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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.

Key words: premature atherosclerosis, cardiovascular risk factors, pulmonary edema.

Case Report

We describe the case of a 48-years old male with a known history of coronary artery disease (PTCA and stenting of circumflex coronary artery and left coronary artery in 2012 for STEMI) and uncontrolled CV risk factors: hypertension (unknown systolic and diastolic pressure values), dyslipidemia (previous hematochemical tests in November 2022 reported total cholesterol 228 mg/dl, LDL-c 163 mg/dl, HDL 34 mg/dl, tryglicerides 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). Family history was negative for CV events. Home therapy was comprehensive of aspirin 100 mg, ezetimibe plus statin and beta-blocker. The patient presented at the ED with acute chest pain, dyspnea, and uncontrolled hypertension (220/130 mmHg). The scenario was consistent with acute pulmonary oedema no chest pain, and treated accordingly. ECG didn't show acute modifications. Laboratory results showed negative troponin (three consecutive points under the cut-off for normality), NT pro-BNP 838 ng/L (consistent with cardiogenic dyspnea). After stabilization, it was noted that the BP was significantly different between the two arms, and right radial and omeral pulse were hyposphigmic. He underwent CT angiography of the thorax and abdomen, which showed occlusion of 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 an extensive aortic stenosis due to a large circumferential atheromatous plaque which extended from the thoracic aorta, to 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 on 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 intravenous infusion of heparin was stopped. Balancing hemorrhagic and thrombotic risk, aspirin was shifted to 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. CT scan of intracranial arteries showed moderate to severe stenosis of left internal carotid artery and subocclusion of 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 didn't show arrhythmic events. Invasive procedures like surgical or intra arterial thrombolytic therapy were not taken in consideration, due to improvement of the neurological status with medical therapy alone.

Hematochemical tests showed a normal leucocytes and platelets count, normal values of hemoglobin. 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, homocistein within normal limits. The research of autoantibodies as anti phospolipid antibodies, Lupus anticoagulant test were negative. Genetic tests showed normal homozygosis for G20210A Prothrombin mutation and G1691A V Leiden factor, etherozygosis for 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 PET CT scan was performed on the suspicion of generalized vasculitis, but it didn't 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, Glargine insulin 12 UI per day.

Discussion

This is a case of a middle age male with several uncontrolled cardiovascular risk factors that put the patient in a "very high risk" profile for cardiovascular events and the 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 lifestyle is still high also 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 strong independent predictor of outcomes in primary and secondary prevention of atherosclerotic cardiovascular disease [3,4].

Furthermore, literature shows that several traditional risk factors combined together have additive or multiplicative effect. The joint presence of hypertension, hypercholesterolemia and diabetes has a multiplicative effect on global CV level of risk [5-7]. Our patient was also a heavy smoker. Smoking independently increases risk for atherosclerotic cardiovascular 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 nonfasting 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 cardiovascular risk factors and better application of guideline-based care (even adequate pharmacological therapy and adherence to therapy) can prevent premature deaths from cardiovascular diseases [10].

Conclusions

Atherosclerosis is a generalized process and results from interaction of several risk factors. We described the case of a middle age male, with history of coronary artery disease in young age, with multiple CV risk factors not properly addressed by pharmacological therapy and with a 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 cardiovascular events in premature atherosclerosis is composed by a radical change in lifestyle (healty diet, moderate physical activity, weight loss, smoking cessation) and adeguate pharmcological treatment of hypertension, diabetes and dyslipidemia, if present. According to the most recent European guidelines on cardiovascular prevention, patients with premature atherosclerosis are on a very high risk of cardiovascular events, so: target levels of blood pressure < 130/80 mmHg, of HbA1c <7.0% (53 mmol/mol) (for diabetic patients), of LDL-c < 55 mg/dl are recommended [9].

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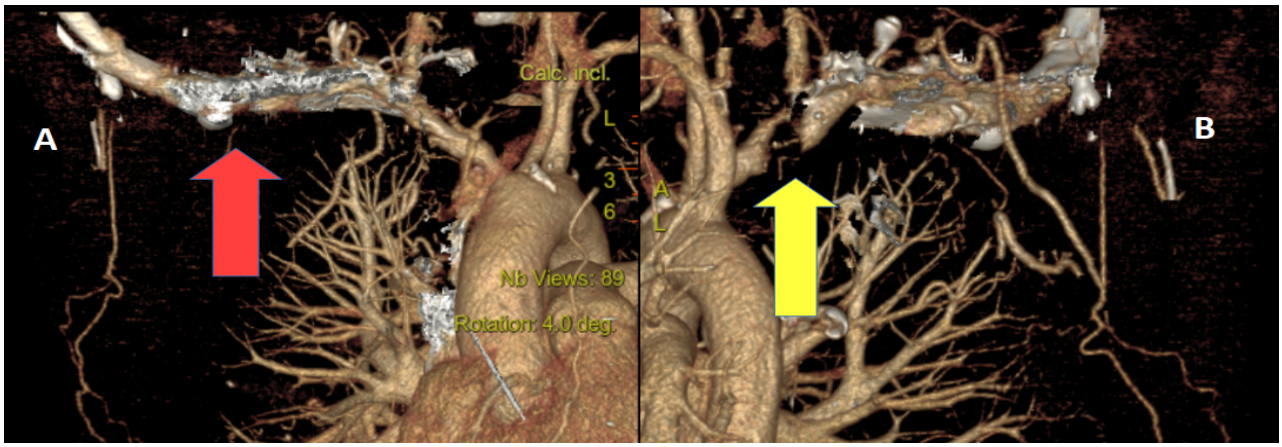

Figure 1. 3D tomographic reconstruction showing wide calcifications of right subclavian artery (red arrow on the left, anterior view) and right subclavian artery proximal occlusion with downriver reperfusion (yellow arrow, on the right; from the back).

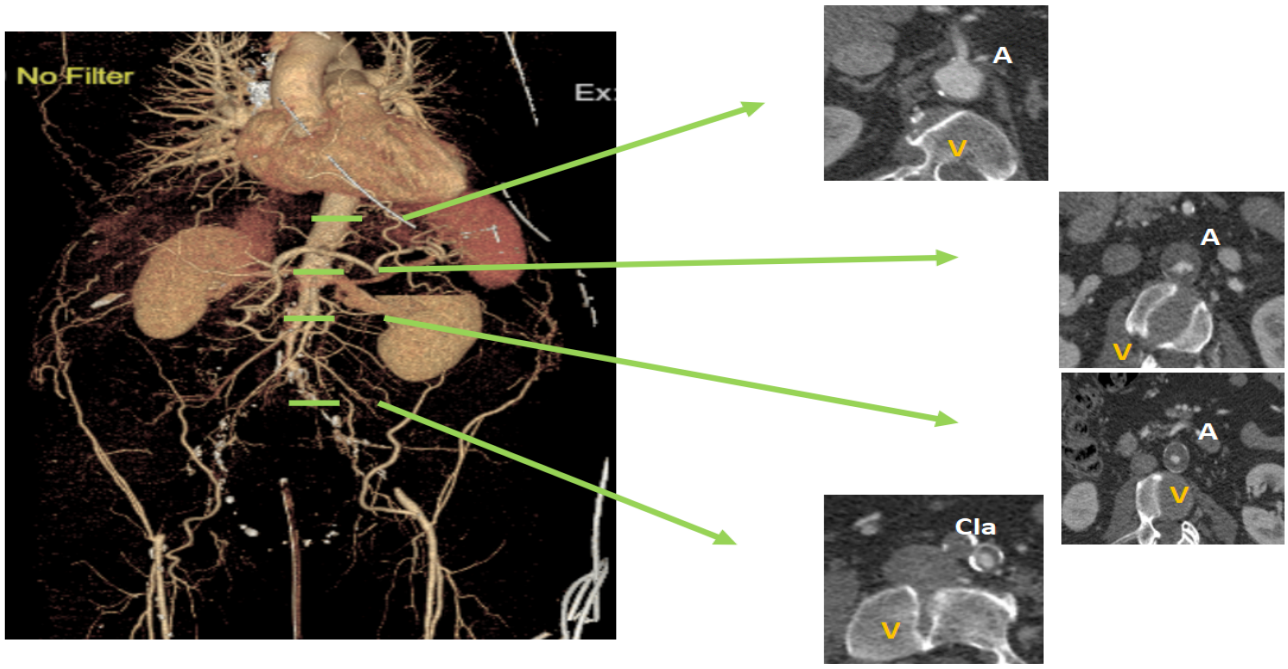

Figure 2. Extensive aortic stenosis due to a large circumferential atheromatous plaque which extended from the thoracic aorta to iliac-femoral artery (left side) and the corresponding transvers view on the right side.

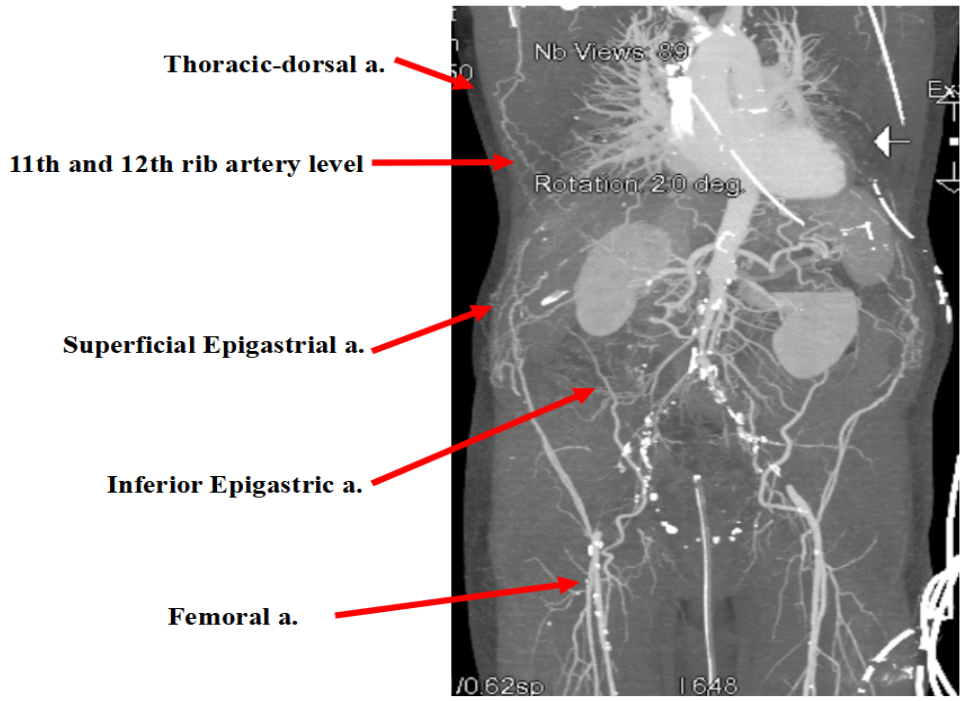

Figure 3. Recanalization of femoral arteries due to epigastric and intercostal arteries.

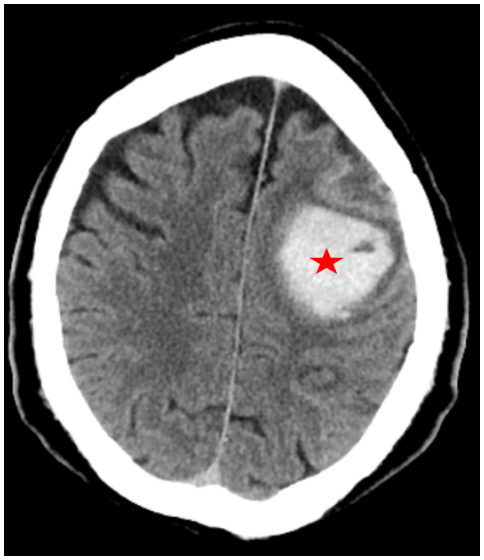

Figure 4. Left frontal cerebral hemorrhage (red star).