, and electrocardiography [3].

Syncope has been reported in 13 to 23% of patients with pulmonary thromboembolism [3,4]. When present, syncope is, most of the time, the initial manifestation of the embolic accident and is usually reported as resulting from a sudden decrease in cardiac output due to massive pulmonary arterial obliteration [3,4].

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The co-occurrence of syncope and complete atrioventricular block associated with pulmonary thromboembolism is very rare, and only a few cases have been reported in the literature [4-8]. This association was a complicating factor for the initial diagnosis of pulmonary thromboembolism and had clear implications in the outcome of most cases reported [5,7]. This study aimed at reporting the case of a patient with this form of presentation and at discussing the clinical, electrocardiographic, pathophysiological, prognostic, and therapeutic aspects of that rare manifestation of pulmonary thromboembolism.

Case Report

We report the case of a 68-year-old male patient with diabetes mellitus and systemic arterial hypertension, who was bedridden due to the treatment of an infected ulcerated lesion in the right lower limb and was followed up at home. The patient regularly used insulin, oral antidiabetic drugs, and an angiotensin-converting enzyme inhibitor. He experienced a sudden episode of chest pain followed by syncope and was referred to the emergency service of the Hospital Geral. His findings were typical of shock: cutaneous-mucous paleness, disorientation, tachydyspnea, blood pressure of 70/40 mmHg, heart rate of 34 bpm, and no significant alterations on pulmonary auscultation. He did not have signs and symptoms suggestive of deep venous thrombosis. The electrocardiogram showed complete atrioventricular block and idioventricular rhythm (fig. 1). The patient underwent provisory artificial pacemaker implantation through puncture of the right subclavian vein, which allowed, in association with general measures, the initial stabilization of the clinical parameters. The curve of the MB fraction of creatine phosphokinase (CKMB) was normal. Lactic dehydrogenase (DHL) was 518, glycemia was 476, and the leukogram showed 12,600 leukocytes with a shift to the left.

Two-dimensional Doppler echocardiography was performed for the etiological stratification of cardiovascular shock. The relevant findings on 2-dimensional Doppler echocardiography were normal left atrial and ventricular thickness, volume, and systolic functions, and significant hypokinesia of the inferior wall. The right ventricle showed an enlarged volume and severe diffuse hypokinesia. The right atrial volume was enlarged. Moderate tricuspid insufficiency was observed, and the estimated pulmonary artery pressure was 64 mmHg. The initial diagnostic hypothesis was inferior infarction with right ventricular impairment.

The patient evolved with progressive clinical worsening. After

6 hours, he required ventilatory support, being referred to the hemodynamics laboratory, where he initially underwent cine coronary angiography. After confirming the nonexistence of obstructive coronary lesions to justify the clinical findings, a pulmonary arteriography was performed. The study of the pulmonary circulation revealed opacification defects in the right pulmonary artery from its trunk to the superior and inferior lobar arteries, with impairment of some segmentary branches, patent left pulmonary artery, and an opacification defect in the inferior lobar artery and its segmentary branches (fig. 2). The clinical and arteriographic findings indicated massive pulmonary thromboembolism. Mechanical fragmentation of the thrombi was attempted with a 6F pigtail catheter, and systemic thrombolytic therapy with streptokinase was initiated at the dosage of 250,000 IU, for 30 minutes, followed by 100,000 IU per hour. The patient evolved with progressive hemodynamic worsening and refractory hypoxemia, and died 1 hour after the hemodynamic study. The retrospective analysis of the routine examinations showed complete left bundle-branch block in an electrocardiogram performed 6 months prior to the event (fig. 3).

Discussion

The diagnosis of pulmonary thromboembolism is very often difficult to establish [1-2], because it has a wide clinical spectrum, differing considerably in its dimension, clinical presentation, and presence or absence of associated diseases [1].

In the case of massive pulmonary thromboembolism, the differential diagnosis comprises myocardial infarction, cardiac tamponade, aortic dissection, acute mitral insufficiency, left ventricular failure, septicemia, hemorrhage, arrhythmia, and, occasionally, stroke [9].

The extension of the embolic occlusion, the patient's cardiovascular and pulmonary status prior to the embolic phenomenon, and the humoral and reflex factors are the 3 major determinants of the severity of the hemodynamic impairment in pulmonary thromboembolism [9].

Although the occurrence of syncope related to pulmonary thromboembolism has been well established [8], its presence causes difficulty in making an appropriate diagnosis, as reported in some studies about the diagnosis of syncope [1,10]. Visual blurring and syncope may be caused by pulmonary thromboembolism, but many other entities may result in central hypoxemia or hypotension [11].

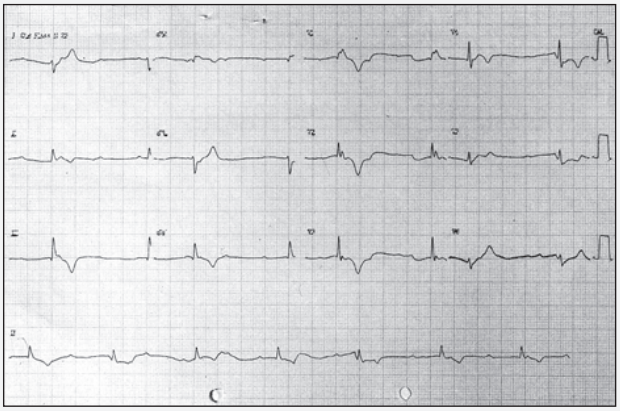

Fig. 1 - Twelve-lead electrocardiogram of our patient during medical care. Note complete atrioventricular block with idioventricular rhythm.

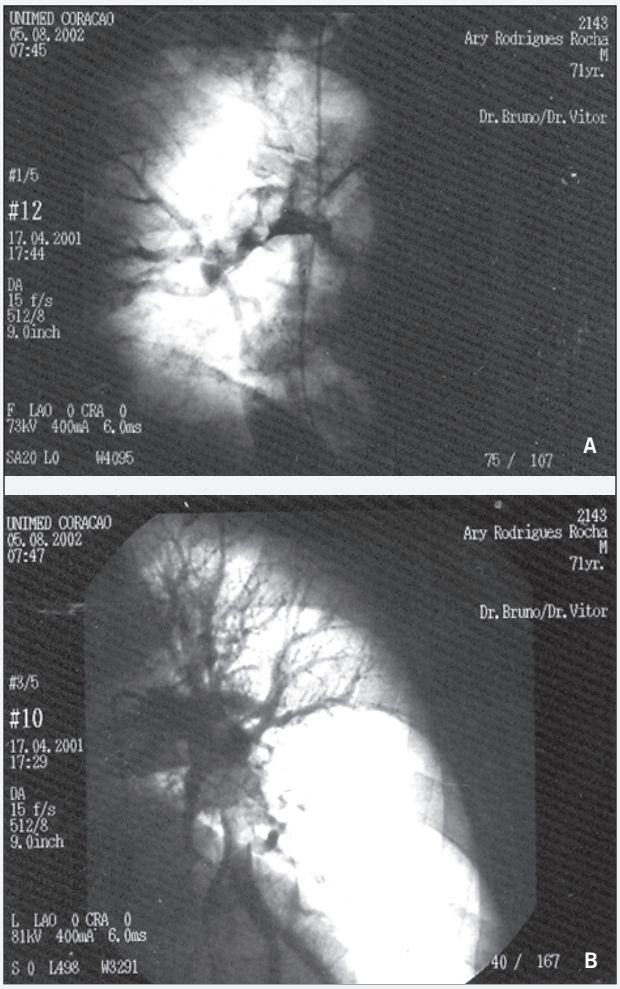

Fig. 2 - Angiographic images of the pulmonary arteries of our patient: A) large intraluminal defect in the bifurcation of the right pulmonary artery and its branches; B) filling defect in the inferior lobar artery and its segmentary branches.

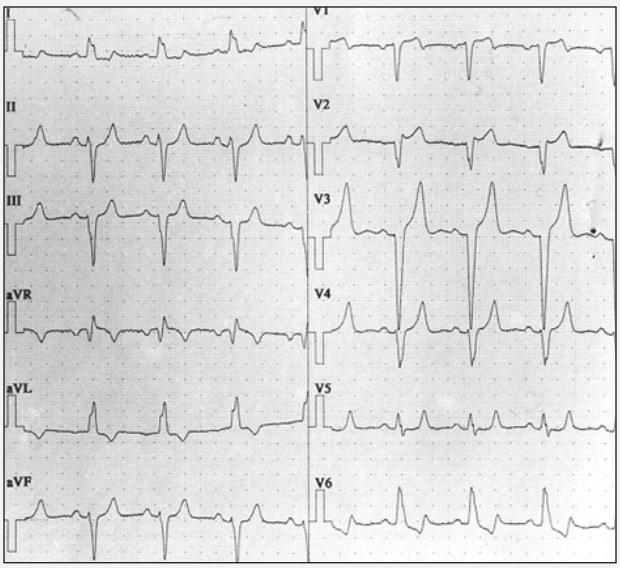

Fig. 3 - Twelve-lead electrocardiogram of our patient during a routine medical visit 6 months before the massive pulmonary thromboembolism episode.

According to the literature, syncope seems to be associated with massive pulmonary thromboembolism rather than with pulmonary thromboembolic events of smaller hemodynamic repercussion [9].

The occurrence of syncope during pulmonary thromboembolism

may result from 3 different possibilities. The first possibility is acute right ventricular failure caused by massive embolism consequent to a reduction in the cross-sectional pulmonary vascular area and pulmonary arterial hypertension. This failure could trigger a significant decrease in left ventricular filling, with concomitant tachycardia, arterial hypotension, and low cerebral flow [3,9], which may be the most probable mechanism of syncope in the presence of acute pulmonary thromboembolism [1]. In addition to the hemodynamic alterations, respiratory disorders, such as bronchoconstriction, an increase in the dead space, and a reduction in the pulmonary surfactant contribute to the clinical findings in these patients [12].

In some cases, syncope progresses to cardiac arrest; in others, it is brief. In the latter, the embolic occlusion of the central pulmonary artery may change to a partial occlusion [1].

The second possibility is the reflex syncope triggered by pulmonary thromboembolism [3,5].

In acute pulmonary thromboembolism, when an embolus lodges in a large branch of the pulmonary artery, it may trigger a hyperadrenergic state, resulting in an increase in the left ventricular contractility with restriction of the diastolic filling. This could stimulate the ventricular mechanoreceptors (type C afferent fibers) involved in the Bezold-Jarisch reflex and lead to an increase in the efferent vagal response, causing a decrease in heart rate, a delay in atrioventricular conduction, and a decrease in sympathetic tonus, resulting in peripheral vasodilation, and, finally, syncope [1,4,8]. In these cases, varied degrees of atrioventricular block could occur, being frequently associated with sinus bradycardia [3,6]. This reflex, however, is transient, lasting no more than the initial 15 minutes after massive pulmonary embolism. The prognosis during this period is difficult to assess due to reflex hypotension and the tendency toward spontaneous lysis of the thrombus. If hypotension persists, it is more likely to result from the mechanical occlusion of the pulmonary arterial system, being related to an extremely poor prognosis [1].

The third possibility is complete atrioventricular block in the presence of preexisting complete left bundle-branch block [3,5,6]. Our patient belongs to this subgroup. The rarity of this form of presentation of pulmonary thromboembolism may significantly contribute to the delay or even lack of a diagnosis of this clinical syndrome. In fact, Simpson et al [5] and Akinboboye et al [7] reported on 3 patients with recurring pulmonary thromboembolism with complete second-degree atrioventricular block and presyncope. The treatment of these patients was directed only to the atrioventricular conduction disorder; all patients underwent definitive artificial pacemaker implantation and died, and the diagnosis of massive pulmonary thromboembolism was established on autopsy [5,7]. The development of acute right bundle-branch block due to pulmonary embolism supposedly accounted for complete atrioventricular blockage and syncope in these individuals [8].

Sixty percent of the patients with pulmonary thromboembolism and syncope are known to have electrocardiographic signs of acute cor pulmonale (abrupt appearance of the S1Q3 type of the QRS pattern in the frontal plane, negative and pointed T wave in D3, and/or complete or incomplete right bundle-branch block) [4]. When analyzed in isolation, the presence of right bundle-branch block is frequent in pulmonary thromboembolism, mainly in massive pulmonary thromboembolism, right bundle-branch block being observed in 16 to 26% of the cases [4,13].

The mechanisms to which right bundle-branch block is usually attributed in pulmonary thromboembolism are myocardial ischemia and significant right ventricular dilation [4,13].

According to Wilner et al [4], only a few elements favor the first hypothesis. Those authors stated that experimental and clinical studies favor the increase in coronary flow in pulmonary thromboembolism.

The following fact favors the second hypothesis: the right branch of the His bundle is particularly exposed due to its superficial subendocardial trajectory on the right ventricular face of the septum, being, therefore, very sensitive to a sudden distension of the right cavities [4].

Nielsen et al [13] assessed the electrocardiographic alterations occurring in 87 patients affected by pulmonary thromboembolism and correlated them with the extension of the embolism (scintigraphic and angiographic score). Those authors observed that the presence of complete and incomplete right bundle-branch block and change in the QRS axis in the frontal plane correlated positively with the severity of pulmonary thromboembolism. Another relevant finding of that study was the fact that, in 9 of the 11 patients undergoing embolectomy, who had complete right bundle-branch block, the intraventricular conduction disorder disappeared in the first 24 postoperative hours, confirming, therefore, the hypothesis that intraventricular conduction disorders may be transient in the evolution of pulmonary thromboembolism [4,13]. This final observation led the authors to suggest that the presence of complete right bundle-branch block not only suggests the presence of a very extensive obstructive vascular process but also a high frequency of severe hemodynamic disorder, due to early symptom onset. As it indicates a massive and acute vascular obstruction, the authors proposed the need for immediate pulmonary angiography, aiming at assessing a possible surgical correction through pulmonary embolectomy [13].

Because approximately 2/3 of the patients with massive pulmonary thromboembolism die in the first hour, fast diagnosis and therapeutic intervention at the time of pulmonary embolism presentation are essential [12].

According to the multicenter study Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED), pulmonary thromboembolism is not a disease that can be clinically diagnosed, and ventilation/perfusion scintigraphy in combination with clinical suspicion is occasionally useful, but most patients need to undergo pulmonary angiography so a more accurate diagnosis may be established [2]. However, considering the severity of the patients, the complexity of the examination, and its possible complications, only 12% of the patients with pulmonary thromboembolism are referred for pulmonary angiography [2]. In addition, in the cases of pulmonary thromboembolism with pulmonary artery pressure levels > 40 mmHg, which are usually observed during massive pulmonary thromboembolism, the relative risk of the procedure is greater [14]. Furthermore, other techniques, such as computerized tomography and chest magnetic angioresonance, have shown promise in the diagnostic assessment of pulmonary thromboembolism [2].

Although pulmonary angiography has been considered the gold-standard test for acute pulmonary thromboembolism [11], the guidelines for the diagnosis and treatment of that disorder recently published by the European Society of Cardiology recommend the initial performance of noninvasive procedures (ventilation/perfusion scintigraphy, angioresonance, chest computed tomography with

contrast medium and specific protocol); pulmonary angiography should be reserved only for the cases with a strong clinical suspicion in which one of those tests is normal [14].

When massive pulmonary thromboembolism is suspected, echocardiography is recommended, because it may frequently show indirect signs of acute pulmonary hypertension and right ventricular overload, if the hemodynamic instability results from acute pulmonary thromboembolism, in addition to helping in the differential diagnosis [14].

A study [10] including 1,001 patients with massive pulmonary thromboembolism showed that 93% of the patients had evidence of right ventricular overload or pulmonary hypertension on the echocardiogram or right ventricular catheterization. Therefore, it is important to search for evidence of right ventricular overload when the diagnosis of massive pulmonary thromboembolism is suspected. Consequently, a more invasive approach is justified in patients with clinical findings suggestive of acute pulmonary thromboembolism associated with hemodynamic instability, which, as in the present case, is associated with echocardiographic findings of an unexplained right ventricular hypokinesia or right ventricular dilation, or both [9].

The most frequent therapeutic approaches proposed for massive pulmonary thromboembolism are therapy with systemic thrombolytic agents or surgical embolectomy [9].

Although no difference in mortality was observed between the different controlled studies using recombinant tissue-type plasminogen activator (rtPA), streptokinase, or urokinase, several differences were observed in regard to the early hemodynamic effects and safety [9,14]. Recombinant tissue-type plasminogen activator has proved to be the thrombolytic agent with the most significant hemodynamic response in the first hour of use when compared with urokinase or streptokinase [14]. Although all thrombolytic agents are effective in managing pulmonary thromboembolism, the option for using rtPA may be relevant in the evolution of patients with massive pulmonary thromboembolism [14].

Recently, De Gregório et al [12] studied 59 cases of massive pulmonary thromboembolism undergoing mechanical fragmentation with a catheter in association with in situ thrombolytic therapy. Those authors reported clinical improvement in 56 (94.9%) patients and 3 deaths due to refractory ventricular failure. The justification for this combined intervention was that the mechanical fragmentation of the thrombus could allow rapid recanalization of the central pulmonary arteries. In addition, rupture of the thrombus could cause dispersion of the clot to more peripheral branches, generating a decrease in pulmonary artery pressure and an increase in pulmonary vascular flow [12]. Finally, mechanical fragmentation, theoretically, could also allow an increase in the area of the thrombus exposed to the fibrinolytic agent, therefore increasing its lytic action [12].

In the present case, the use of the angiographic study was based on 2 points: the clinical and echocardiographic findings, which justified the need for establishing the differential diagnosis with acute coronary artery disease; and the existence of a severe atrioventricular conduction disorder, which is an exceptional finding in the presence of massive pulmonary thromboembolism.

In reality, in patients with a strong clinical suspicion and severe hemodynamic instability, the thrombolytic (or even surgical) therapy for pulmonary thromboembolism may even be adopted based only on echocardiographic signs [14].

Although in the present case both the diagnosis of massive pulmonary thromboembolism and the attempt at the mechanical fragmentation of the thrombi in association with the use of thrombolytic therapy were performed, the late diagnosis due to the co-occurrence of complete atrioventricular block may have been the fundamental factor in the patient's clinical outcome.

In conclusion, the occurrence of syncope in association with complete atrioventricular block, due to its rarity, may have been a factor in delaying the diagnosis of pulmonary thromboembolism. The intraventricular conduction disorder, in this situation, results from a maintained interruption in the conduction in the right branch of the His bundle triggered by right ventricular distension secondary to a massive pulmonary thromboembolism, which makes the time factor fundamental for the patient's survival. Knowledge about the possible outcome of pulmonary thromboembolism, in addition to the patient's clinical findings, should lead to the performance of complementary tests, allowing for immediate diagnosis and adequate intervention.

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