Disseminated Intravascular Coagulation with Congestive Heart Failure and Left Ventricular Thrombus: A Case Report with Literature Review of 7 Cases

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
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Patient:	**Male, 55**
Final Diagnosis:	**Disseminated intravascular coagulation**
Symptoms:	**Leg pain • short of breath • swelling legs**
Medication:	**—**
Clinical Procedure:	**—**
Specialty:	**Cardiology**

Objective:	**Unusual clinical course**
Background:	Coagulation abnormalities can accompany acute congestive heart failure (CHF). However, disseminated intravascular coagulation (DIC) is rarely documented in such patients. DIC is characterized by generalized excessive activation of coagulation pathways followed by their depletion with secondary activation of anticoagulation and fibrinolysis. Treatment of the cause is an integral part of management of DIC; thus, recognition of the cause is critical.
Case Report:	A 55-year-old previously healthy man presented with breathlessness, swelling of both legs, and left leg pain. His physical exam result was consistent with decompensated heart failure. Further testing revealed multiple deep venous thrombi in the upper and lower extremities, arterial occlusion in the left popliteal artery, and an unusual cyst-like left ventricular thrombus. His laboratory evaluation was consistent with severe acute DIC. The patient was managed aggressively with diuretics, transfusions of platelets, and cryoprecipitate and was subsequently anticoagulated. His platelet count and coagulation parameters normalized and coronary angiography did not reveal any obstructive lesions. On day 22, an echocardiogram revealed and MRI confirmed that the intracardiac thrombus had disappeared. He underwent revascularization of the left leg and was successfully discharged from the hospital.
Conclusions:	Severe biventricular non-ischemic cardiac dysfunction with intra-cardiac thrombi should be considered in patients presenting with DIC. In addition to anticoagulation, treatment of underlying heart failure is critical in such cases.
MeSH Keywords:	**Disseminated Intravascular Coagulation • Embolism and Thrombosis • Heart Failure • Tricuspid Valve Insufficiency**
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Background

Several abnormalities of the coagulation system have been described in patients with heart failure, including elevated levels of thrombin activation markers and D-dimer, and increased expression of platelet-derived adhesion molecules [1]. However, overt disseminated intravascular coagulation is rarely described in association with congestive heart failure. Only 7 well-documented cases of DIC with heart failure have been reported and only 2 of the patients survived [2–6]. Here, we report a patient with this unusual association and a left ventricular thrombus, who was managed successfully. In our patient, treatment of heart failure and anticoagulation led to a complete resolution of severe thrombocytopenia, coagulation abnormalities, and LV thrombus.

Case Report

A 55-year-old Caucasian computer engineer presented with progressive breathlessness, severe swelling of both legs, and left leg pain since the night before. Aside from intermittent alcohol abuse since age 19, he denied any history of medical problems and was not taking any medications.

On physical examination he appeared jaundiced and older than his stated age and had bilateral rales, jugular vein distension, irregularly irregular rhythm, distended abdomen, and edema. Multiple petechiae were present on both legs. There was no palpable pulse in the left foot, but active movements were preserved.

The laboratory evaluation revealed elevated transaminases (AST 170 U/L, ALT 98 U/L) and markedly elevated bilirubin (12.2 mg/dL), profound thrombocytopenia (23,000 per µL),

acute kidney failure (creatinine 2.1 mg/dL), and coagulopathy with INR 2.7. The fibrinogen level was low (<50 mg/dL) and there were signs of excessive fibrinolysis (D-dimer 26 mg/L and fibrin degradation products >20 µg/mL). EKG demonstrated atrial fibrillation. Further work-up revealed multiple bilateral thrombi in the right popliteal, left gastrocnemius, right posterior tibial vein, and bilateral peroneal veins, and right cephalic vein, as well as a pulmonary embolus. Occlusion of the left popliteal artery was detected by Doppler ultrasound and later confirmed on an angiogram. Transthoracic echocardiogram revealed 4-chamber enlargement with severe bi-ventricular systolic dysfunction and a cystic structure in the LV apex (Figure 1A, 1B). Due to the location of the structure, we did not feel that transesophageal echocardiography would add any additional diagnostic value.

Initial management consisted of intravenous diuretics and prompt transfusion of cryoprecipitate to correct coagulopathy, and single-donor platelets. Platelet count and fibrinogen increased rapidly; the next day becoming 80,000 per µL and 104 mg/dL, respectively. Anticoagulation with intravenous unfractionated heparin without initial bolus was commenced with APTT goal 40–70 s when fibrinogen levels rose above 150 mg/dL. Coronary angiography revealed angiographically normal coronary arteries. Sequential echocardiograms (on day 8) revealed loss of the cystic character of the mass and, ultimately, complete disappearance of the intraventricular mass (on day 22) without a clinically significant embolism. This mass was ultimately considered to be a thrombus. The following week, he underwent left peripheral arterial bypass. The postoperative course was complicated by sepsis from aspirational pneumonia and another episode of rapid ventricular response. Amiodarone initially failed to control his heart rate, but with continuous treatment the rate normalized on beta-blockers and digoxin. Four weeks after admission, the patient
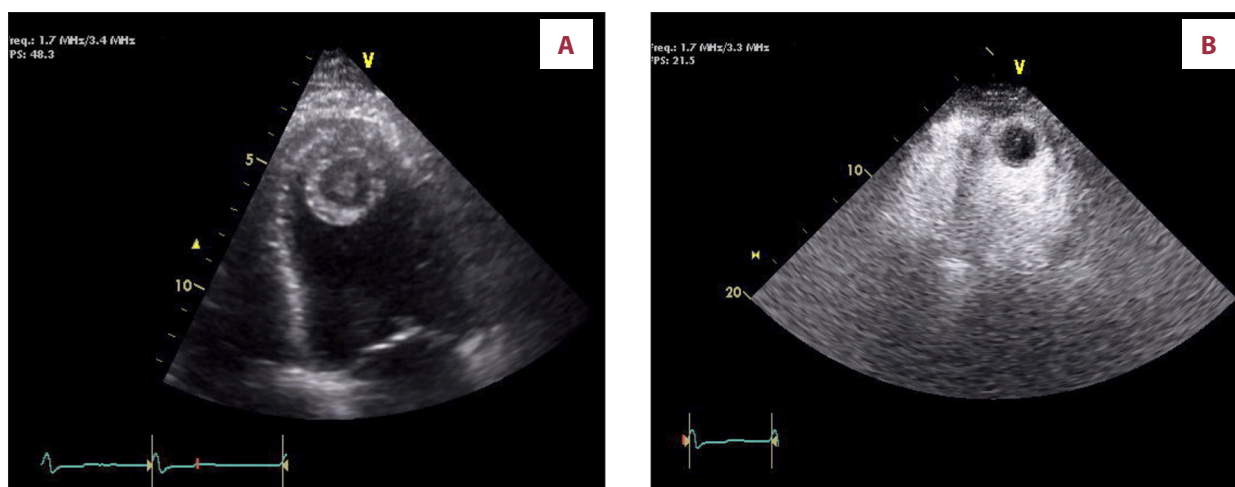
Figure 1. (**A**) Apical 4-chamber view showing a round, cyst-like thrombus in the left ventricle. (**B**) The same view after administration of 10 microliter per kilogram of Definity echo-contrast. The scale shows depth in cm.

developed patchy erythema with scaling on the torso and ex-tremities, which responded to treatment with topical cortico-steroids. A skin biopsy showed psoriasis (the result of this bi-opsy became available only after discharge). His transaminase levels returned to normal, his bilirubin remained only mildly elevated (1.4 mg/DL), platelet count was 497,000 per µL, and creatinine was 0.8 mg/DL. Indirect immunofluorescence re-vealed the presence of antinuclear antibodies (ANA, titer of 1: 160) and perinuclear-anti-neutrophil cytoplasmic antibod-ies in the serum (p-ANCA, titer of 1: 20); however, there was no clinical evidence of systemic vasculitis. His antiphospholip-id antibody panel was unremarkable. Eventually, he improved and was discharged from the hospital on oral anticoagulation. Other medications were lisinopril 5 mg daily, metoprolol succi-nate 75 mg daily, and digoxin 0.125 mg daily. The patient was alive and doing well 2 months after discharge.

Discussion

This case illustrates an unusual association of congestive heart failure with DIC, left ventricular thrombus, arterial occlusion with lower extremity ischemia, deep venous thrombosis, and pulmonary embolism. We were unable to find any reports of DIC with heart failure caused by non-ischemic LV dysfunc-tion and complicated by LV thrombus. Upon review of the sparse clinical reports of DIC associated with heart failure, 5 of those patients had a history of myocardial infarction with LV thrombus [2–4], 1 had a left atrial thrombus as a compli-cation of mitral stenosis [5], and 1 had a right atrial throm-bus with presumed non-ischemic cardiomyopathy [6]. In 1 case, there was evidence of widespread fibrin microthrombi on post-mortem examination (this is not required to confirm the presence of DIC); acute DIC was diagnosed in 6 cases and chronic in 1. Possible causation between intra-cardiac throm-bosis and DIC has been proposed [3,4] because in all report-ed cases of patients with heart failure, intra-cardiac thrombi were present [2–7].

Although DIC most often manifests with abnormal bleeding, both heart failure and DIC can predispose to thrombosis. A unique form of intracardiac thrombosis associated with DIC, marantic endocarditis, was not present in our patient. Contrary to heart failure, in which intracavitary thrombosis is com-mon [8], thrombosis in DIC is most often detected on autopsy [9]. Most of the DIC-related thrombi tend to be small, short-lived and highly susceptible to fibrinolysis [9,10]. Large-vessel thrombosis may occur when a stable foundation for platelet growth (eg., an intravascular catheter) is provided [11]. A cys-tic shape of the intracardiac thrombus is extremely unusual *per se* [12], indicating a relatively fresh thrombi with poten-tially higher embolic potential. On review of the literature, all LV thrombi and 1 atrial thrombus were mural [2–5], but often

described as large (occupying up to 50% of the left ventricu-lar cavity [3]) or biventricular [4].

Besides appearing to be a "chicken or the egg" question, rec-ognition of the cause of DIC is critical for successful DIC man-agement. Solomon et al. [4] proposed that disruption of the normal flow pattern in the LV cavity over a large (more then 1 cm in diameter) intraventricular thrombus results in damage to red blood cells, monocytes, and platelets, with activation of coagulation and widespread dispersion of activated coagula-tion factors. However, unless there is a specific interaction be-tween the thrombus and the blood components, such hemo-dynamic perturbations are unlikely to be significant, because an increased rate of DIC has not been reported with cardiac tumors. Alternatively, local consumption of coagulation factors at the site of massive fibrin deposition might be a factor that pushes the coagulation system "over the edge" and causes consumptive coagulopathy. Fresh, organizing thrombi or throm-bi attributed to recent myocardial infarction were reported in all 4 cases in which histological examination was performed [3,4]. Local consumption of coagulation factors leading to fi-brin generation has been previously suggested as a possible underlying mechanism of DIC in cases with aortic aneurysms or hemangiomas [13,14]. While a diagnosis of psoriasis was recently linked to an increased risk of venous thromboembo-lism in 2 large cohort studies [15,16], there are no reports that coagulation abnormalities precede cutaneous manifestation of psoriasis. Our patient developed psoriatic lesions 4 weeks after his admission, shortly after initiation of beta-blockers.

We believe that another factor, liver dysfunction, contributed significantly to the development of DIC in this case. Because most of the procoagulant and anticoagulant factors are synthe-sized in the liver, hepatic impairment predisposes to depletion of these factors [17,18]. Heart failure can cause hepatic dys-function by 2 mechanisms: hypotension with hypoperfusion, or venous congestion secondary to right ventricular failure. Due to the latter, the degree of tricuspid valve regurgitation correlates well with the degree of liver function abnormality [17]. There were no episodes of hypotension documented in this patient. We believe that liver congestion secondary to se-vere tricuspid valve insufficiency and biventricular failure with a chronic alcohol abuse background have likely contributed to synthetic liver dysfunction and predisposed to DIC develop-ment. In the same case series by Solomon et al. [4], autopsies of all 3 patients who died from heart failure complicated by DIC showed evidence of hepatic infarcts, chronic passive con-gestion, and centrilobular hepatic necrosis, which are chang-es that were previously associated with heart failure [18]. In all other patients described, signs of right ventricular failure were present on exam [2,6] or on cardiac catheterization [3]. Even so, development of overt DIC arguably requires a trigger-ing event, which may have been formation of the LV thrombus.

If treatment of the underlying disease is the integral part of DIC therapy, then normalization of hemodynamic status is the mainstay of DIC management in the setting of acute CHF. Our patient had evidence of severe fluid overload, and aggressive therapy with diuretics was justified to improve cardiac filling pressures and to decrease liver congestion. We found ample justification to raise the levels of platelets and fibrinogen above 50,000 per μL and 150 mg/Dl, respectively, before initiation of intravenous unfractionated heparin [19]. Overcorrection of thrombocytopenia and hypofibrinogenemia can "fuel the fire" of DIC and is generally not recommended. We omitted a heparin bolus and despite standard-dose heparin anticoagulation, no bleeding was observed. Frequent blood tests were done to insure that fibrinogen and platelet levels were maintained. In addition to treatment of thromboembolic complications, heparin counteracts the generation of excess thrombin and limits DIC [19]. In all patients who survived, anticoagulation with unfractionated heparin was used [2,6] and out of 4 patients who died, 3 did not have thrombus before death diagnosed by echocardiography and there were no references to heparin use [3,4].

Conclusions

Significant cardiac dysfunction with intra-cardiac thrombi should be considered in patients presenting with DIC. In addition to anticoagulation, treatment of underlying heart failure is critical in such cases.

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