Clinical and echocardiographic diagnosis, follow up and management of right-sided cardiac thrombi

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Abstract

Background: Right-sided cardiac masses are infrequent and have varied clinical presentation. The present study describes the clinical features, echocardiographic findings and management of 19 patients presenting with right-sided cardiac thrombi in a tertiary care center in north India.

Methods: This is a retrospective, single center observational study of consecutive patients over the period January 2003–2008 admitted in our emergency intensive care unit (EICU). We identified 38 patients with right-sided cardiac masses admitted to EICU diagnosed by transthoracic echocardiography of which 19 patients had right-sided thrombus. The echocardiographic findings were reviewed by two cardiologists in all patients. Treatment was not standardized and choice of therapy was based on judgment of attending physician.

Results: The mean age of patients with cardiac thrombus was 36.6 ± 11.8 years. Right atrial (n = 17) and right ventricle (n = 2) thrombi were associated with deep vein thrombosis (DVT) in 7 (36.8%) and pulmonary embolism in 3 (15%) patients. 13 (68.4%) patients appeared to have in situ mural thrombus. 12 patients were managed with oral anticoagulants, 3 patients underwent surgery and 4 patients were thrombolysed. All the survivors had a mean follow-up of 40 ± 6 months (range – 18–50 months).

Conclusions: Prompt echocardiographic examination in an appropriate clinical setting facilitates faster diagnosis and management of patients with right-sided cardiac thrombi. High incidence of in situ mural thrombus and varied comorbidities predisposing to right-sided cardiac thrombi besides DVT and pulmonary embolism need to be recognized. Oral anticoagulation and thrombolysis appear to be the mainstay of treatment with surgery limited for selected patients.

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Abbreviations: EICU, emergency intensive care unit; DVT, deep vein thrombosis; TEE, trans-esophageal echocardiography; ELISA, enzyme linked immunosorbent assay; VQ, ventilation perfusion; PA, pulmonary artery; RV, right ventricle; PAH, pulmonary arterial hypertension; CCP, chronic constrictive pericarditis; RA, right atrial; LA, left atrial; LV, left ventricle; CA, carcinoma; CTEPH, chronic thromboembolic pulmonary hypertension; HIV, human immunodeficiency virus; IVC, inferior vena cava; PFO, patent foramen ovale; PASP, pulmonary artery systolic pressure; STK, streptokinase; IV, intravenous; rtPA, recombinant tissue plasminogen activator; MI, myocardial infarction; BMV, balloon mitral valvotomy; MVR, mitral valve replacement; ATT, antitubercular treatment; RVOT, right ventricle outflow tract; CAGB, coronary artery bypass grafting; ASD, atrial septal defect.

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Right-sided cardiac masses are infrequent and do not have a uniform clinical presentation. High index of suspicion and prompt echocardiographic examination in an appropriate clinical setting shall facilitate faster diagnosis and management of patients with right-sided cardiac thrombi. The present study describes the clinical features, echocardiographic findings and management of 19 patients presenting with right-sided cardiac thrombi in a tertiary care center in north India.

1. Methods

This is a retrospective, single center study of all consecutive patients admitted in our ICU from Jan 2003–2008. We identified 38 patients with right-sided cardiac masses admitted to ICU diagnosed by transthoracic echocardiography of which 19 patients had right-sided thrombus. Masses such as vegetation, primary or metastatic tumors and embryological remnants were excluded.

Trans-thoracic echocardiography was done in all patients using a Philips Envisor with a 2.5- or 3.5-MHz probe. Six patients also underwent trans-esophageal echocardiography (TEE) using a 5-MHz monoplane echo probe. Cardiac MRI was needed in one patient to differentiate it from myxoma. All patients underwent vascular Doppler studies, D-dimer assay (by enzyme linked immunosorbant assay [ELISA]) and three blood cultures with the first and last one at least half an hour apart. Ventilation perfusion (VQ) scan was done in 10 patients where high pulmonary artery (PA) pressures or dilation of right ventricle (RV) or excessive mobility of the mass pointed to the possibility of associated pulmonary thromboembolism. The 9 patients who did not undergo VQ scan included 4 patients with rheumatic heart disease, 1 with RV cardiomyopathy, 2 patients with constrictive pericarditis and 2 patients with sepsis where possibility of pulmonary embolism was unlikely in presence of alternative diagnosis.

2. Results

Out of 38 patients identified with right-sided cardiac masses 19 had right-sided thrombus. The mean age of patients with cardiac thrombus was 36.6 ± 11.8 years (age range – 7 days to 64 years; median age – 33 years). There were 7 female and 12 male patients. Clinical and echocardiographic findings of patients are presented in flowcharts (Figs. 1 and 2).

All patients presented with dyspnea; 10, 6 and 3 patients were in NYHA class II, III and IV, respectively at presentation. One patient each presented with palpitations and easy fatigability. Pulmonary arterial hypertension (PAH) was present in 17 patients at presentation. Ten patients (52.6%) presented with mild PAH and 7 patients presented with moderate to severe PAH. The severity of PAH was classified on the basis of mean pulmonary artery pressure as mild (25–40 mmHg), moderate (41–55 mmHg) or severe (>55 mmHg). 1

In all, 36.8% (n = 7) patients presented with deep venous thrombosis (DVT); with ileo-femoral DVT (n = 2), ileo-femoral and popliteal (n = 1) and popliteal vein (n = 4) involvement. One patient had a history of DVT 3 years ago which was not present during the time of enrollment. This patient had developed right atrial (RA) thrombus while he was on oral anticoagulants. 15% (n = 3) patients with right-sided thrombi had evidence of pulmonary embolism.

Only 21% (n = 4) patients had a history of prolonged immobilization and three of these had associated DVT. Similar number of patients (n = 4) had associated tuberculosis (pleural effusion 1, pott’s spine 1, tubercular chronic constrictive pericarditis (CCP) 2), and half of these had associated large vein occult DVT.

Two patients presented with sepsis and infected RA thrombus. One of these patients was a 7 days female, presenting with cerebrovascular accident following umbilical vein cannulation and other patient presented with pyopericardium, pyomyositis and history of acute febrile illness. Four patients had associated rheumatic heart disease all of whom had severe mitral stenosis with associated RV dysfunction (n = 1), left ventricle (LV) dysfunction (n = 1) left atrial (LA) thrombus (n = 1) and organic tricuspid valve disease (n = 1). Associated malignancy (carcinoma (CA) breast post-irradiation and surgery), connective tissue disease (Scleroderma with chronic thromboembolic pulmonary hypertension (CTEPH) with RV thrombus), RV cardiomyopathy and human immunodeficiency virus (HIV) positive status on follow-up was detected in one patient each. Three patients had associated RV dysfunction and 2 patients had LV systolic dysfunction.

2.1. Imaging characteristics

The echocardiographic findings were recorded and reviewed by two cardiologists in all patients. The right-sided thrombi varied in size from 1.1 × 0.9 to 6 × 8.5 cm. Most of these were regular (84%) with varying shapes [spherical (26%), oval/ovoid (36%), vermicular (21%), rhomboid and spindle shaped]. Broad-based pedicle could be identified in one of the cases, rest were non-pedunculated. Barring 3 cases, the attachment of thrombi could be localized from inferior vena cava (IVC) opening (3/19), RA roof (3/19), Eustachian valve (2/19), inter atrial septum (4/19), RV apex (2/19) and from body of RA and RA appendage (2/19). Mobility was preserved in 6 of these with 2 thrombi extending across tricuspid valve and 1 across tricuspid valve upto RV outflow tract. In 3 patients with patent foramen ovale (PFO) the thrombi extended across tricuspid valve and mitral valve; tricuspid, mitral and aortic valve; and across mitral and aortic valve, respectively. Two patients (one with scleroderma, CTEPH and other with RV myocardial infarction and RV dysfunction) had right ventricle thrombi. Mild and moderate to severe PAH was found in 52.6% (n = 10) and 36.8% (n = 7) patients, respectively.

3. Management and follow-up

Treatment was not standardized and choice of therapy was based on judgement of attending physician. Twelve patients were managed with oral anticoagulants, 3 patients underwent surgery and 4 patients were thrombolysed. The dose of thrombolytic agents used was – Streptokinase (STK) – intra-venous (IV) bolus 250,000 units over 30 min followed by infusion of 100,000 units/h for 12–24 h and Recombinant tissue plasminogen activator (rtPA) – IV bolus of 15 mg in 10 min followed
of 17 survivors 15 patients had no right-sided thrombi on echocardiography follow up at 6 months. Two patients had persistence of thrombus; one of these had a history of DVT 3 years prior to presentation. The second patient had Inferior wall and RV myocardial infarction (MI) with RV thrombi persisting for first 6 months but thereafter completely disappearing at 3rd visit (9 months). Fungal and bacterial etiology, respectively, was found in the two patients presenting with infected RA thrombus (Fig. 3) and each of them responded to heparin infusion along with prolonged parenteral antibiotics/antifungals. Amongst the four patients presenting with severe mitral stenosis (MS) (Fig. 4), two patients underwent balloon mitral valvotomy (BMV) and mitral valve replacement (MVR) successfully after 6 weeks of disappearance of RA thrombus. The other two patients with severe MS were kept on medical management. Both patients with chronic constrictive pericarditis (tubercular etiology) underwent surgery, received 9 months antitubercular treatment (ATT) and remained on oral anticoagulation for one year (Fig. 5).

Three patients with extension of thrombus into the left side of heart (Fig. 6) were either thrombolysed (2 cases with streptokinase) or sent for surgery (1 case). One patient who was thrombolysed and the other patient who underwent surgery expired immediately after thrombolysis and intraoperatively, respectively. One survival in the medical group was free of thrombi at 6 months of follow up. His thrombophilia profile for inherited hyper coagulant states was negative though he was continued on lifelong anticoagulation. Two patients with thrombi extending across the TV up to the RV outflow tract (RVOT) had associated pulmonary embolism and were successfully thrombolysed.

4. Discussion

Right heart thrombi can be classified into two groups. The first group represents embolized deep venous thrombi that are temporarily lodged in the right atrium or ventricle and are often referred to as “emboli in transit” or thromboembolism and the second group represents thrombi in situ or the mural thrombi which are immobile. They present a distinctive appearance on two-dimensional transthoracic and transesophageal echocardiography. Since the initial case report by Covarrubias and colleagues, many authors have described thrombus in transit as highly mobile, coiled, or serpiginous masses moving within the right atrium or ventricle. These often prolapse into the tricuspid or pulmonic valve during the cardiac cycle. A point of attachment often is unseen or is
Thromboemboli are difficult to distinguish from myxomas, and acoustic difference allows the discrimination.\textsuperscript{5}

Mural thrombi, show less motion during the cardiac cycle, a broad-based attachment to the heart wall, and occasional focal calcification. Mural RA thrombi are seen in conditions like cardiomyopathies, post coronary artery bypass grafting (CABG), post atrial septal defect (ASD) repair, patients with permanent pacemaker leads or hyper alimentation catheters or ventriculoatrial shunts in situ.\textsuperscript{7} Such patients usually have enlarged RA or decreased cardiac output with relative stasis of blood or have evidence of endocardial damage to RA after

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Fig. 2 – Flow chart depicting imaging characteristics of right-sided masses and the treatment strategy.

Fig. 3 – TTE image (sub costal view) showing round well circumscribed heterogenous mass attached to inter atrial septum in a seven day old new born.

Fig. 4 – TEE (bicaval view) showing oval homogenous mass with translucency at periphery. Mass was immobile below RA appendage in a patient of severe mitral stenosis, PAH with severe RV systolic dysfunction.
surgery. In this series only one patient had PPI leads in situ and three had associated RV dysfunction.

The present study signifies the importance of high incidence of in situ thrombus rather than thrombus in transit. The incidence of mural thrombi is believed to be more in this series owing to characteristics of thrombi; \( n = 13 \) (68.4%) thrombi were immobile with localized attachments as depicted in flow chart. Moreover, underlying enlarged RA and decreased cardiac output with relative stasis of blood predisposed to formation of mural RA thrombi as in patients with severe mitral stenosis and associated organic tricuspid valve disease, RV dysfunction and LV dysfunction; constrictive pericarditis, RV cardiomypathy, Inferior and RV myocardial infarction with RV dysfunction.

Most of the RA thrombi in this series were regular homogenous or multi lobed structures with or without central echolucency. They were without a pedicle but appeared attached to a particular point in right atrium or to one of the inlets in right atrium. None of them was attached to the tricuspid leaflet, though if mobile across the tricuspid valve they appeared to move along the tricuspid leaflets into the RV in diastole unlike vegetation on tricuspid leaflet. Unlike LV thrombus, none had a layered appearance, except the RV thrombus. The infected thrombus had a more heterogenous and mottled appearance, were immobile without any extension, had a short clinical history without significant immobilization and were not associated with pulmonary embolization or any signs of persistent bacteremia. The RV thrombi were immobile homogenous regular structures attached to the RV apex, taking its shape and associated with RV dysfunction.

15% (\( n = 3 \)) patients were diagnosed to have pulmonary embolism. Echocardiographic studies in patients with pulmonary embolism show an incidence of right heart thromboembolism between 3% and 23%, with a combined incidence of 9% across several large series studying consecutive patients.\(^8\)\(^{12}\) On the other hand, pulmonary thromboembolism may be seen up to 98% of cases of right atrial thromboembolism.\(^13\)\(^\)\(^7\) cases of right heart thromboembolism were analyzed in a retrospective meta-analysis by Peter et al\(^13\) with pulmonary thromboembolism present in 98% of cases. The treatments administered were none (9%), anticoagulation therapy (35.0%), surgical procedure (35.6%), or thrombolytic therapy (19.8%). The overall mortality rate was 27.1%. The mortality rate associated with no therapy, anticoagulation therapy, surgical embolectomy, and thrombolysis was 100.0%, 28.6%, 23.8%, and 11.3%, respectively. Using multivariate modeling, thrombolytic therapy was associated with an improved survival rate (\( p < 0.05 \)) when compared either to anticoagulation therapy or surgery.

In the present study, right heart thrombi were associated with mortality of 10.5% over 18-month follow up. Treatment administered was only anticoagulants in 12 (63%), thrombolysis in 4 (21%), and surgery in 3 (15.7%) cases. Oral anticoagulation remains to be the gold standard for mural thrombus given their success rate of 91.6% in dissolving such masses. Thrombolysis should be given for compelling indications like right atrial thromboembolism, pulmonary thromboembolism, increased fragility and mobility of these masses, and extension of thrombi into left side across PFO. Surgery is indicated for indications other than just mere presence of right-sided thrombus, for instance, chronic constrictive pericarditis. Valve surgery and simultaneous removal of RA clot is also recommended though in the present series it was done only after resolution of clot.

The RA thrombi-behaves same as platelet rich red thrombi disappearing slowly with oral anticoagulants or more early with thrombolysis. Infected thrombus is a form intermittent between a thrombus and vegetation caused by local seeding of a thrombus by the highly virulent infected material during transient bacteremia in appropriate clinical conditions. In the present series, two patients had infected thrombi one with pyomyositis and other with septicemia and a history of umbilical vein cannulation. One of these cases had an undulating membrane over the RA thrombi. Thrombus is generally hypo vascular tissue, so ingress of antibiotics and immune system antibodies via vasculature is thought to be poor and prompt surgical resection of the infected thrombus should be performed, followed by prolonged administration of antibiotics. However both our patients responded to antibiotics along with oral anticoagulants.
Tuberculosis, a widely prevalent infectious disease in India, was seen in 21% cases. Half of these cases also had associated DVT. Deep vein thrombosis was occult in more than 50% of cases. Tuberculosis as a risk factor for venous thrombosis has been mentioned in various studies. Deep vein thrombosis occurred in 50% of patients in a series of 380 patients of tuberculosis along with various hematological abnormalities. The hypercoagulable state in tuberculosis is caused by increased anti-phospholipid antibodies, decreased protein C and protein S, decreased anti-thrombin III, thrombocytosis, increased fibrinogen levels, increased fibrinogen degradation products and t-PA causing impaired fibrinolysis. Mechanical factors like lymphadenopathy causing venous obstruction and subsequent thrombosis has also been reported, as is antitubercular drug rifampicin causing hypercoagulable state.

Patients having RA mass extending into the left side had the worst prognosis of all. Two out of three patients in this series expired with one immediately after thrombolysis while the second one expired intraoperatively.

The most effective therapy for patients with right heart thrombi remains unknown. This issue is critical because the presence of a right heart thromboembolus complicating a pulmonary thromboembolism appears to carry a poor prognosis. Chartier et al. reported a mortality rate of 45% in the most recent series of 38 consecutive patients with right heart thromboembolism. All of these deaths occurred within the first 24 h of hospitalization, signifying the need to rapidly diagnose and treat right heart thromboembolism.

Existing published reports differ in their recommendations for treatment by advocating surgical removal, administration of thrombolytic agents or anticoagulation therapy with heparin. The last analysis of patients with right heart thromboembolism (n = 119) found similar mortality rates for surgery, thrombolysis, and heparin anticoagulation therapy (38%, 38%, and 30%, respectively) and thus concluded that heparin therapy was the treatment of choice.

Unfortunately, there are no prospective trials to definitively answer this question or to assess other risk factors that may be related to mortality. Our results suggest that thrombolytic therapy was associated with a reduction in mortality for thromboembolism while oral anticoagulation was enough for mural thrombus. Oral anticoagulants alone for free floating thrombus may be hazardous with the possibility of thrombus embolizing to pulmonary circulation.

Surgical embolectomy has its own set of potential complications including an inherent delay of at least hours, general anesthesia, cardiopulmonary bypass, and the inability to remove coexisting pulmonary thromboemboli beyond the central pulmonary arteries. One of the major advantages of the surgical approach is the ability to simultaneously repair a PFO, thus reducing the risk of a subsequent paradoxical embolism. The percutaneous catheter directed retrieval of clots is a promising possibility, but only few cases have been reported to date. In contrast, thrombolytic therapy can be administered quickly and results in the simultaneous thrombolysis of cardiac and pulmonary arterial thromboemboli as well as a thrombus in the femoral venous circulation. The major complication of thrombolytic therapy is significant bleeding, which occurs in as many as 22% of patients.

5. Limitations

This study is relatively small sized retrospective study with wide variability in clinical aspects of the studied patients. However, in absence of any previous published reports on the entity in this region, our findings might be an impetus for future work in this field. PE was diagnosed in 3 (15%) patients in the present study. However, VQ scan employed for the diagnosis is not a sensitive modality to detect small thrombi and hence there might be an under estimation of the prevalence of PE. Also, of the 19 studied patients, 9 patients did not undergo VQ scan as there were alternative explanations available for PAH and/or RV dilatation. These patients could still have had PE. As regards management, the treatment with thrombolysis and anticoagulation resulted in good outcome in these patients with right heart thrombi, most of which appeared to be mural thrombi. However, in the small patient population comparison amongst the treatment modalities was not possible. In our experience, thrombolysis appears to be a better modality in patients with severe PAH and right-sided thrombi.

6. Conclusion

Prompt echocardiographic examination in an appropriate clinical setting facilitates faster diagnosis and management of patients with right-sided cardiac thrombi. High incidence of in situ mural thrombus and varied comorbidities predisposing to right-sided cardiac thrombi besides DVT and pulmonary embolism need to be recognized. Oral anticoagulation and thrombolysis are the mainstay of treatment with surgery limited for selected patients. Oral anticoagulation for all and thrombolysis for high risk thrombi associated with mobile fragile thrombus or with PE is recommended. However, in transit thrombus presenting across PFO is the most difficult group with uncertain prognosis.

Conflicts of interest

All authors have none to declare.

References