CARDIOVASCULAR MEDICINE

Splenectomy: a strong risk factor for pulmonary hypertension in patients with thalassaemia

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Objective: To determine the association between splenectomy and pulmonary hypertension in patients with thalassaemia with anaemia.

Design: Prospective cross-sectional study.

Methods: 68 patients with thalassaemia, who had a haemoglobin concentration of less than 100 g/l, were recruited into this study. Echocardiography was performed before clinical data were reviewed. Pulmonary artery pressure was estimated by measuring the systolic transtricuspid pressure gradient from tricuspid regurgitation and adding it to the right atrial pressure, which was estimated by the response of the inferior vena cava to inspiration. Pulmonary hypertension was defined as systolic pulmonary artery pressure > 35 mm Hg. History of splenectomy and other clinical data were compared between patients with and without pulmonary hypertension.

Results: 29 patients had pulmonary hypertension and 39 did not. Patients with pulmonary hypertension had significantly more nucleated red blood cells and higher platelet counts, and a higher prevalence of splenectomy (75.8% v 25.6%, odds ratio 9.1, 95% confidence interval 3.0 to 27.7). In multivariate analysis, splenectomy was the only factor significantly related to pulmonary hypertension.

Conclusion: Splenectomy is a strong risk factor for pulmonary hypertension in patients with thalassaemia.

Heart disease is a major cause of mortality and morbidity in patients with thalassaemia after the first decade of life,¹ despite improved prognosis with iron chelation. The common cardiac abnormalities that have been reported in patients with thalassaemia are cardiac hypertrophy, ventricular systolic dysfunction, pericarditis and pulmonary hypertension.²⁻³

Pulmonary hypertension is found in about 59–75% of patients with thalassaemia and can be the leading cause of heart failure in these patients.²⁻⁵ Factors affecting pulmonary artery pressure include high cardiac output caused by anaemia, left ventricular (LV) systolic dysfunction, chronic pulmonary haemosiderosis, recurrent respiratory tract infections, hypoxaemia and pulmonary fibrosis.⁵⁻⁶ Another proposed cause is the hypercoagulable state with thrombotic obstruction of the pulmonary arteries.⁷⁻⁹ Although most of the reported patients with thalassaemia with pulmonary hypertension were splenectomised,²⁻⁵⁻⁶ non-splenectomised patients can also have pulmonary hypertension whereas some of them have normal pulmonary arterial pressure.² The relationship between splenectomy and pulmonary hypertension in thalassaemia has not been clearly established. The purpose of this study was to explore this relationship.

METHODS

Patients

We studied patients with thalassaemia with haemoglobin concentration less than 100 g/l who were being treated at the haematology outpatient clinic from January 2000 to December 2001. They were free from cardiac symptoms and had no evidence of clinical heart failure or signs of chronic liver disease. None were taking cardioactive drugs at the time of examination. We excluded patients with significant valvular heart disease, congenital heart disease, more than mildly diminished LV systolic function (LV ejection fraction (LVEF) less than 40%), documented cardiac arrhythmia, known risk factors for secondary pulmonary hypertension (chronic pulmonary diseases, asthma, chronic smoking and

recurrent pulmonary infections) and poor echocardiographic imaging. The study protocol was approved by the institutional research ethics committee and was carried out in accordance with the Declaration of Helsinki. All participants gave written informed consent.

Study protocol

One hundred patients with thalassaemia who regularly visited our adult haematology clinic were screened. All patients without exclusion criteria were examined by echocardiography, other than those with poor echocardiographic imaging. Echocardiographic examinations were done by only one investigator, who was kept blinded to the patient's clinical information. Splenectomy status was hidden before and during echocardiographic examinations by covering the upper abdomen. Clinical data including additional history, complete physical examination and oxygen saturation by pulse oximetry were recorded after the echocardiographic examination was completed.

Echocardiography

Complete two-dimensional, M mode and Doppler (pulsed wave, continuous wave and colour) echocardiography was performed at rest with a Sonos 5500 (Hewlett Packard, Andover, Massachusetts, USA) equipped with 2.5–3.5 MHz transducers. LV dimensions were measured according to the recommendations of the American Society of Echocardiography. Modified Simpson's rule was used to measure the LVEF.¹⁰ Doppler flow of the mitral valve was recorded by pulsed wave Doppler with the sampling volume at the tips of the mitral valve. Peak early diastolic flow velocity (E velocity), early flow deceleration time, peak flow velocity during atrial contraction (A velocity) and the ratio of E to A velocity (E:A ratio) were measured to assess ventricular diastolic function.

In a given patient, a tricuspid regurgitation jet was sought from all available mid-precordial and apical positions until a flow signal with the maximum spectral representation of the

highest velocities could be obtained. Peak velocity was then recorded from a holosystolic regurgitant jet. Intravenously agitated saline injection into the antecubital vein was also used in selected cases to obtain measurable tricuspid regurgitation. If a clear holosystolic regurgitant jet could not be obtained, the patient was excluded from the study. From the maximum velocity (V) of the regurgitant jet, the systolic pressure gradient (ΔP) between the right ventricle and right atrium was calculated by the modified Bernoulli equation ($\Delta P = 4V^2$). Right atrial pressure was estimated by the response of the inferior vena cava diameter to inspiration. Right atrial pressure was assumed to be 5 mm Hg if the inferior vena cava completely collapsed with inspiration, 10 mm Hg if the inferior vena cava diameter decreased more than 50% during inspiration, and 15 mm Hg if it decreased less than 50%. If the inferior vena cava diameter was larger than 2.5 cm and reduced by less than 50% during inspiration, right atrial pressure was assumed to be 20 mm Hg.¹⁰ Adding the transtricuspid gradient to the mean right atrial pressure provided the right ventricular systolic pressure or peak systolic pulmonary arterial pressure in the absence of right ventricular outflow tract obstruction.^{10–11} Pulmonary hypertension was defined as a systolic pulmonary artery pressure greater than 35 mm Hg.¹²

Statistical analysis

The estimated sample size was calculated from the result of our pilot study performed between October and November 2000. At least 68 patients were required to test this hypothesis, with a predicted confidence interval (CI) of at least 95%. Data were statistically analysed with the SPSS V.10.0 (SPSS Inc, Chicago, Illinois, USA) statistical software package. Continuous variables were expressed as mean (SD). Student's t test and the χ^2 test were used to compare variables between groups. Continuous data were compared between the three groups by analysis of variance. Multivariate regression analysis was used to identify potential relationships between variables.

RESULTS

Of the 100 patients initially recruited from the haematology outpatient clinic, 32 were excluded. The reasons for exclusion were inadequate holosystolic regurgitant flow in 30 patients, significant pulmonary valvular stenosis in one patient, and a history of chronic smoking in one patient. Among the 32 excluded patients, 28 were non-splenectomised and four were splenectomised. Of the remaining 68 patients, 25 were men and 43 were women ranging in age from 15–58 years. The haemoglobin concentration varied from 36 to 99 (mean 65) g/L. Forty had β thalassaemia/haemoglobin E disease, 13 had homozygous β thalassaemia and 15 had haemoglobin H disease. The history of blood transfusion in the previous 12 months was completely recorded for 39 of 68 patients (57.4%). The amount of blood transfused during the 12 months varied from 0–9 units (mean 1.9 (2.9) units). The average number of units of blood transfused was 4.85 (1.4) for patients with homozygous β thalassaemia and 1.6 (1.1) for patients with β thalassaemia/haemoglobin E disease. None of the patients with haemoglobin H disease received a blood transfusion. Iron chelation was not given to any patients. Mean LVEF was 64.5% (range 52.4–79.0%). Of the 68 patients, 29 (43%) had significant pulmonary hypertension. None of the patients had clinical evidence of thromboembolism such as deep vein thrombosis or pulmonary embolism.

Clinical characteristics and pulmonary artery pressure differences

Among 68 patients, 32 (47%) underwent splenectomy. Table 1 compares clinical characteristics between splenectomised and

non-splenectomised patients. All patients who underwent splenectomy had either homozygous β thalassaemia or β thalassaemia/haemoglobin E disease. None of the patients with haemoglobin H disease underwent splenectomy. All of the splenectomised patients underwent splenectomy for treatment of hypersplenism at a mean age of 10.8 (6.8) years. The splenectomised patients had higher nucleated red blood cell counts and higher platelet counts than non-splenectomised patients (316.7 (188) ν 11.7 (58) cells/100 white cells, $p < 0.001$; and 593 (277) ν 271 (146) $\times 10^9$ cells/L, $p < 0.001$ respectively). A higher percentage of splenectomised patients (10/17, 59%) than of non-splenectomised patients (4/22, 18%; $p = 0.009$) received a blood transfusion. Splenectomised patients received more blood transfusions during the preceding 12 months (3.65 (3.5) ν 0.5 (1.3) units, $p = 0.002$). Despite being younger, the splenectomised patients had significantly higher pulmonary artery pressure and lower oxygen saturation than non-splenectomised patients (43.3 (20.5) ν 28.9 (8.3) mm Hg, $p = 0.001$; and 94.7 (2.6) ν 96.5 (1.9)%, $p = 0.009$, respectively).

Although LVEF was similar in both splenectomised and non-splenectomised patients, diastolic function differed. The mitral valve E:A ratio was higher in splenectomised than in non-splenectomised patients (1.55 (0.5) ν 1.15 (0.3), $p = 0.001$). Significantly more splenectomised than non-splenectomised patients (37% ν 7.4%, $p = 0.023$) had restrictive LV filling (mitral valve E:A > 1.5 and deceleration time < 160 ms).¹³

Factors influencing pulmonary hypertension

Table 2 shows clinical and echocardiographic findings in patients with and without pulmonary hypertension. There were 29 patients with and 39 patients without pulmonary hypertension. In the univariate analysis, these two groups did not differ in age, sex and oxygen saturation. Haemoglobin typing and haemoglobin concentrations did not differ. A higher percentage of patients (8/15, 53%) with than without pulmonary hypertension (6/24, 25%) received blood transfusion. Patients with pulmonary hypertension received more blood transfusions during the preceding 12 months than those without pulmonary hypertension (3.53 (3.7) ν 0.88 (1.7) units, $p = 0.018$). LVEF was not different between the two groups. The mitral valve E:A ratio was higher in patients with than in patients without pulmonary hypertension (1.5 (0.5) ν 1.19 (0.4), $p = 0.013$). The percentage of patients with restrictive LV filling was not different between the two groups (29.6% ν 14.8%, $p = 0.118$). Patients with pulmonary hypertension had significantly more nucleated red blood cells and higher platelet counts (290 (320) ν 54 (112) cells/100 white cells, $p = 0.001$; and 530 (260) ν 335 (251) $\times 10^9$ cells/L, $p = 0.003$, respectively). The prevalence of splenectomy was higher in patients with pulmonary hypertension than in patients without pulmonary hypertension (75.8% ν 25.6%, $p < 0.001$). The odds ratio for splenectomy in patients with pulmonary hypertension was 9.1 (95% CI 3.0 to 27.7), compared with the patients without pulmonary hypertension. In multivariate analysis, the only significant factor associated with development of pulmonary hypertension was splenectomy ($p < 0.001$).

Determinants of pulmonary hypertension in splenectomised patients

Comparing splenectomised patients who developed pulmonary hypertension with those splenectomised who did not, the only difference in the variables was higher nucleated red blood cells in those who developed pulmonary hypertension (table 3).

Table 1 Clinical and echocardiographic characteristics of splenectomised and non-splenectomised patients

	Splenectomy (n = 32)	No splenectomy (n = 36)	p Value
Clinical findings			
Age (years)	22.8 (7.8)	35.2 (12.2)	<0.001
Women	66% (n = 21)	61% (n = 22)	0.70
Type of thalassaemia			
Homozygous β thalassaemia	10	3	
β thalassaemia/Hb E disease	22	18	<0.001
Hb H disease	0	15	
Hb (g/l)	61 (16)	68 (19)	0.10
NRBCs (cells/100 WCs)	316 (188)	11.7 (58)	<0.001
Platelet count ($\times 10^9$ cells/l)	593 (277)	271 (146)	<0.001
Blood transfusion (units)	3.65 (3.5)*	0.55 (1.3)†	0.002
Oxygen saturation (%)	94.7 (2.6)	96.5 (1.9)	0.009
Echocardiographic findings			
PAP (mm Hg)	43.3 (20.5)	28.9 (8.3)	0.001
LVEF (%)	64.2 (7.0)	64.7 (6.8)	0.78
LVEDd (mm)	50.1 (11.8)	51.8 (5.0)	0.48
LVESd (mm)	33.4 (6.8)	33.1 (5.0)	0.34
MPAd (mm)	22.1 (5.7)	19.3 (3.3)	0.02
RVd (mm)	35.8 (6.2)	31.8 (7.3)	0.04
Mitral valve E:A ratio	1.55 (0.5)	1.15 (0.3)	0.001
Mitral valve DT (ms)	155.8 (38.2)	163.5 (31.4)	0.61

Continuous variables are mean (SD).

*n = 17; †n = 22.

DT, deceleration time; Hb, haemoglobin; LVEDd, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVESd, left ventricular end systolic diameter; MPAd, main pulmonary artery diameter; NRBCs, nucleated red blood cells; PAP, pulmonary artery pressure; RVd, right ventricular diameter; WCs, white cells.

DISCUSSION

Impaired LV systolic and diastolic function have been investigated in patients with thalassaemia.^{14–18} A few studies have shown that right ventricular dysfunction may be more prevalent and present earlier than LV dysfunction, and it has been speculated that pulmonary hypertension may be the cause.^{14–19} Our study showed that of 68 patients with normal LV systolic function and measurable tricuspid regurgitation, 29 (43%) had significant pulmonary hypertension. This finding is consistent with a recent report, which also found that 59.1% of patients with thalassaemia intermedia with

normal LV contractility had significant pulmonary hypertension.² In that study, the role of splenectomy as a cause of the development of pulmonary hypertension was obscured by the confounding effect of age. To our knowledge, our study is the first to show a strong relationship between splenectomy and the development of pulmonary hypertension in patients with thalassaemia. Our splenectomised patients had significantly higher systolic pulmonary artery pressure than non-splenectomised patient (43.3 (20.5) v 28.9 (8.3) mm Hg, $p = 0.001$) despite their younger age (22.8 (7.8) v 35.2 (12.2), $p < 0.001$).

Table 2 Clinical and echocardiographic findings in patients with and without pulmonary hypertension

	Pulmonary hypertension (n = 29)	No pulmonary hypertension (n = 39)	p Value
Clinical findings			
Age (years)	26.5 (10.2)	31.6 (12.9)	0.50
Women	59% (n = 17)	67% (n = 26)	0.50
Type of thalassaemia			
Homozygous β thalassaemia	8	5	
β thalassaemia/HbE disease	18	22	0.07
Hb H disease	3	12	
Hb (g/l)	61 (17)	67 (18)	0.18
NRBCs (cells/100 WCs)	290.2 (320.5)	54.2 (111.9)	0.001
Platelet count ($\times 10^9$ cells/l)	530 (260)	336 (251)	0.003
Blood transfusion (unit)	3.53 (3.7)*	0.88 (1.7)†	0.018
Oxygen saturation (%)	95.1 (2.8)	96.1 (2.0)	0.16
Splenectomy	75.8%	25.6%	<0.001
Echocardiographic findings			
LVEF (%)	64.7 (7.4)	64.2 (6.4)	0.78
LVEDd (mm)	49.4 (11.4)	52.2 (6.8)	0.12
LVESd (mm)	33.1 (7.2)	33.3 (4.7)	0.22
MPAd (mm)	22.9 (5.4)	19.0 (3.6)	0.002
RVd (mm)	35.5 (8.7)	31.9 (5.5)	0.10
Mitral valve E:A ratio	1.50 (0.5)	1.19 (0.4)	0.013
Mitral valve DT (ms)	160.6 (34.2)	160.8 (33.9)	0.985

Continuous variables are mean (SD).

*n = 15; †n = 24.

DT, deceleration time; Hb, haemoglobin; LVEDd, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVESd, left ventricular end systolic diameter; MPAd, main pulmonary artery diameter; NRBCs, nucleated red blood cells; RVd, right ventricular diameter; WCs, white cells.

Table 3 Clinical and echocardiographic findings in splenectomised patients with and without pulmonary hypertension

	Pulmonary hypertension (n = 23)	No pulmonary hypertension (n = 9)	p Value
Clinical findings			
Age (years)	23.54 (8.0)	21.3 (7.4)	0.51
Women	70% (n = 16)	56% (n = 26)	0.65
Type of thalassaemia			
Homozygous β thalassaemia	7	3	0.87
β thalassaemia/Hb E disease	16	6	
Hb H disease	0	0	
Hb (g/l)	61 (18)	62 (12)	0.94
NRBCs (cells/100 WCs)	382.8 (308.4)	155.1 (41.7)	0.009
Platelet count ($\times 10^9$ cells/l)	631 (252)	443 (335)	0.20
Blood transfusion (units)	2.80 (2.7)*	4.00 (3.8)†	0.53
Oxygen saturation (%)	94.7 (2.7)	94.7 (1.9)	0.98
Time since splenectomy (years)	12.1 (7.3)	11.6 (4.5)	0.82
Echocardiographic findings			
LVEF (%)	64.5 (7.5)	63.5 (5.9)	0.73
LVEDd (mm)	48.4 (12.0)	54.7 (10.6)	0.17
LVESd (mm)	32.9 (6.7)	34.5 (7.4)	0.50
MPAd (mm)	23.2 (5.9)	19.4 (4.4)	0.09
RVd (mm)	35.2 (6.0)	36.7 (6.8)	0.63
Mitral valve E:A ratio	1.43 (0.4)	1.58 (0.5)	0.510
Mitral valve DT (ms)	157.35 (30.8)	155.75 (38.1)	0.885

Continuous variables are mean (SD).

*n = 5; †n = 12.

DT, deceleration time; Hb, haemoglobin; LVEDd, left ventricular end diastolic diameter; LVEF, left ventricular ejection fraction; LVESd, left ventricular end systolic diameter; MPAd, main pulmonary artery diameter; NRBCs, nucleated red blood cells; RVd, right ventricular diameter; WCs, white cells.

We have also studied other factors that can influence pulmonary artery pressure in our patients. Regular blood transfusion and iron chelation had been reported to prevent pulmonary hypertension in thalassaemia major and to lower the incidence of splenectomy.^{13–20} Contrary to this, we found that the patients with pulmonary hypertension received more blood transfusion than the patients without pulmonary hypertension. Moreover, we found that the splenectomised patients had more blood transfusion than non-splenectomised patients. This higher level of blood transfusion may imply more severe disease in splenectomised patients. The lower intensity and the inadequacy of blood transfusion shown by lower haemoglobin concentration were evident in this studied population. These observations may account for the discordant findings of the effect of blood transfusion on pulmonary artery pressure in our study compared with previous reports. However, owing to a lack of blood transfusion data for all our patients, we did not incorporate blood transfusion into multivariate analysis.

Although anaemia can affect cardiac output and cause pulmonary hypertension in the similar level of pulmonary vascular resistance, we did not observe this effect in our study. Owing to a wide range in the haemoglobin concentration, we stratified haemoglobin into tertiles to study the effect of anaemia on pulmonary artery pressure. Mean pulmonary artery pressure was 36.0 (14.7) mm Hg in patients with a haemoglobin concentration between 36 and 57 g/l, 38.3 (19.5) mm Hg in patients with a haemoglobin concentration between 57 and 79 g/l, and 32.0 (16.1) mm Hg in patients with a haemoglobin concentration between 79 and 99 g/l. There was no statistical difference between the three groups ($p > 0.05$).

LV systolic and diastolic dysfunction can contribute to pulmonary hypertension, but these factors seem to be less dominant in patients with thalassaemia. Du *et al*⁴ showed that pulmonary systolic pressure in patients with thalassaemia major correlated with LV systolic and diastolic dysfunction. But 77% and 55% of their patients with pulmonary hypertension had normal systolic and diastolic function, respectively.⁴ Moreover, pulmonary artery pressure also

correlated with age and the amount of blood transfusion. On the contrary, the other studies of patients with thalassaemia intermedia² and well-treated patients with thalassaemia major¹³ found no correlation between systolic or diastolic LV dysfunction and pulmonary artery pressure. Consistently, LV systolic function was not different between patients with and without pulmonary hypertension in our study. Patients with pulmonary hypertension had a higher mitral valve E:A ratio than did patients without pulmonary hypertension. However, the percentage of patients with a restrictive filling pattern was not different between the two groups. Therefore, LV ventricular systolic and diastolic dysfunction is unlikely to be a major contributing factor to pulmonary hypertension in our study.

The possible mechanisms leading to pulmonary hypertension after splenectomy may involve nucleated red blood cells, platelets and the coagulation cascade. Abnormalities of these entities have been well described in patients with thalassaemia. Eldor *et al*²¹ reported a shorter life span of platelets in both splenectomised and non-splenectomised patients with thalassaemia than in non-thalassaemic splenectomised patients. There is also evidence of endogenous platelet activation in patients with thalassaemia.^{21–22} Although thrombocytosis associated with splenectomy may have a role in favouring a thrombotic tendency, there is some evidence against it being the major factor. Specifically, thrombocytosis was maximal in the early post-splenectomy phase, but thrombosis was not seen.²³

With regard to red blood cells, thalassaemic red blood cells can induce thromboembolic complications.^{24–31} These cells have increased membrane expression of anionic phospholipids that accelerate thrombin generation, which in turn activates platelets.^{26–28–30} The high oxidative state of these red blood cells, due to iron accumulation in the membrane, induces a similarly high oxidative state in platelets leading to their activation.^{24–25–29–32} Furthermore, rheological abnormality of thalassaemic red blood cells favours their aggregation.²⁷ In addition to mature thalassaemic red blood cells, nucleated red blood cells have been studied for their effect on the coagulation system. Garozzo and colleagues³³ reported the

presence of adhesion molecules (intercellular adhesion molecules 1, 2 and 3, platelet-endothelial cell adhesion molecule 1, and vascular cell adhesion molecule 1) on nucleated red blood cells of patients with thalassaemia intermedia and major. This may well contribute to the hypercoagulable state seen in these patients.

The aforementioned mechanisms are likely to be intensified in splenectomised patients with thalassaemia, as they have more abnormal red blood cells and red blood cell precursors than their non-splenectomised counterparts.²³ We postulate that this may be the predominant mechanism responsible for splenectomy-induced pulmonary hypertension, as it would favour more pulmonary thrombosis and subsequent increased pulmonary vascular resistance.

In a previous study by Du *et al*⁴ of a group of patients with poorly treated thalassaemia major, two thirds of patients had undergone splenectomy and almost all of them had pulmonary hypertension at a mean age of 12 years. Similarly, our patients had a low haemoglobin concentration and high rate of splenectomy, which may reflect inadequate treatment that eventually led to pulmonary hypertension. In contrast, according to two recently published reports, well-treated thalassaemia major populations have a low incidence of both splenectomy and pulmonary hypertension. Moreover, intensification of transfusion had been shown to reduce hypercoagulability and reduce pulmonary artery pressure in splenectomised patients with thalassaemia intermedia.³⁴ Regular blood transfusions and iron chelation to prevent splenomegaly and consequent splenectomy may well be the key to preventing pulmonary hypertension in patients with thalassaemia. Nevertheless, there are risks of blood transfusion that should be considered in the therapeutic approach.

Study limitations

The study exclusion rate was high and could have caused a significant bias. However, the main reason for exclusion was inadequate holosystolic tricuspid regurgitation (30 of 32 excluded patients), which tends to occur in patients with lower pulmonary artery pressure. Most of the excluded patients (28 of 32 excluded patients) were non-splenectomised, so the effect of excluding them, if there was any, would minimise rather than maximise the relationship between splenectomy and pulmonary hypertension. Another limitation was the relatively small study population, which may have been a confounding factor in the multivariate analysis. Additionally, inadequate blood transfusion data could have compromised the result of the study. Blood transfusion seemed to be higher in the splenectomised and pulmonary hypertensive patients and this may reflect more severe disease with the greater possibility of developing pulmonary hypertension.

Conclusion

Our findings indicate that splenectomy is a strong risk factor for pulmonary hypertension in patients with thalassaemia. Regular blood transfusions and iron chelation to prevent splenomegaly and consequent splenectomy may well be the key to preventing pulmonary hypertension in this patient group. Further studies evaluating the role of antithrombotic and chronic intensive blood transfusion in lowering pulmonary artery pressure in splenectomised patients with thalassaemia are warranted.

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IMAGES IN CARDIOLOGY

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Multiple intracardiac thrombi in a patient with dilated cardiomyopathy

Two dimensional transthoracic echocardiography of a modified apical four chamber view showing multiple mobile clots in both the left and right ventricles on admission (A) and complete resolution of the thrombi in left ventricle with only a small residual thrombus in the right ventricle after 10 days of anticoagulation treatment (B).

The occurrence of multiple biventricular thrombi in patients with dilated cardiomyopathy is extremely rare. A 47-year-old man with a history of 25 years of cocaine and amphetamine use presented with recent onset of weakness, palpitations, persistent dry cough and shortness of breath on minimal exertion. At admission, physical examination revealed sinus tachycardia with pulse 100/min, blood pressure 94/64 mm Hg, elevated jugular venous pressure, bilateral basal rales, S3 gallop, 2/6 midsystolic murmur at the apex, and mild hepatomegaly. Relevant laboratory tests were normal (including troponin I) except for an elevated natriuretic peptide (578 pg/ml, normal < 100 pg/ml).

Chest x-ray showed cardiomegaly, patchy bilateral pulmonary infiltrates (pulmonary congestion with suspected superimposed pneumonia) and a small pleural effusion. Abdominal ultrasound revealed mild hepatomegaly with dilatation of hepatic veins and inferior vena cava. Blood cultures and serology for HIV and hepatitis were negative. The ECG showed sinus rhythm and poor R wave progression in leads V1–V4. Echocardiography demonstrated a dilated left ventricle with severely depressed left ventricular function (ejection fraction –15%) with global biventricular hypokinesis, right ventricle dysfunction, severe mitral and severe tricuspid valve regurgitation and mobile multiple clots in both the left and right ventricles (to view video footage visit the *Heart* website—<http://www.heartjnl.com/supplemental>). Adenosine single photon emission computed tomography (SPECT) was performed to exclude obstructive coronary artery disease and was negative for ischaemia. The evaluation for hypercoagulable disorder was negative. The working diagnosis was dilated cardiomyopathy possibly related to amphetamine and/or cocaine use with recent onset of congestive heart failure, multiple intracardiac thrombi and bilateral pneumonia. Conventional treatment for congestive heart failure was started. Antibiotics were given for bilateral pneumonia. Intravenous heparin was administered for the multiple intracardiac thrombi.

After seven days of heparin the patient was put on warfarin and the echocardiogram on the 10th day of treatment showed resolution of the clots in the left ventricle and only a small residual clot in the right ventricle. There was no evidence of embolism on physical examination or on chest and brain CT. The patient's general condition stabilised and the symptoms of heart failure improved. Biventricular pacing and automatic implantable cardioverter-defibrillator implantation are planned after complete clot resolution.

In this patient the severe biventricular dysfunction most likely led to the formation of multiple biventricular thrombi and the thrombi resolved on anticoagulation treatment.

To view video footage visit the *Heart* website—<http://www.heartjnl.com/supplemental>

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