Pulmonary edema in a young male with severe uncontrolled cardiovascular risk factors and pan-vascular atherosclerosis: a case report

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Abstract

Cardiovascular risk factors are the cause of atherosclerotic disease, which can involve all the elastic and muscolo-elastic arteries. The etiopathogenesis of atherosclerosis is multifactorial since genetics, lifestyle, and comorbidities can be simultaneously involved. Clinical manifestations can be heterogeneous and include myocardial infarction, stroke, aortic aneurysms, renal artery stenosis, renal insufficiency, peripheral artery disease, *etc*. Currently, 70% of clinical events cannot be prevented with available drug therapy, statins included, and at least 10% of coronary events occur in apparently healthy individuals in the absence of major traditional risk factors. The case of a young male with a history of coronary artery disease and multiple atherosclerotic risk factors not properly treated who was admitted to the emergency department for pulmonary edema and high blood pressure is presented. During the diagnostic workup, a dramatic atherosclerotic involvement of all arterial trees emerged. Moreover, the patient presented with thrombosis of the right subclavian artery, which was treated with a heparin infusion and later complicated by cerebral hemorrhage with residual hemiplegia.

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Case Report

We describe the case of a 48-year-old male with a known history of coronary artery disease (percutaneous transluminal coronary angioplasty and stenting of circumflex coronary artery and left coronary artery in 2012 for ST elevation myocardial infarction) and uncontrolled cardiovascular (CV) risk factors: hypertension (unknown systolic and diastolic pressure values), dyslipidemia [previous hematochemical tests in November 2022 reported total cholesterol 228 mg/dL, low-density lipoprotein-cholesterol (LDL-c) 163 mg/dL, high-density lipoprotein 34 mg/dL, triglycerides 152 mg/dL), diabetes (diagnostic levels of glycemia for 1 year but no specific therapy), and heavy active smoking (20 cigarettes per day since 1995). His family history was negative for CV events. Home therapy was comprehensive of aspirin 100 mg, ezetimibe plus statin, and β-blocker. The patient presented at the emergency department with acute chest pain, dyspnea, and uncontrolled hypertension (220/130 mmHg). The scenario was consistent with acute pulmonary edema, no chest pain, and treated accordingly. The electrocardiogram (ECG) did not show acute modifications.

Laboratory results showed negative troponin (three consecutive points under the cut-off for normality) and N-terminal pro b-type natriuretic peptide 838 ng/L (consistent with cardiogenic dyspnea). After stabilization, it was noted that the blood pressure was significantly different between the two arms, and the right radial and omeral pulse were hyposphigmic. He underwent computed tomography (CT) angiography of the thorax and abdomen, which showed occlusion of the right subclavian artery at the origin by a large thrombus with re-perfusion immediately below the obstruction and heavy calcification of the other segments of the

artery (Figure 1). In addition, there was extensive aortic stenosis due to a large circumferential atheromatous plaque, which extended from the thoracic aorta to the iliac-femoral artery with intercostal arteries, epi- and hypogastric collateralization (Figures 2 and 3); however, renal arteries were patent. Because of the right subclavian thrombotic occlusion, intravenous heparin infusion was started. Two days later, the patient developed progressive aphasia with strength deficit and loss of sensibility in the right arm. Ischemic stroke was suspected, and a brain CT angiography was done, which showed a left frontal intracerebral hemorrhage (40 mm diameter) (Figure 4). At this point, the intravenous infusion of heparin was stopped. Balancing hemorrhagic and thrombotic risk, aspirin was shifted to a lower dosage (75 mg), and subcutaneous heparin prophylactic dosage (4000 IU) was given. High-dose statin was also started.

Serial head CT angiographies were repeated, and an initial reduction of the hemorrhagic lesion in densitometric values was recorded after 12 days. A CT scan of intracranial arteries showed moderate to severe stenosis of the left internal carotid artery and subocclusion of the right external and internal carotid arteries. Transthoracic echocardiography showed preserved ejection fraction, absence of new regionals, no significant valvular abnormalities, and no intracavitary thrombi. ECG monitoring did not show arrhythmic events. Invasive procedures like surgical or intra-arterial thrombolytic therapy were not taken into consideration due to the

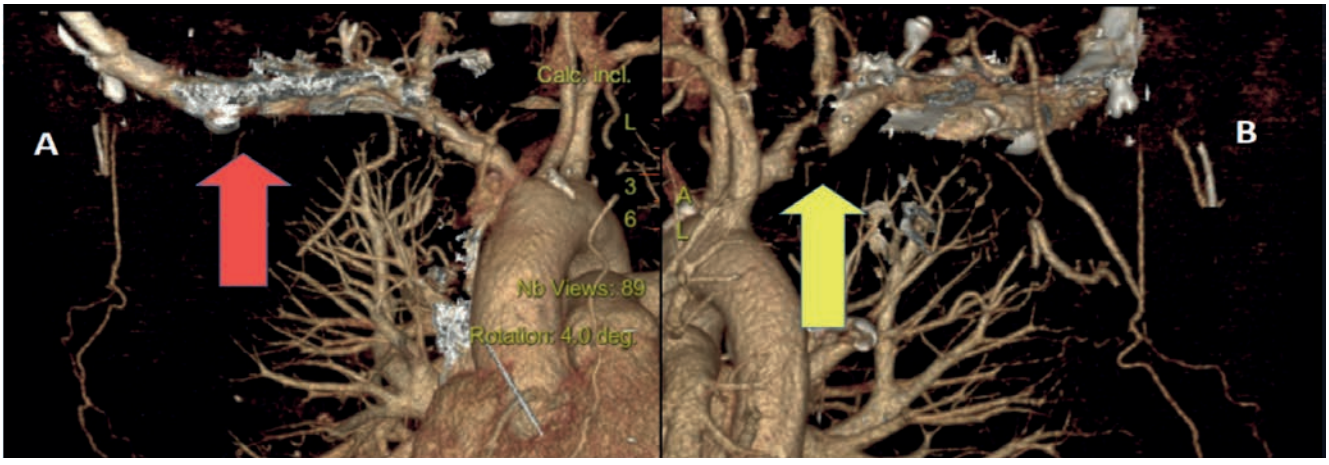

Figure 1. 3D tomographic reconstruction showing wide calcifications of right subclavian artery (red arrow on the left, anterior view) and right subclavian artery proximal occlusion with downriver reperfusion (yellow arrow on the right; from the back).

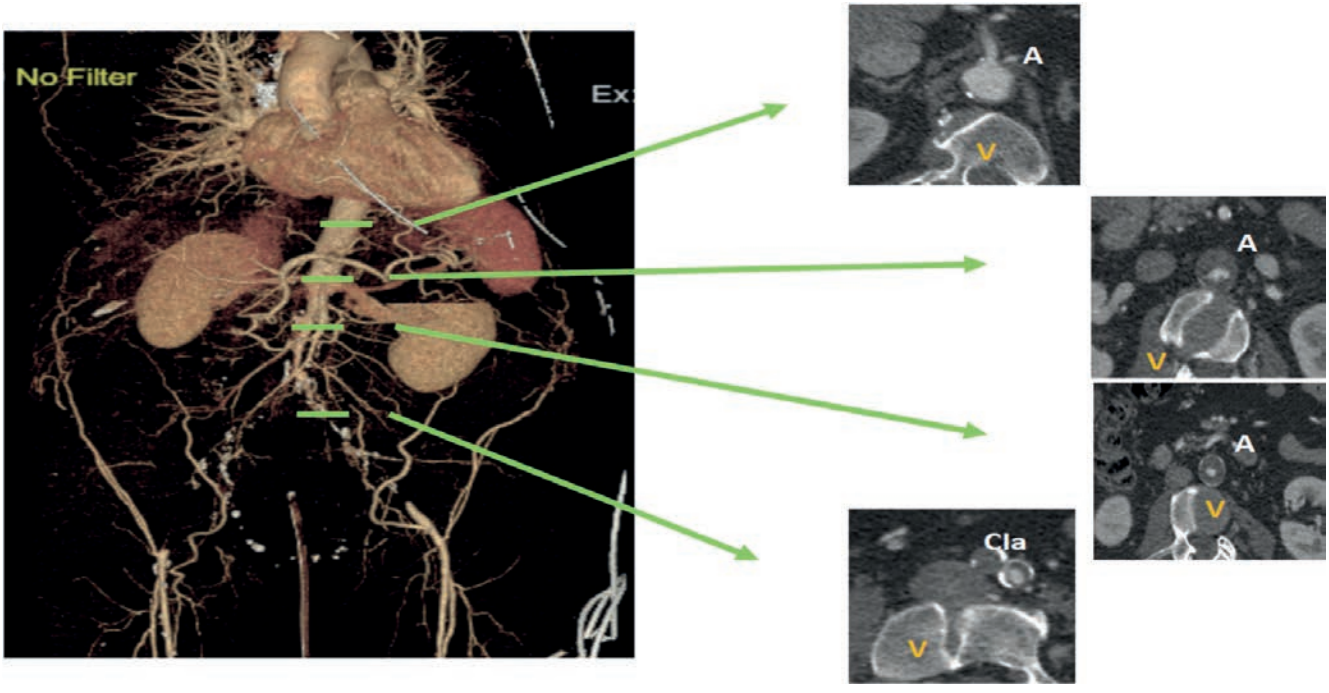

Figure 2. Extensive aortic stenosis due to a large circumferential atheromatous plaque which extended from the thoracic aorta to iliac-femoral artery (left side) and the corresponding transvers view on the right side.

improvement of the neurological status with medical therapy alone.

Hematochemical tests showed normal leucocytes and platelets count, and normal values of hemoglobin (Hb). Renal function and all electrolytes were normal, same for hepatic and thyroid function. A complete study of hemocoagulative parameters showed protein C, protein S level, activated protein C resistance test, antithrombin III, fibrinogen, and homocistein within normal limits. The research of autoantibodies as anti-phospholipid antibodies, and lupus anticoagulant tests were negative. Genetic tests showed normal homozygosis for the G20210A prothrombin mutation and G1691A V Leiden factor, and etherozygosis for the C677T MTHFR mutation. Tumoral markers (on the suspicion of paraneoplastic thrombosis) were also negative. Glycemia levels in the emergency department were elevated (317 mg/dL); blood levels of HbA1c (8.1%) confirmed the diagnosis of diabetes mellitus, so specific therapy with metformin and insulin was started. A total body positron emission tomography CT scan was performed on the suspicion of generalized vasculitis, but it did not show any findings consistent with it. After the acute phase, the patient was transferred to a long-term care hospital, where he pursued physiotherapy with regression of aphasia and improvement of right arm strength. Our patient was dismissed with the following pharmacological therapy: aspirin 75 mg per day, bisoprolol 1.25 mg per day, amlodipin 10 mg per day, olmesartan 40 mg per day, spironolacton 25 mg per day, atorvastatin 80 mg per day, pantoprazole 40 mg per day, metformin 1000 mg per day, and glargine insulin 12 UI per day.

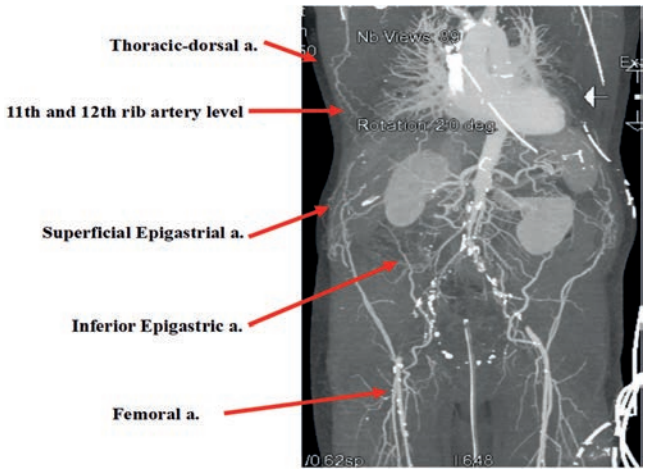

Figure 3. Recanalization of femoral arteries due to epigastric and intercostal arteries.

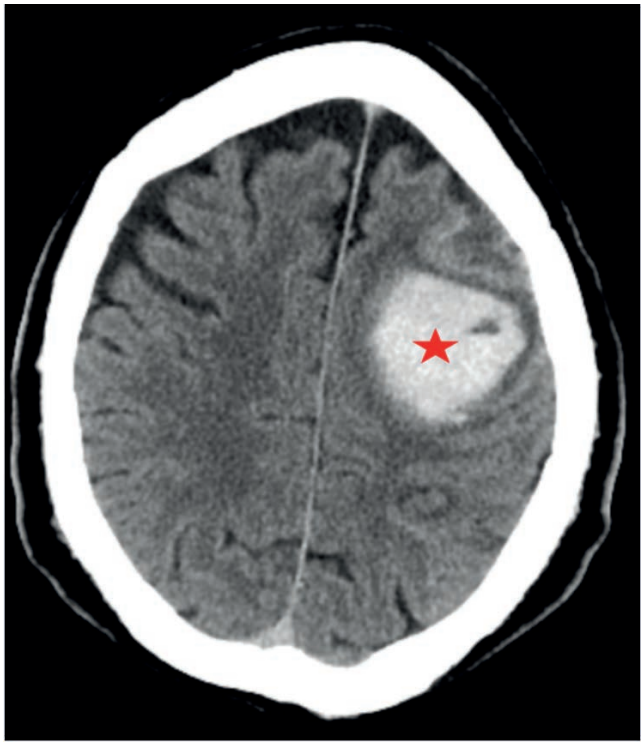

Figure 4. Left frontal cerebral hemorrhage (red star).

Discussion

This is the case of a middle-aged male with several uncontrolled CV risk factors that put the patient in a "very high risk" profile for CV events; he developed the so-called premature atherosclerosis, a condition diagnosed before the age of 50 that has a tremendous impact on quality of life [1,2]. All the arterial districts were dramatically involved.

The prevalence of unhealthy lifestyles is still high nowadays; particularly, smoking and CV risk factors like sedentary lifestyle and obesity are often poorly treated, even in patients considered to be at high CV risk like the present case. A sedentary lifestyle leads to visceral fat accumulation-induced chronic inflammation and is an under-recognized cardiometabolic risk factor and a strong independent predictor of outcomes in primary and secondary prevention of atherosclerotic CV disease [3,4].

Furthermore, the literature shows that several traditional risk factors combined have an additive or multiplicative effect. The joint presence of hypertension, hypercholesterolemia, and diabetes has a multiplicative effect on the global CV level of risk [5-7]. Our patient was also a heavy smoker. Smoking independently increases the risk for atherosclerotic CV disease and has a multiplicative effect on CV disease when combined with other traditional risk factors [7,8]. In the case of early and severe atherosclerosis, also the impact of nontraditional risk factors for premature atherosclerosis has to be considered, which include human immunodeficiency virus infection, highly active antiretroviral therapy, chemotherapy, radiation, lifestyle, diet, metabolic syndrome, recreational substance use, preeclampsia, inflammatory and autoimmune conditions, plus hereditary disorders (like clotting abnormalities, lipid derangements, and vessel disorders) [2]. Other non-traditional risk markers are non-fasting lipids, triglycerides, Lp(a), and apoB levels [6,9].

Many heart attacks, strokes, and hypertensive conditions are preventable with early detection and awareness of risk factors: lifestyle changes, early recognition of CV risk factors, and better application of guideline-based care (even adequate pharmacological therapy and adherence to therapy) can prevent premature deaths from CV diseases [10].

Conclusions

Atherosclerosis is a generalized process and results from the interaction of several risk factors. We described the case of a middle-aged male with a history of coronary artery disease at a young age,

with multiple CV risk factors not properly addressed by pharmacological therapy, and with dramatic atherosclerotic disease and iatrogenic complications.

These patients should be treated early and very aggressively, including lifestyle changes, in order to at least slow down, if it is not possible to stop, the atherosclerotic process and its complications.

A reasonable strategy to prevent CV events in premature atherosclerosis is composed of a radical change in lifestyle (healthy diet, moderate physical activity, weight loss, smoking cessation) and adequate pharmacological treatment of hypertension, diabetes, and dyslipidemia, if present. According to the most recent European guidelines on CV prevention, patients with premature atherosclerosis are at a very high risk of CV events, so target levels of blood pressure <130/80 mmHg, of HbA1c <7.0% (53 mmol/mol) (for diabetic patients), and of LDL-c <55 mg/dL are recommended [9].

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