

Case Report

Spontaneous Thrombus Formation in a Normal Left Ventricle Following Administration of Large Doses of Epoietin

ILIAS K. KARABINOS¹, SPYRIDON KOULOURIS², ATHANASIOS KRANIDIS², MAHMOUT EL ALI³, ANTONIOS MARSONIS², VASILIKI KOKKINO³, NIKOLAOS EXADAKTYLOS²

¹Cardiology Dept. Euroclinic of Athens, ²1st Department of Cardiology, ³Haematology Dept, "Evangelismos" Hospital, Athens, Greece

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We present a case of a thrombus formation within the left ventricle of a patient with a normal heart, who had previously been receiving high doses of erythropoietin for an inappropriately prolonged period.

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Address:
Ilias K. Karabinos

17 Solomou St.
11147 Galatsi
Athens, Greece
e-mail:
iliaskk@in.gr

A 60-year-old female with a known history of rheumatoid arthritis was initially admitted to the orthopaedic department of our hospital in order to have a total joint replacement of her right hip. Since the patient had chronic mild anaemia (haematocrit: 35%), previously attributed to rheumatoid arthritis, and she was to have an operation with expected heavy blood loss, she was started on 10000 U/day alpha epoietin subcutaneously for seven days before the procedure. Postoperatively, she had the standard prophylactic antithrombotic treatment with low molecular weight heparin, while remaining on alpha epoietin.

On the eighth postoperative day, the patient complained of atypical mild chest discomfort. Physical examination was normal. The electrocardiogram revealed sinus tachycardia. Chest X-ray examination was normal, while a lung perfusion scan was negative for pulmonary embolism. Trans-thoracic echocardiography through a very poor acoustic window revealed normal systolic function of the left ventricle without any regional hypokinesis, normal valves and a slight pericardial effusion. However, a mobile mass 3-4 cm in diameter was de-

tected, attached to the apex and the apical septum of the left ventricle and giving the impression of fresh thrombus (Figure 1, arrow).

The patient was transferred to the coronary care unit. The administration of alpha epoietin was discontinued and unfractionated heparin and aspirin were started. Full blood count revealed increased haematocrit (48%) compared to baseline, with normal white blood cell and platelet count. Serial measurements of serum cardiac markers during the next three days (CK-MB, myoglobin, troponin I) were negative for any myocardial necrosis. Thoracic and upper abdominal computed tomography examination confirmed the echocardiographic finding (Figure 2, arrow) and also revealed a spleen infarct. Plasma tests for protein C, protein S, von Willebrand and antithrombin III activity, and activated protein C resistance, were found to be normal. Serum levels of tissue plasminogen activator, plasminogen activator inhibitor-1 and homocysteine were also normal. Lupus anticoagulant test was negative. Serum levels of IgG and IgM antibodies against cardiolipins were found to be within the normal limits. During the following week, our pa-

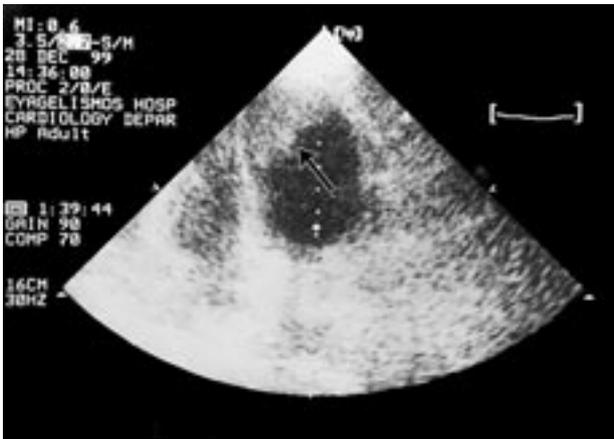


Figure 1. Transthoracic echocardiography (modified four-chamber view): a mobile mass attached to the apex, giving the impression of a fresh thrombus (arrow).

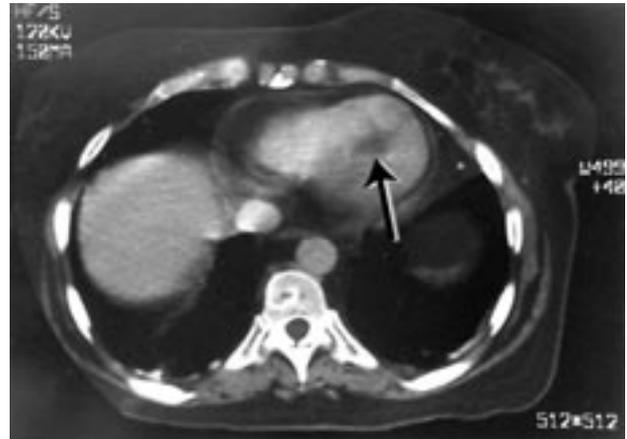


Figure 2. Thoracic computed tomography examination identified a fresh thrombus inside the left ventricle (arrow).

tient suffered two episodes of left femoral artery embolus which was removed surgically. The pathological examination documented that the embolus was of recent thrombotic origin. Serial daily transthoracic echocardiograms revealed a gradual impressive reduction of the size of the mass over time and it disappeared fifteen days later. The patient was then discharged and advised to take acenocoumarol for 6 months. Twenty-four months after discharge the patient remained asymptomatic without any evidence of left ventricular thrombus.

We followed up our patient with phone calls every 6 months for the next 3 years. She was doing well without any symptoms. Three years after her discharge she had another transthoracic echocardiogram, which documented a normal heart and the absence of any intraventricular thrombus (Figure 3).

Discussion

In the setting of a normal heart¹ the pathogenesis of left ventricular thrombus formation can be attributed to either a hypercoagulant state or an undetectable disorder of the endocardium. Apparently, our patient did not suffer a myocardial infarction or myocarditis, as was documented both by the normal electrocardiographic findings and the absence of any elevation of serum titres of cardiac markers. Moreover, no regional hypokinesis was detected during serial echocardiograms.

Inherited thrombophilia is a thrombogenic entity whose main causes include G1691A mutation of factor

V gene,² G20210A mutation of prothrombin gene, antithrombin deficiency, protein C and protein S deficiency. It has never been reported to provoke endocardial thrombus formation in a normal heart. Antiphospholipid antibody syndrome³ and hypereosinophilic syndrome⁴ have been reported as causes of left ventricular thrombus formation. However, our patient had all the relevant laboratory diagnostic tests within normal limits. In addition, autoimmune disorders have been suggested to promote thrombogenicity, while cases of left ventricular thrombus formation have been reported in Adamantiadis-Behcet's disease⁵ and lupus erythematosus,⁶ but never in rheumatoid arthritis.



Figure 3. Transthoracic echocardiography (modified four-chamber view) three years later: absence of any left ventricular thrombus.

The administration of high doses of alpha epoietin constitutes the most plausible explanation of intraventricular thrombus formation in our patient. The rapid increase of haematocrit following alpha epoietin administration and the resolution of the thrombus, which was facilitated by discontinuing the drug and giving heparin, support this hypothesis. It is well known that administration of high doses of alpha epoietin⁷ can lead to an increased blood viscosity and a subsequent hypercoagulant state. Alpha epoietin must be administered cautiously and haematocrit should not be expected to rise more than 30% above baseline within 10 days.

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