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CASE REPORT

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Elevated lipoprotein A in acute on chronic CTEPH with cardiogenic shock: a case report

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ABSTRACT

The natural history of most thrombi undergoes total or near total resolution, but the thrombi in chronic thromboembolic pulmonary hypertension (CTEPH) do not resolve completely and subsequently increase the pulmonary vascular resistance. We hypothesised that the elevated lipoprotein A in acute pulmonary embolism could lessen the autoresorption of the emboli and ultimately lead to CTEPH.

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1. Introduction

Chronic thromboembolic pulmonary hypertension (CTEPH) is the result of single or recurrent pulmonary emboli arising from the sites of venous thrombosis. Lipoprotein A can reduce thrombolysis and cause the failure of autoresorption of the pulmonary emboli. Chronic pulmonary emboli will eventually increase the pulmonary arterial pressure. Here, we report an interesting case where elevated lipoprotein A can be associated with CTEPH.

2. Case presentation

A 62-year-old man presented with a 1-week history of worsening shortness of breath and reduced exercise tolerance on early December 2019. He denied chest pain, cough or fever. Past medical history had a notable essential hypertension, diabetes mellitus, asthma and a remote history of hepatitis C s/p treatment. Allergies include penicillin. Family history is relevant for deep vein thrombosis in mother, sister and daughter. Social history is notable for half pack per day smoking history since teens, as well as prior opioid use disorder maintained on methadone. On admission exam: 98 F, 107/62, respiratory rate was 20, pulse rate was 96 and oxygen saturation was 96% on 3 L of oxygen. Patient was not in acute distress. Cardiac exam noted normal s1s2 and no murmurs rubs or gallops. Abdomen was soft and non-tender with no organomegaly appreciated. Patient had right-leg pitting edema and chronic venous skin changes in both legs. There were dorsalis pedis pulses bilaterally.

The differential diagnosis includes cute coronary syndrome, new onset heart failure, cardiac tamponade, pulmonary hypertension due to unrecognized CTEPH, community acquired pneumonia and acute pulmonary embolism.

The admission laboratory was significant for D-dimer 2,518 ng/ml (normal 0–243 ng/ml), troponin 0.031 (normal ≤0.010 ng/ml), BUN 21 mg/dl (normal 7–18 mg/dl), Creatinine 1.3 mg/dl (normal 0.7–1.2 mg/dl), ESR 10 (normal 0–22 mm/h), CRP 1 (normal <4 mg/l) and ferritin 113 (normal 15–150 ng/ml). Chest X ray was unremarkable. The EKG reported T wave inversion in V2 to V5. CT angiogram chest showed bilateral subsegmental pulmonary embolism and mild right-heart strain (Figure 1). The echocardiogram revealed no obvious valvular abnormalities, normal left-ventricle systolic function, mild right-ventricular hypertrophy, pulmonary arterial pressure 50–55 mmHg, severe right ventricular dilatation and dysfunction (Figure 2). The hypercoagulability work-up was remarkable for elevated lipoprotein A 461.7 nmol/L (normal <75 nmol/L) and elevated homocysteine level 28.7 umol/L (normal <15 umol/L).

The patient was admitted to medical floors and anticoagulated with low-molecular weight heparin. On hospital day 4, the patient remained oriented and hemodynamically stable but became lethargic with higher oxygen requirements; now low 90s on 4 liters nasal cannula. The labs on the same day were notable for AST 15,842 U/L (normal ≤40 U/L), ALT 5,624 U/L (normal ≤41 U/L), total bilirubin 3.9 mg/dL (normal ≤1.2 mg/dL), LDH 7,943 U/L (normal 135–225 U/L), INR 7.6, BNP 1,666 pg/mL (normal 0–100 pg/mL), creatinine 4.2 mg /dL, BUN 64 mg/dL and potassium 5.8 mol/L (normal 3.5–5.1 mol/L).

Decision was made to transfer to outside hospital for consideration of thrombolysis or embolectomy;

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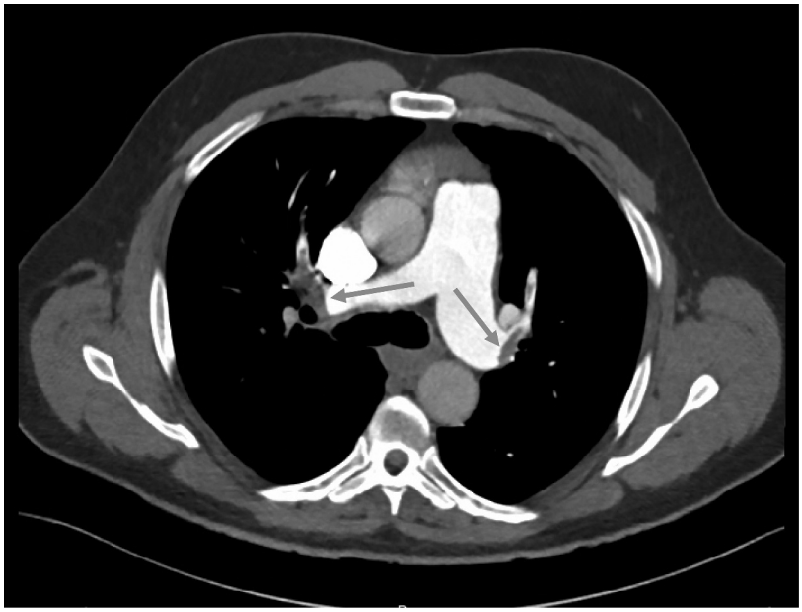

Figure 1.

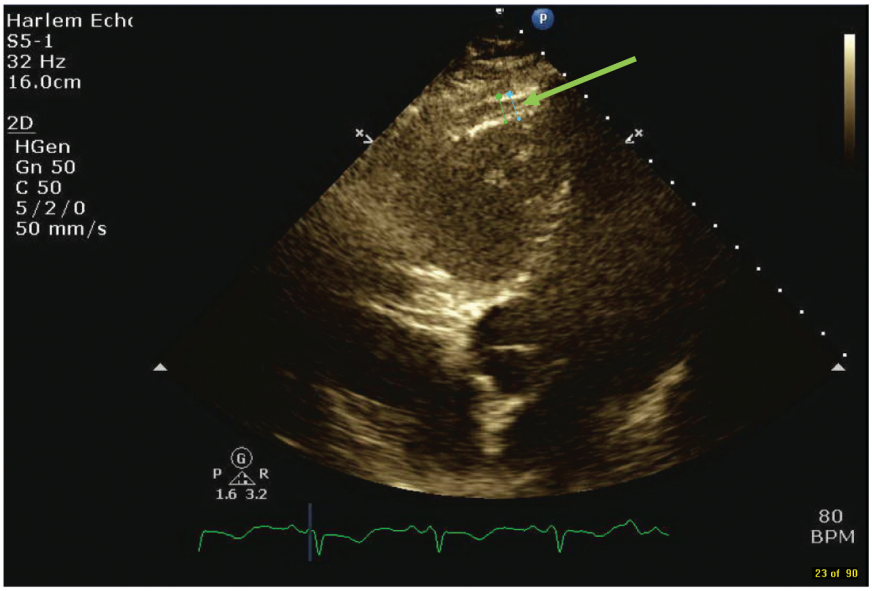

Figure 2.

however, patient deemed not to be a candidate due to worsening coagulopathy. Here, the patient was treated with IV heparin and pressor support. Supplemental oxygen was provided via facemask. A repeat echocardiogram showed normal left ventricle systolic function, dilated and hypokinetic right ventricle, and severe pulmonary hypertension with pulmonary artery systolic pressure of 73 mmHg. Nitric oxide use was started for severe pulmonary hypertension. Patient subsequently developed sepsis with thought given to pancreatitis as a source, and he was started on broad spectrum antibiotics with norepinephrine added to dobutamine. Continuous Veno-Venous Hemofiltration (CVVH) was started for volume overload. He was evaluated for Extracorporeal Membrane Oxygenation (ECMO) but was not a candidate due to severe multi-organ failure. Patient eventually suffered pulmonary endarterectomy (PEA) arrest 10 days after initial presentation.

3. Discussion

CTEPH is the result of single or recurrent pulmonary emboli arising from the sites of venous thrombosis [1]. The Sixth World Symposium on Pulmonary Hypertension (WSPH) defined pulmonary hypertension as a combination of mPAP >20 mmHg, pulmonary arterial wedge pressure $\leqslant$15 mmHg and pulmonary vascular resistance (PVR) $\geqslant$3 Wood Units. CTEPH is classified as group 4 pulmonary

hypertension. The precise incidence of CTEPH remains unknown because it is often underdiagnosed. The pooled incidence of CTEPH after symptomatic acute pulmonary embolism was reported to be 3.4% [2]. The pathophysiology of CTEPH is not well understood. The natural history of most thrombi undergoes total or near total resolution, but the thrombi in CTEPH do not resolve completely and subsequently increase the pulmonary vascular resistance [1]. The failure of thrombolysis could be due to the fact that the fibrin in patients with CTEPH is more resistant to lysis by plasminogen [3]. The mechanism of CTEPH is thought to be a result of the obstruction of organized clot in the proximal vessels and the formation of vascular remodeling in the distal pulmonary circulation [4]. The risks of CTEPH are increased in patients with previous pulmonary embolism, unprovoked pulmonary embolism, right-ventricular dysfunction, age above 60 years old, ventriculo-atrial shunts, non-O blood group, high level of clotting factor VIII, high level of von Willebrand factor, positive antiphospholipid antibody, positive lupus anticoagulant, thyroid replacement therapy, history of malignancy, chronic infections and chronic inflammations [4–6]. The clinical presentations of CTEPH are dyspnea on exertion, reduced exercise tolerance, chest pain, palpitation, cough, hemoptysis, legs swelling, dizziness, syncope, deoxygenation, loud pulmonic sound (P2), distended jugular veins and signs of right-heart failure [4]. Transthoracic echocardiogram can detect elevated pulmonary arterial pressure and right-heart dysfunction. CTEPH is diagnosed with ventilation/perfusion scan (V/Q scan) (sensitivity 100%, specificity 93.7% and accuracy 96.5%) or computed tomography pulmonary angiography (CTPA) (sensitivity 92.2%, specificity 95.2% and accuracy 93.9%) [7]. Normal V/Q scan essentially rules out CTEPH. CTPA is useful to distinguish other differential diagnoses of CTEPH. The differential diagnoses of CTEPH include angiosarcoma of pulmonary artery, pulmonary arteritis, fibrous mediastinitis and other venous occlusive diseases of the pulmonary artery [4,8]. Other tests such as magnetic resonance pulmonary angiography (MRA), digital subtraction angiography (DSA) or pulmonary angiography can also be used to diagnose CTEPH. PEA is the first-line treatment for patients with CTEPH. For patients who are not the candidates for PEA, medical therapy with riociguat, balloon pulmonary angioplasty or lung transplantation can be considered [2,4].

Our patient had remarkably elevated lipoprotein A and elevated homocysteine. Whether hyperhomocysteinemia or elevated lipoprotein A is associated with venous thromboembolism is controversial based on the current literature [9,10]. Lipoprotein A has been shown to have reduced thrombolysis [11,12]. Lipoprotein A is a complex plasma protein in which apolipoprotein B-100 is covalently linked by a disulfide bridge to a unique apolipoprotein (a). Lipoprotein A is structurally similar to plasminogen, and it competes the binding site of plasminogen on fibrin and diminishes its fibrinolytic activity [11]. Our patient most likely had undiagnosed single or multiple pulmonary emboli in the past because his initial echocardiogram reported pulmonary arterial pressure of 50–55 mmHg (normal ≤20 mmHg) and mild right-ventricular hypertrophy. On top of that, he probably suffered another acute pulmonary embolism or broken pulmonary emboli to distal pulmonary given that the repeat echocardiogram reported pulmonary arterial pressure 73 mmHg 6 days later. We hypothesis that the elevated lipoprotein A could have lessened the autoresorption of the emboli in his lungs and ultimately led to CTEPH. Morris et al. demonstrated that fibrin is resistant to lysis in patients with CTEPH [3].

4. Conclusion

There is no study between the association of lipoprotein A and CTEPH. We would like to present the case to raise the awareness of researchers and encourage more study to be done in the future. We would also like to propose a follow-up question for future researchers whether decreasing the elevated lipoprotein A in patient with acute pulmonary embolism can reduce the incidence of CTEPH if there is a possible association between elevated lipoprotein A and CTEPH.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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