CASE REPORT

Biventricular thrombosis in a structurally normal heart at high altitude

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Accepted 9 May 2014

SUMMARY

We present a rare case of biventricular thrombus in a young patient with a structurally normal heart at high altitude, complicated with pulmonary embolism. Detailed evaluation revealed him to have protein S deficiency. Altered environmental conditions at high altitude associated with protein S deficiency resulted in thrombus formation at an unusual location; the same is discussed in this case report.

BACKGROUND

Exposure to high altitude (HA) has been observed to result in a hypercoagulable state, thus predisposing individuals to thromboembolic events.^{1 2} Environmental conditions at HA such as hypoxia; dehydration; enforced stasis and use of constrictive clothing due to low temperatures predispose individuals to the occurrence of thrombotic events.^{1 2} The condition gets further compounded in individuals with underlying hereditary thrombophilic disorders which may result in the occurrence of thrombosis at unusual sites.^{3 4} In this case report we present a case of biventricular thrombosis with pulmonary embolism and pulmonary infarction in a young patient with a structurally normal heart, posted at HA, who was detected to have protein S deficiency.

CASE PRESENTATION

A 31-year-old male patient residing in a HA (17 400 ft above mean sea level) area reported with acute onset fever, pleuritic chest pain over the left side, haemoptysis and breathlessness. Physical examination revealed him to be feverish (oral temperature 102°F) with tachycardia (110/min) and tachypnoea (respiratory rate 28/min); his SpO₂ on room air was 98%; general examination otherwise was unremarkable. Systemic examination revealed a dull note on percussion along with decreased breath sound in the left infrascapular region; examination of the other systems was normal.

INVESTIGATIONS

Investigations revealed normal haemogram and biochemical parameters. Sputum examination for cytology and culture was unremarkable. Chest radiograph (figure 1) revealed blunting of the left costophrenic angle along with a non-homogenous opacity in the left lower zone. He was seronegative for Venereal Disease Research Laboratory and HIV infection. Antiphospholipid IgG antibody was 5.43 GPL U/mL (0.5–10.0) and IgM antibody was 3.67 MPL U/mL (0.5–10.0). Antineutrophil cytoplasmic antibody and rheumatoid factor were negative. ECG

Figure 1 Chest radiograph revealed blunting of the left costophrenic angle along with a non-homogenous opacity in the left lower zone.

showed sinus tachycardia along with T wave inversion in the inferolateral leads. Two-dimensional (2D) echo revealed a thrombus at the origin of the left pulmonary artery with no flow (figure 2A). Contrast-enhanced CT of the chest showed left pulmonary artery thrombosis along with multifocal infarcts in the left lung (figure 2B). Colour Doppler flow imaging of the lower limbs and pelvis did not reveal any evidence of deep venous thrombosis. 99mTc-macroaggregated albumin lung perfusion scan revealed minimal perfusion of the left lung with normal perfusion of the right lung (figure 2C). In addition, thrombi were also noted at the apex of the right and left ventricles (figure 3). The right and left ventricular systolic/diastolic and valvular functions were normal. Interatrial septum was intact. The thrombi appeared to be shaggy and mobile with echogenic lucency suggesting fresh onset.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of prothrombotic states includes hereditary disorders such as protein C or S deficiency, antithrombin deficiency, activated protein C resistance due to factor V gene mutation, prothrombin gene mutation and dysfibrinogenemia. Acquired prothrombotic states include antiphospholipid syndrome and hyperhomocysteinaemia. The differential diagnosis of pulmonary embolism includes acute coronary syndrome, community-acquired pneumonia, pericarditis, exacerbation of chronic airway disease, pneumothorax and panic disorder.

TREATMENT

The morphological characteristics of the thrombi on echocardiogram combined with high intracavitary

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To cite: Malani S, Chadha D, Banerji A. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2014-204520

Figure 2 (A) Two-dimensional echocardiogram revealed thrombotic occlusion of the left pulmonary artery (LPA), the main pulmonary artery (MPA) was patent, (B) contrast-enhanced CT of the chest showed multifocal infarcts in the left lung, (C) 99mTc-macroaggregated albumin lung perfusion scan revealed minimal perfusion of the left lung with normal perfusion of the right lung.

motion resulting from normal contractility of the ventricle predisposed the patient to a high risk of embolisation. In view of this, the patient was subjected to thrombolytic therapy with alteplase 100 mg over 2 h followed by infusion of unfractionated heparin once thrombin time was less than twice the normal. The patient attained gratifying recovery following thrombolysis and became asymptomatic within 48 h. Repeat 2D-echo showed complete resolution of the left and right ventricle thrombus (figure 4). Oral anticoagulants were subsequently added and continued. The plan is to continue with anticoagulants for at least

6 months and to continue them lifelong in case of recurrence of thrombosis.

OUTCOME AND FOLLOW-UP

Procoagulant workup after 3 months on discontinuation of oral anticoagulants for 2 weeks showed protein S (PT-based functional assay) 41% (ref range 60–140%) and protein C 107.10% (ref range 70–140%); factor V Leiden mutation, methylene tetrahydrofolate reductase (MTHFR) gene mutation (C677T) and prothrombin gene G20210A mutation were not detected.

Figure 3 Two-dimensional echocardiogram in four-chamber view showing presence of thrombus in the left ventricular (LV) and right ventricular (RV) apex.

Figure 4 Two-dimensional echocardiogram in four-chamber view post-thrombolytic therapy showing complete resolution of the thrombi from both the ventricular chambers. RA, right atrium; RV, right ventricular; LA, left atrium; LV, left ventricular.

Serum homocysteine levels were 16.72 $\mu\text{mol/L}$, (ref range 5.46–16.20). Oral anticoagulants were reintroduced and continued. In the absence of hepatic disease, factor V Leiden mutation, HIV infection, vitamin K deficiency or co-administration of K antagonist, protein S deficiency noted in the present case is unlikely to be acquired. However, the hereditary nature of our patient's protein S deficiency could not be established as his family members have not been screened.

DISCUSSION

There are several case reports of biventricular intracardiac thrombi diagnosed by echocardiography, but to our knowledge, this finding in patients with normal biventricular systolic function has not been reported.

Vascular thrombosis is an uncommon peril of exposure to HA during travel or ascension of mountains.¹ The exact underlying mechanism of this is not known but it is postulated to be multifactorial resulting from altered coagulation cascade, haematocrit values and platelet reactivity.^{1 2} Platelet adhesiveness and aggregation has been shown to be increased at HA. In addition, hyperviscosity resulting from hypoxia mediated by increased red cell counts along with dehydration also increases the risk of thrombosis.^{1 2} Associated hereditary thrombophilic state may compound the above mentioned altered physiological state leading to an increased risk of thrombosis. Hereditary thrombophilia is suspected when thrombosis occurs in a young patient with a family history of similar disorder, if thrombosis is noted in unusual sites or if there is a history of recurrent thrombosis.^{3 4} Although venous thrombosis is commonly noted in these patients, there are case reports of arterial thrombosis involving the cerebral, visceral and coronary arteries and even the aorta.^{5–7} The unusual site of thrombosis noted in this patient was probably linked to double hit resulting from altered physiological state at HA and underlying protein S deficiency. In the absence of acquired causes of protein S deficiency, the possibility of having hereditary thrombophilia was high in the present case but the same could not be established in the absence of family studies. Protein S is a vitamin K-dependent plasma protein produced by the liver that inhibits blood coagulation by acting as a cofactor for protein C.^{3 4} It is an autosomal dominant inherited disorder with prevalence in the range of 0.03–0.13% causing spontaneous and recurrent episodes of deep venous thrombosis in young adults. Pulmonary embolism, as noted in the present case, occurs in about 38% of patients with protein S deficiency.^{3 8} The association of this deficiency with arterial thrombosis is rare, with a frequency of 6.3% compared with 61.7% noted for venous thrombosis.⁸ In the arterial bed, mesenteric and cerebral vessels are the most affected.⁸ Intracardiac thrombus in patients with protein S deficiency has been reported in the past but only among patients with underlying severe left ventricular dysfunction.^{9 10}

There is no accepted consensus regarding the management of intracardiac thrombi.^{8 11} Therapy is guided by efficacy of the antithrombotic agent and risk of bleeding or embolisation. Thrombolytic therapy has been used successfully but its effectiveness is dependent on the age of the thrombus, being most effective in fresh onset thrombi. Although a lot of thrombolytic agents have been tried, the more rapidly infused t-PA has been the most widely and successfully used thrombolytic agent.^{12 13} Surgery is preferred to medical treatment in patients with pedunculated or floating thrombi which have a high risk of embolisation. In the present case, thrombolytic therapy was preferred in view of echocardiographic features suggesting it to be a fresh

thrombus. The duration of oral anticoagulants in patients with hereditary thrombophilia is lifelong with recurrent spontaneous thrombosis. In patients where thrombosis is precipitated by transient risk factors a trial off these drugs can be given after a period of 6 months.^{4 8}

In summary, we have presented a case of intracardiac thrombosis in a structurally normal heart occurring at HA. Thrombosis at an unusual site in the young patient resulted possibly from an underlying protein S deficiency and altered physiology at HA.

Learning points

- ▶ Vascular thrombosis is an uncommon peril of exposure to high altitude.
- ▶ Environmental conditions at high altitude such as hypoxia; dehydration; enforced stasis and use of constrictive clothing due to low temperatures predispose individuals to the occurrence of thrombotic events.
- ▶ Hereditary thrombophilia should be suspected when thrombosis occurs in a young patient with a family history of similar disorder, if thrombosis is noted in unusual sites or if there is a history of recurrent thrombosis.
- ▶ Thrombolytic therapy can be used successfully for fresh intracardiac thrombus with good results.

Contributors SM was involved in patient care and preparation of the manuscript. DC was involved in preparation of the manuscript. AB was involved in patient care and revision of the manuscript.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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