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Veganism and hypercoagulable state-hyperhomocysteinemia presenting as pulmonary thrombo-embolism in a vegetarian living at high altitude

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Abstract: Hyperhomocysteinemia as a hypercoagulable state has been debatable, but when associated with other high-risk factors like severe vitamin B12 and folate deficiency, smoking, high altitude, and antiphospholipid syndrome can present with thromboembolism. Vegans are at high risk of severe B12 deficiency as the primary source is animal products. Right now, the total number of vegans, vegetarians, and all related categories, is close to 14 per cent of the world population. We here present a young vegan with severe B12 deficiency presenting with sub-massive thromboembolism.

Keywords: Hyperhomocysteinemia; Pulmonary Thromboembolism; Vegan; Vitamin B12 Deficiency

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1. Introduction

Hyperhomocysteinemia has been identified as an associated factor with increased chances of thrombosis and thromboembolic events.

The chances of these events increases when there is concomitant vitamin B12 and folate deficiency, residing at high altitude and associated hypercoagulable states like antiphospholipid syndrome (1). Vitamin B12 deficiency is well identified entity in veganism as the primary source of the vitamin is from animal source (2). Here we present an interesting case of a young male with self-adopted veganism with severe vitamin B12 deficiency and hyperhomocysteinemia presented with sub-massive pulmonary embolism.

2. Case presentation

A 30-year-old gentleman, residing in a hilly district of North India (average elevation of 369 meters/1,210 feet), non-smoker, belonging to ethical community that follows exclusive vegan diet to the emergency department with sudden onset and rapidly progressive breathlessness. The patient had no history of trauma, chest pain, fever, cough, coryza or expectoration or history of any recent vaccination. On physical examination, he had tachypnea with respiratory rate 28 breaths per minute and oxygen saturation of 92% with FiO2 of 40% supplied with venturi mask. He had oxygen saturation of 76% on room air. The blood pressure and pulse rate were 150/80 mmHg and 120 beats per minute, respectively. The auscultation of chest and heart was unremarkable and no clinical evidence of deep vein thrombosis in the lower limbs. The initial laboratory investigation revealed hemoglobin of 16 gram/dl with mean corpuscular volume of 112 fl, platelet count of 2 lakh/mcl. The renal function and liver function tests were within normal range. The cardiac troponin levels were within normal range, but B-type natriuretic peptide (BNP) was elevated to 350 pg/ml and D-dimer levels of 1540 ng/ml. Normal laboratory parameters for BNP and D-dimer was 0-100pg/ml and 0-240 ng/ml respectively. Electrocardiogram (EKG) showed sinus tachycardia with Q3T3 pattern (Figure 1) and the chest X-ray posteroanterior view was unremarkable. A Wells' score of 4.5 was calculated with moderate risk of pulmonary embolism (PE). The patient was subjected to point of care 2D-echocardiography which showed right ventricle systolic dysfunction, pulmonary artery hypertension, mild tricuspid regurgitation. The CT pulmonary angiography (CTPA) revealed partial thrombosis of the main pulmonary artery at the bifurcation extending into the left pulmonary artery origin and right pulmonary artery extending to the lower lobe branches (Figure 2).

Given the unprovoked nature and the clot burden, the extensive thrombophilia work up revealed no factor V Leiden mutation, protein C and protein S levels, anti-neutrophil antibody, anti β2 glycoprotein, anticardiolipin antibody and lupus anticoagulant within normal limits. The vitamin B12 level was low at 63 pg/ml (normal level- 200 to 600 pg/mL), normal serum folic acid level of 6.87ng/ml (normal level- 2.7 to 17.0 ng/mL) and hyperhomocysteinemia of level 22 micromol/L (normal level- <15μmol/L). The procoagulant work up was although sent during acute phase, however it was sent before starting any anticoagulant.

The patient was managed on low molecular-weight heparin (LMWH) and oxygen support and later switched to rivarox-

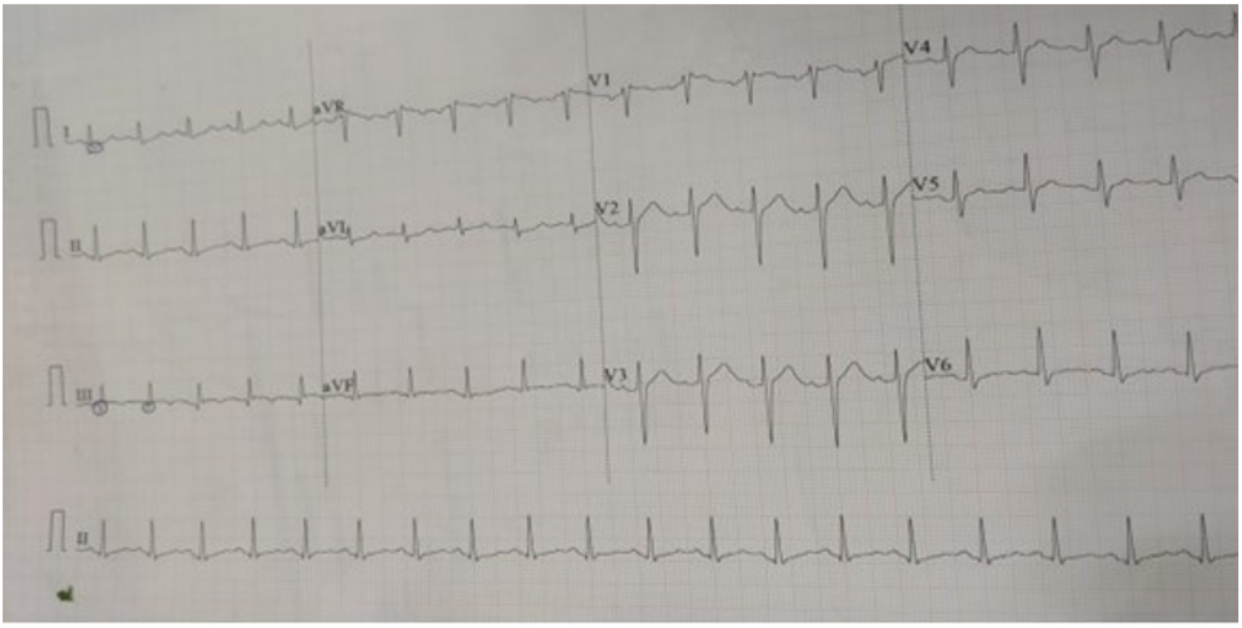

Figure 1 EKG showed sinus tachycardia with Q3T3 pattern

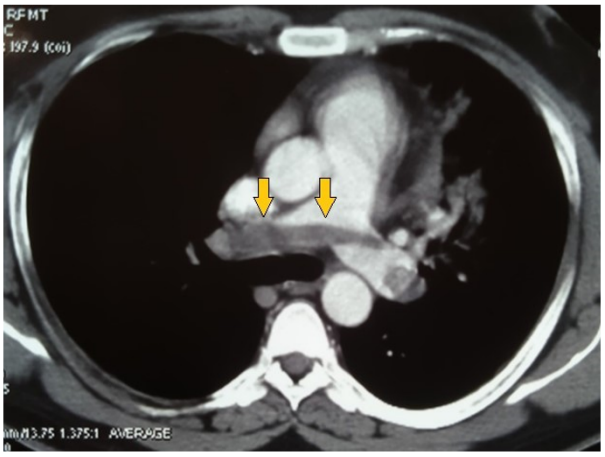

Figure 2 CT pulmonary angiography (CTPA) revealed partial thrombosis of the main pulmonary artery at the bifurcation extending into the left pulmonary artery origin and the right pulmonary artery (arrows)

aban. In addition to the anticoagulation, the patient was supplemented with vitamin B12 and folic acid. The patient symptomatically improved and respiratory distress resolved within a week and patient was counselled for taking the continuation of the anticoagulants and regular follow up.

3. Discussion

Methionine is converted to cysteine in the cells and homocysteine is an intermediate product is this pathway. The various steps in the pathway requires the vitamin B6 and B12 for the functioning of the enzymes required for transsulfuration and remethylation.

Hyperhomocysteinemia results when there is deficiency of vitamin B12 (dietary deficiency or pernicious anemia), vitamin B6, folate, mutation of enzyme methylenetetrahydrofolate reductase (MTHFR) or in tobacco smoking and chronic kidney disease (3). Prospective studies and meta-analysis done has found that elevated homocysteine levels are associated with unprovoked, first venous thromboembolic events in middle-aged and older women (<60 years) (4,5). In the recent years, social media and celebrities have brought the trend of veganism which is evident from the increase of about 580% in the google search for veganism in the last five years (6). Right now, the total number of vegans, vegetarians, and all related categories, is close to 14 percent of the world population.

Veganism has been followed by various ethical community especially in the southeast Asian countries like the Jain, Hindus, Buddhist community (6). Vitamin B12 is vitamin which has exclusive animal source and low vitamin B and hyperhomocysteinemia has been identified as independent risk factor for thromboembolism (7). High altitude has been hypothesized as one of associated factors with hyperhomocysteinemia to increased chances of thromboembolism as also present in our index case (1).

4. Conclusion

The veganism has led to severe vitamin 12 deficiency and the associated hyperhomocysteinemia and the high altitude in our index case may have contributed to the hypercoagulability which presented as multiple pulmonary emboli. Ultimately, this case illustrates the interplay of genetic, iatrogenic, environmental and social factors leading to metabolic derangements and thrombosis, as well as the wide differential in unprovoked PE. It also provides further evidence in favor of the association between hyperhomocysteinemia and

thrombosis. This also emphasizes the importance of checking of vitamin B12 levels in obligatory veganism so that the deficiency can be treated and supplementation of various micronutrients according to the recommended dietary allowance.

5. Declarations

5.1. Acknowledgement

None.

5.2. Authors' contribution

All authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

5.3. Conflict of interest

None.

5.4. Funding

None.

5.5. Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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