CASE REPORT

Acute right ventricular myocarditis presenting with chest pain and syncope

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SUMMARY

Myocarditis is assumed to involve both ventricles equally. Right ventricular predominant involvement is rarely described. A case of acute viral right ventricular myocarditis presenting with chest pain and syncope, grade 3 atrioventricular block, right ventricular dilatation and free wall hypokinesia is reported. Cardiac MRI showed late enhancement of the right ventricular free wall without involvement of the left ventricle. Anti-Coxsackie A9 virus neutralising IgM-type antibodies titre was elevated. This case emphasises that manifestations of myocarditis can be limited to the right ventricle and should be considered in the differential diagnosis of right ventricular enlargement.

BACKGROUND

Myocarditis may present with a wide range of symptoms including chest pain, new-onset heart failure, atrial or ventricular arrhythmias, cardiogenic shock and sudden death. Dilated cardiomyopathy with chronic heart failure is the major long-term sequel of myocarditis.¹ Myocardial inflammation per se is a non-specific response to various triggers such as viral or bacterial infection, cardiotoxic agents, catecholamines, infarction or mechanical injury. These triggers are generally assumed to involve both ventricles equally.^{1–4} The lymphocyte infiltration is distributed focally and despite patchy myocardial involvement there is limited information on differences between ventricles in the progression of the disease. Necropsy, cardiac MRI (CMR) and endomyocardial biopsy (EMB) studies comparing right and left ventricular involvement have shown that myocarditis more

frequently affects the left ventricular free wall than the interventricular septum.⁵ Literature search shows few reports of myocarditis with predominant right ventricular involvement.^{6–11}

The authors present a case of acute viral myocarditis with predominant involvement of the right ventricle (RV) and discuss the differential diagnosis of right ventricular dilation in the absence of left abnormalities.

CASE PRESENTATION

A 49-year-old Caucasian man with a history of hypertension, diabetes mellitus, dyslipidemia and obstructive sleep apnoea was admitted to the emergency room with chest pain. The patient had been asymptomatic up to 3 days before admission when he developed generalised myalgia, asthenia, nausea and vomiting. In the morning of admission he experienced an episode of intense anterior chest pain followed by syncope. Rapid recovery of awareness followed and the patient maintained mild thoracic pain exacerbated by cough and deep inspiration.

Arterial hypertension, diabetes mellitus and hypercholesterolaemia had been diagnosed 2 years before. Regular habits included moderate alcohol consumption but there was no history of smoking or illicit drug consumption. He worked in a school and lived with his wife and two healthy children in a suburban community with no pets. He had not travelled in the year before.

Regular medication consisted of lercanidipin, enalapril, metformin and rosuvastatin. There were no known allergies and no new medication had been started prior to the onset of symptoms.

Figure 1 ECG tracing. On admission to the emergency room the ECG showed grade 3 atrioventricular block with a wide QRS (140 ms) escape rhythm of 40 bpm (A). At discharge the ECG showed normal sinus rhythm with right bundle branch block pattern (B).

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Figure 2 Chest X-ray at presentation. The anteroposterior chest X-ray showed a mildly enlarged cardiac silhouette and a mildly ingurgitated hilar and interstitial vasculature.

The patient arrived at the emergency room with ongoing chest pain and dyspnoea. Mucous membranes were moist and there was no scleral icterus. His peripheral pulse was irregular at about 40 bpm. Blood pressure was 100/60 mm Hg. Respiratory rate was 30 breaths/min and peripheral oxygen saturation 98% while breathing room air. Axillary temperature was 37.1 °C.

Cardiac and pulmonary auscultation showed no abnormal findings apart from irregular heart sounds. No jugular venous pulse was discernible at 45° neck elevation. There was no peripheral oedema. Abdominal, neurological and skin examinations were unremarkable and no adenopathy or thyromegaly were documented.

The ECG revealed grade 3 atrioventricular block with a wide QRS escape rhythm of 40 bpm (figure 1A).

A chest X-ray showed mildly enlarged cardiac silhouette and mildly ingurgitated hilar and interstitial vasculature (figure 2).

A transthoracic echocardiogram was performed in the emergency room and depicted: (A) right ventricular enlargement (on apical four chambers—right ventricular diameter at midlevel: 43 mm; longitudinal right ventricular dimension: 88 mm); (B) right-ventricular wall hypokinesia with mildly reduced right ventricular function (tricuspid annular plane systolic excursion: 16 mm) and (C) moderate tricuspid regurgitation with an

estimated systolic pulmonary arterial pressure of 33 mm Hg and (D) normal left ventricular function (left ventricular ejection fraction estimated in 55%) (figure 3A).

Serum levels of creatine (CK), liver enzymes, CK MB isoenzymes, cardiac troponin I and C reactive protein (CRP) were elevated; D-dimer levels were within normal range (table 1).

The patient was admitted to the intensive cardiac care unit. Right ventricular pacing was started after insertion of a pacing wire through the right femoral vein and pharmacological therapy consisting of aspirin, sublingual nitroglycerine and statin was initiated.

Decision to undergo urgent invasive coronary angiography was taken once considered the high pretest probability of coronary artery disease (CAD) and relevance for further treatment decisions. No relevant coronary disease was found (figure 4).

Myocardial inflammatory conditions were then considered, given the prior flu-like syndrome, CRP elevation and absence of CAD. Lysine acetylsalicylate therapy (1800 mg, twice daily) was initiated and an extensive workup for the cause of myocarditis (specific viral and bacterial pathogens and autoimmunity serology) was performed.

Over the course of 24 h the chest pain resolved and the patient remained haemodynamically stable. On the third day of hospital admission, CK levels normalised but troponin I remained elevated with an oscillatory pattern. Hepatocyte cytolysis markers normalised, and the CRP levels peaked at 15 mg/dL. On the sixth day the temporary pacing wire was removed as the patient had been electrically stable in sinus rhythm with 'de novo' right bundle branch block pattern (figure 1B).

On the seventh day the patient was referred to CMR. CMR findings included normal dimensions of the cardiac chambers, interventricular and intraventricular asynchrony with mild depression of biventricular systolic function and moderate-volume pleural effusion. Notably, CMR late-enhancement technique showed right ventricular free wall hypersignal evident in subepicardial, non-ischaemic pattern and myocarditis with preferential involvement of the RV was assumed (figure 5A,B).

A rise in anti-Coxsackie A9 virus neutralising IgM-type antibodies titre suggested acute infection.

The patient was kept under treatment with non-steroidal anti-inflammatory agents during 8 days; additional medication included oral furosemide, bisoprolol, enalapril and insulin.

Figure 3 Selective coronary angiography. Left coronary artery catheterisation showed 40% stenosis on the middle portion of the left anterior descending artery and no relevant stenosis on the circumflex artery (A); right coronary artery catheterisation showed a dominant right coronary artery without significant stenosis (B).

Table 1 Laboratory data

Variable	Reference range	Admission	1st day after admission	3rd day after admission	5th day after admission
Haematocrit (%)	40–52	41	38.7	36.3	34.2
White cell count (per mm ³)	3.8–10.6	8.47	12.87	11.6	12.87
Platelets count (per mm ³)	150–440	185	183	208	173
Creatine (mg/dL)	0.7–1.2	1.3	1.6	1.3	0.9
Urea (mg/dL)	1–50	67	120	97	81
Sodium (mmol/L)	136–145	137	134	132	133
Potassium (mmol/L)	3.4–4.5	4.3	4	3.7	3.9
Alanine aminotransferase (U/L)	1–37	496	500	467	247
Aspartate aminotransferase (U/L)	1–41	370	481	458	468
Lactate dehydrogenase (U/L)	240–480	1894	1689	1188	1370
Bilirubin (mg/dL)	0.1–1.1	1	1.4	0.9	0.7
Reactive C protein (mg/dL)	0.01–0.5	8.45	10.77	14.77	8.05
NT-pro-B-type natriuretic peptide (pg/mL)	0–125	6280			1787
I-type cardiac troponine (ng/mL)	0.01–0.03	8.94	10.55	8.26	9.32
Dimer-D (ug/mL)	<0.5	0.34			

Symptoms improved and the patient remained haemodynamically and electrically stable. Finally, 14 days after hospital admission, he was discharged home, asymptomatic and on medication with enalapril, bisoprolol, metformin and rosuvastatin.

OUTCOME AND FOLLOW-UP

At 1 month follow-up, the patient remained asymptomatic and was back to work. An echocardiogram then obtained showed normal heart chambers without regional wall motion

Figure 4 Echocardiography imaging. The admission transthoracic echocardiogram showed right ventricular enlargement (A) and free right ventricular wall hypokinesia with mildly reduced right ventricular function (tricuspid annular plane systolic excursion was 16 mm; B). By 1-month follow-up, the heart chambers were normal without segmental or global wall motion abnormalities and good systolic function of right and left ventricles (C and D).

abnormalities and preserved biventricular systolic function (figure 3C,D). Six months later he remained asymptomatic and the follow-up CMR evaluation evidenced complete resolution of the initial findings (figure 5C,D).

DISCUSSION

CAD constitutes the main cause of troponin elevation in patients presenting with acute chest pain and must be excluded. However, non-obstructive CAD is found on immediate cardiac catheterisation in more than 10% of these patients.¹² The absence of CAD confronts the clinician with a broad variety of possible underlying aetiologies including myocarditis, different cardiomyopathies, aortic disease, embolic and vasospastic infarction, pulmonary embolism, arrhythmias, valvular heart disease, sepsis and further rare conditions. Overall, myocarditis is the most frequent diagnosis in this setting.^{1 12}

In the case reported acute myocarditis was considered the most probable diagnosis based on inflammatory markers elevation and flu-like syndrome. However, the main involvement of the RV represents a challenge as differential diagnosis including acute pulmonary embolism, non-atherosclerotic right ventricular myocardial infarction or arrhythmogenic right ventricular cardiomyopathy (ARVC) should be considered.

Predominant right ventricular disease in the absence of CAD

Pulmonary embolism (PE) is a relatively common cardiovascular emergency. Large and/or multiple emboli might abruptly increase pulmonary vascular resistance to an afterload level that cannot be matched by the RV leading to acute RV failure.¹³ In the reported case, the D-dimer test was negative allowing for almost certain exclusion of PE without need of further investigation. Also, the echocardiographic signs of RV pressure overload (typically flattened ventricular septum and D shape left ventricle in short axis) were not seen.

An isolated right ventricular infarction accounts for less than 3% of all cases of infarction but may result in considerable morbidity. It is associated with atherosclerotic disease of marginal arteries or of a non-dominant right coronary artery but it may occur in the absence of CAD when substantial right ventricular hypertrophy is present. Although rare this should be considered as a possible diagnosis in the presented clinical case. The patient's history of obstructive sleep apnoea could be a cause of right ventricular hypertrophy and increased susceptibility of the RV to ischaemia.^{14–16}

ARVC is a heart muscle disease characterised by atrophy and fibrofatty replacement of RV myocardium, leading to dilation, systolic dysfunction and electrical instability of the RV. The disease is a frequent cause of life-threatening ventricular

Figure 5 Cardiac MRI. Balanced steady-state free precession image in four-chambers view (A–D) showed late enhancement of the free-wall of the right ventricle (A, arrow); pleural and pericardial effusion is also seen (B, arrow). Six months later no late enhancement (C) or pericardial or pleural effusion were found (D). Image quality was limited by the patient's tachypnoea.

Table 2 Presentation, diagnostic workflow and clinical course of reported patients with myocarditis with predominant right ventricular involvement

Patient	Author and year of publication	Age and gender	Presentation	Aetiology	Diagnostic procedure	Result
Patient 1	Hayes <i>et al</i> (1961)	64 years, male	Syncope	Idiopathic	Necropsy	Death (sudden death)
Patient 2	Matsuoka <i>et al</i> (1987)	7 years, male	Fever, eyelids oedema	Idiopathic	Necropsy	Death (advanced heart failure)
Patient 3	Matsuoka <i>et al</i> (1987)	1 year, male	PSVT, eyelids oedema	Idiopathic	Necropsy	Death (advanced heart failure)
Patient 4	McFalls <i>et al</i> (1993)	67 years, female	Dyspnoea, peripheral oedema	Idiopathic	Necropsy	Death (sudden death)
Patient 5	Sir <i>et al</i> (2004)	68 years, female	Chest pain, dyspnoea	Idiopathic	ECHO	Survival
Patient 6	Hama <i>et al</i> (2009)	65 years, male	AAVB, MVT	Idiopathic	CMR and EBM	Survival
Patient 7	Ho <i>et al</i> (2010)	28 years, female	Postural hypotension	Idiopathic	EBM	Death (CS)

AAVB, advanced atrioventricular block; CMR, cardiac MR; CS, cardiogenic shock; EBM, endomyocardial biopsy; ECHO, echocardiogram; MVT, monomorphic ventricular tachycardia, PSVT, paroxysmal supraventricular tachycardia.

arrhythmias in young individuals with an apparently normal heart. Its prevalence has been estimated to vary from 1:2500 to 1:5000, but in Spain and Italy the estimated prevalence was reported to be higher. ARVC is familiar in almost one-third of cases and genetic studies have recently identified causative mutations in genes encoding proteins of the desmosomal cell junction. Clinical diagnosis is currently made on the basis of established criteria but their value, mostly when dealing with non-familial cases, is increasingly questioned.^{17–19} The patient in the clinical case presented only one minor morphological criterion (moderate dilation of RV with mildly reduced systolic function), there was no familial history of ARVC or sudden death, the baseline ECG was normal and afterwards developed right bundle branch block.

Myocarditis is assumed to involve both ventricles equally. Right ventricular predominant involvement is rarely described. To the date of submission of this article only few reports of right ventricular myocarditis can be found. Literature search shows seven reports.^{6–11}

The identification of the cause for troponin elevation in the absence of CAD is not a simple task since there is no acceptable diagnostic pathway to guide the clinician. This investigation is usually made using either CMR (non-invasive) or EMB (invasive). In spite of their good diagnostic performance—80% versus 88%, respectively—EMB appears to be more powerful than CMR because it allows for immunohistochemistry and PCR analysis. Indeed, 20% of the patients cannot be diagnosed using CMR alone. Despite this, some authors have previously suggested performing CMR in all patients: if CMR is able to establish a diagnosis, EMB is unlikely to change it. EMB should be employed if clinically relevant (eg, patients with persistent symptoms) as a second-step management tool in situations with ‘negative’ CMR.¹² Another advantage of performing CMR first is to allow for a CMR-guided EMB-procedure, thus increasing sensitivity.^{12–20}

CMR in myocarditis typically shows a pattern of late contrast enhancement that originates primarily from the epicardium towards the midwall, sparing the subendocardial layer. The presence of subepicardial and midwall enhancement is highly suggestive of myocarditis in cases where there is clinical suspicion of such condition and enables exclusion of ischaemia-related myocardial damage, since this disease starts in the subendocardium and spreads in transmural direction.¹² These findings were patent in the described clinical case, and the subepicardial late-enhancement pattern matched the wall motion abnormalities detected by echocardiography. Ultimately this suggested acute myocarditis with preferential involvement of the RV excluding right ventricular infarction and ARVC diagnosis.

EMB was not performed once CMR imaging results and the clinical stability of the patient were considered.

Right ventricular myocarditis may have different course

The clinical presentation, diagnostic workflow and clinical course of patients of myocarditis with predominant right ventricular involvement are summarised in table 2. Most of the cases published so far were fatal.^{6–8 11} It is possible, however, that this may be a biased interpretation and that only the most serious cases have been submitted for publication. Asymptomatic cases may not have been taken into account. Importantly, in a series of 23 patients with EBM-confirmed myocarditis, the loss of right ventricular function was the most powerful predictor of death or cardiac transplantation.¹ This emphasises that the clinical and pathological course of myocarditis may be different depending on the predominant involvement of the left or right ventricles, or both.

Learning points

- ▶ Although myocarditis is assumed to involve both ventricles, predominant involvement of the right ventricle may occur with different course.
- ▶ Differential diagnosis of right ventricular dilation without left ventricular abnormalities should include right ventricular myocarditis, pulmonary embolism, arrhythmogenic right ventricular cardiomyopathy and right ventricular infarction.
- ▶ Cardiac MR should be considered in the setting of troponin elevation without coronary artery disease as it may alone establish the diagnosis or, if not the case, it may guide the most appropriate site for endomyocardial biopsy.

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