Primary pulmonary arteries atherosclerosis: discovering an unusual cause of death in forensic practice

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Abstract: Background: In the literature, there are few studies on atherosclerosis in the pulmonary artery in human beings and no cases similar to the one presented has been reported until now. The aim of the study is to describe a particularly unusual case of primary severe pulmonary atherosclerosis, in a 40-year old man, reporting its pathological aspects associated with interstitial lung disease as a cause of a mild pulmonary fibrosis.

Case presentation: The patient had marked atherosclerosis in the pulmonary trunk and its branches, probably caused by a series of hemodynamic and endothelial changes, subsequent to the pulmonary hypertension. An autopsy was performed a few days after death in order to explain the reasons of the sudden death. Despite the typical pattern of pulmonary atherosclerosis is generally associated with many co-morbidities, we have found only a significant right ventricular hypertrophy. A complete forensic approach led to attribute the cause of death to cardiorespiratory failure due to severe pulmonary atherosclerosis.

Conclusion: in the light of the limited number of reports in the literature, this paper seeks to widen knowledge in the area of atherosclerosis in the pulmonary artery.

Key Words: primary pulmonary arteries atherosclerosis, forensic practice, unusual cause of death, acute cardiorespiratory failure.

Atherosclerosis is a chronic inflammatory disease characterized by the accumulation of lipids and inflammatory cells along the inner walls of arteries, and it is an underlying cause of cardiovascular disease. Atherosclerotic lesions develop predominantly at branches, bends, and bifurcations in the arterial tree because these sites are exposed to low or disturbed blood flow, which exerts low/oscillatory shear stress on the vessel wall. This mechanical environment alters endothelial cell physiology by enhancing inflammatory activation. In contrast, regions of the arterial tree that are exposed to uniform, unidirectional blood flow and experience high shear stress are protected from inflammation and lesion development [1].

Although a wide range of global risk factors such as age, high cholesterol, and obesity significantly increase the risk of developing atherosclerosis, plaque formation predominately occurs at specific sites within the arterial tree, suggesting a critical role for local factors within the vasculature.

Mild atherosclerosis is said to be common with advanced age [2], but yellow (presumably "fatty") streaks have been historically noted in pulmonary arteries of healthy 40-year-olds [3], mainly at branching points of the trunk and in intrapulmonary arteries [4].

Atherosclerosis limited to the pulmonary artery (PA) is not common in human beings. The PAs and its branches are rarely affected by atherosclerosis. Even after systemic damage, these usually remain intact. Several factors might lead to such a condition. Normally, the pressure in the PAs is much lower than that in the systemic arteries, due to the low pulmonary resistance.

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This results in lower shear stress, therefore, less endothelial damage, which might trigger atherogenesis[5]. Some cases of pulmonary atherosclerosis have been reported in the literature, but all of them were associated with an atrial septal defect [6-7]. Pulmonary hypertension is one of the most serious and frequent consequence, varying between 9% and 22% among patients with atrial septal defect.

### Case report

A 40-year old man was found lifeless in his home by some relatives. He was known to be a non-smoker but he had a some years clinical history of dyspnea and chest pain. These symptoms were initially supposed to be associated with interstitial lung disease as a cause of pulmonary fibrosis. In that year he had undergone a number of radiological exams and invasive procedures. Particularly, a chest X-ray showed hilar congestion and mild cardiomegaly. Few months later a CT scan presented interstitial thickness due to fibrosis and mediastinal linfoadenopaties. Therefore clinicians hypothesized an interstitial lung disease. Malignancies was excluded with broncho-alveolar lavage investigation while macrophages and leucocytes, mainly neutrophils, appeared during microscopic studies.

### Materials and methods

Patient’s data were obtained from the clinical and anatomic pathological records. An autopsy was performed few days after death in order to explain the reasons of the unexpected death. Tissue sample were fixed in formalin, processed, and embedded in paraffin. For light microscopic examination, the sections were stained with haematoxylin–eosin.

### Pathological findings

Internal examination revealed cardiomegaly (12,5 x13,1 cm; 595 g) with the sole evidence of right ventricle hypertrophy (0,7 cm). Pulmonary arteries showed the presence of soft, elastic and yellowish plaques adhering to the walls (figure 1 A, B) spreading throughout the entire vessels as far as the terminal branches with a significant sub-occlusion of those on the right (figure 1 C, D). No other arteries were affected by atherosclerosis. Other evidence concerned oedema and vascular congestion of the lungs. Light microscopy examination of histology samples stained with haematoxylin-eosin revealed: effacement of the pulmonary artery walls; lumen of the vessels obliterated by thrombi in various stages of organization (figure 2 A, B); diffusely ulcerated intima; media of the vessels replaced by granulomatous tissue with cholesterol clefts and fibrosis (figure 2 C). A few areas showed deposition of calcium (figure 2 D).

### Discussion

Postmortem examination revealed substantial atherosclerosis of the large pulmonary arteries, with lesions extending into the medium-size arteries. The cause of death was attributed to cardiorespiratory failure due to severe pulmonary atherosclerosis. The complete anatomo-clinical approach, based on autopic and histologic investigation allowed us to exclude the pulmonary fibrosis suspected by clinicians, with our hypothesizing a primary form of pulmonary atherosclerosis.

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**Figure 1.** A and B: pulmonary arteries show the presence of soft, elastic and yellowish plaques adhering to the walls; C and D: a significant subocclusion of right terminal branches is present.
The latter is known to be a rare condition, affecting middle-aged individuals, men and women alike, and it is characterized by right ventricular failure (dyspnea, cyanosis, precordial pain) leading to a progressive worsening of clinical conditions and death, which usually occurs within 1-2 years after the onset of symptoms [8].

The atherosclerotic disease most commonly affects the systemic and coronary arteries, and pulmonary artery atherosclerosis is significantly correlated with age, right ventricular dilation and hypertrophy, pulmonary emphysema, and aortic atherosclerosis [9]. In contrast we have found only a significant right ventricular hypertrophy in association with pulmonary artery atherosclerosis.

In order to enforce our hypothesis we considered other possible anatomo-clinical conditions which may present a similar pattern.

Particularly, the pathological pattern in itself considered, regardless of the clinical and circumstantial data, could be also suggestive for a pulmonary embolism, an autochthonous thrombosis of the pulmonary arteries or a secondary form of pulmonary arteries atherosclerosis.

The first one has been excluded because of the lack thromboembolic sources which were thoroughly researched.

Moreover, the microscopic findings as well as the deposition of calcium in the vessels wall led to rule a thromboembolic phenomenon out [10].

With regard to the second hypothesis, autochthonous pulmonary arteries thrombosis is generally observed in small and medium size vessels without any anatomical lesions [8]. Instead, in our case, we had the involvement of the entire vessels with the presence of pathological aspects of both tunica media and intima. Finally, the in situ pulmonary artery thrombosis is usually associated with abnormal blood conditions (such as primary or secondary polycythaemia, or thrombotic thrombocytopenic purpura), while our patient had no clinical history of thrombogenic blood disease [11].

The last hypothesis concerned a secondary form of pulmonary atherosclerosis, a well-known pathology that affects the lung vessels due to pulmonary hypertension. The latter is characterized by medial hypertrophy or more often a combination of medial hypertrophy and concentric laminar intimal fibrosis [12, 13]. All of these findings were actually absent in our case.

According to all these considerations, and after a careful examination of the scientific literature published on this field, the most likely cause of the pulmonary artery pattern was identified in an atheromatous noxa which induced the onset of chronic thrombotic episodes.

**Conclusions**

Our study demonstrates a condition that is extremely infrequent. Particularly, in the light of the limited number of reports in the literature, this paper seeks to widen knowledge in the area of primary pulmonary arteries atherosclerosis.

**Conflict of interest.** We declare that we have no conflict of interest.
References