SHORT SERIES REPORT

Idiopathic left ventricular aneurysm and sudden cardiac death in young adults

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Aims We report three young patients presenting with life-threatening ventricular tachycardia (VT) or ventricular fibrillation (VF) and/or survived sudden cardiac arrest, who were admitted to our institution for further diagnostic evaluation.

Methods and results In all patients, idiopathic left ventricular (LV) aneurysms were identified after a detailed non-invasive and invasive evaluation. Sustained VT/VF was inducible during programmed ventricular stimulation in two of the three patients. Left ventricular aneurysms were depicted and characterized by various imaging modalities (echocardiography, magnetic resonance imaging, LV angiography). To elucidate the pathogenesis further, both myocardial viability and regional sympathetic innervation were assessed by radionuclide imaging techniques. Defects of innervation and metabolism were documented in the area of the aneurysm but distal to the aneurysm there were no signs of downstream denervation.

Conclusion Life-threatening arrhythmias may be the first manifestation of an idiopathic LV aneurysm, which can be reliably diagnosed with modern imaging techniques. Radionuclide imaging may yield additional information as to the involvement of the autonomic nervous system potentially associated with arrhythmogenesis. Management strategies in patients with an idiopathic LV aneurysm range from antiarrhythmic drug treatment, implantation of an automatic cardioverter–defibrillator to surgical aneurysmectomy.

Introduction

Left ventricular (LV) aneurysms most frequently develop after myocardial infarction. Other underlying diseases include, for instance, sarcoidosis, Chagas disease, or myocarditis. Idiopathic LV aneurysms without identifiable underlying cause are rare. However, they may be associated with life-threatening ventricular tachyarrhythmias1 and cardiac arrest,2 even as a first manifestation of the disease. Therefore, they represent an uncommon but important cause of sudden death in a young population. Idiopathic LV aneurysms are anatomically distinguished from congenital diverticula, which are denoted to have only a narrow communication with the ventricle3 and which are partly associated with the Cantrell syndrome.4 So far, little is known about the pathogenesis of idiopathic LV aneurysms. The present report summarizes the findings of three young patients with idiopathic LV aneurysms associated with ventricular tachyarrhythmias and reviews the data from the literature. New and interesting pathoanatomical and clinical findings with potential implications for further investigations in larger patient cohorts are presented and discussed.

Patient characteristics

Case 1

A 27-year-old female architect presented in 2001 with palpitations and short episodes of paroxysmal tachycardia associated with dizziness first starting in 1993. During such an attack, ventricular tachycardia (VT) with right bundle branch block morphology (cycle length 333 ms) was documented by 12-lead ECG and terminated by intravenous ajmaline. Initially, the patient refused further diagnostic evaluation and treatment. Treatment with beta-blockers (metoprolol) at a low dose (25 mg daily) was initiated but
was only sporadically taken by the patient due to side effects of hypotension and fatigue.

The family history was unremarkable with respect to cardiac arrest, unexplained syncope, ventricular tachyarrhythmias, or cardiomyopathy. The patient reported moderate physical activity with workout in a gym once weekly. Physical examination, 12-lead surface ECG, bicycle exercise test, laboratory tests, and intravenous ajmaline provocation to unmask a potential Brugada syndrome showed normal findings.

Transthoracic echocardiography revealed an aneurysm of the infero-lateral LV wall. No other structural, wall motion, or valvular abnormalities were detected.

Magnetic resonance imaging (MRI) (Philips Gyroscan Intera, 1.5 T) clearly depicted the aneurysm as an area of circumscript wall thinning showing regional dyskinesia (balanced FFE; short-axis and LV two-chamber views). A region of hyperintensity (‘delayed enhancement’) indicating myocardial fibrosis or scar was identified at the location of the aneurysm in images (inversion recovery T1-weighted 3D turbo-field-echo pulse sequence) acquired 15 min after intravenous administration of gadolinium–DTPA (0.2 mmol/kg) (Figure 1).

Cardiac catheterization with LV angiography also demonstrated the aneurysm with dyskinesia and prolonged dye persistence in the infero-lateral LV (Figure 2). No abnormalities of valves, right ventricle (RV), coronary arteries, or haemodynamics were observed.

Right ventricle endomyocardial biopsy samples from the outflow tract, mid-septal, and apical area of the RV revealed no signs of myocarditis, sarcoidosis, arrhythmogenic right ventricular cardiomyopathy, or storage disease.

Programmed ventricular stimulation in the RV outflow tract (370/210/170 ms basic drive cycle and two extrastimuli) reproducibly induced haemodynamically non-tolerated polymorphic ventricular tachyarrhythmias that were terminated by external defibrillation (Figure 3).

Radionuclide imaging was performed to characterize further the LV aneurysm. 18F-FDG-PET (2-[fluorine-18]fluoro-2-deoxy-D-glucose single photon emission tomography) demonstrated a transmural defect of myocardial glucose uptake matching with the aneurysm as detected by MRI and LV angiography. 123I-MIBG-SPECT scintigraphy was performed to assess the presynaptic cardiac noradrenaline reuptake (innervation) according to a protocol published earlier. The test showed a regional defect in tracer uptake concordant with the location and extent of the LV aneurysm as demonstrated by the other imaging techniques (Figure 4).

Because of the documented spontaneous VT, the inducible fast polymorphic VT, and the presence of a structural LV abnormality, the implantation of an automatic cardioverter-defibrillator (ICD) was strongly recommended but refused by the patient. During a follow-up of 37 months, the patient experienced one further episode of self-limiting tachycardia (no ECG registration) 24 days after discharge.

Case 2

A 24-year-old female student and competitive track and field athlete was referred and admitted to our hospital after an episode of aborted sudden cardiac arrest. While climbing a staircase, she collapsed with cardiac arrest without a prodrome. The emergency physician recorded ventricular fibrillation restored sinus rhythm and systemic circulation by defibrillation (3 × 200 J). In the preceding 4 years, the patient had experienced episodes of palpitations and symptomatic tachycardias (no ECG documentation). Antiarrhythmic drug treatment with sotalol (240 mg/day) was initiated but discontinued 2 months later because of symptomatic bradycardia. The patient remained asymptomatic until the episode of resuscitated cardiac arrest.

The medical history was unremarkable for infectious or inherited diseases, allergies, as well as of surgical procedures. Physical examination, bicycle exercise test, and laboratory tests showed normal findings. Twelve-lead surface ECG revealed no signs of a long or short QT syndrome, arrhythmogenic right ventricular cardiomyopathy, or Brugada syndrome. Provocation with intravenous ajmaline exhibited no signs of Brugada syndrome. The patient had no cardiovascular risk factors: There was no history of unexplained syncope and no family history of premature sudden death or ventricular tachyarrhythmias.

Transthoracic echocardiography revealed a circumscript area with dyskinesia and thinning of the lateral LV wall. No other abnormalities of RV or LV structure, wall motion, or valvular function were detected.
Magnetic resonance imaging depicted a circumscript lateral LV aneurysm with local myocardial thinning and corresponding dyskinesia. Increased signal intensity was observed in the contrast-enhanced delayed images (late enhancement).

Cardiac catheterization with LV angiography confirmed the aneurysm of the LV postero-lateral wall with prolonged dye persistence. During right heart catheterization, a fast sustained polymorphic VT was mechanically induced and successfully converted into sinus rhythm with a single 200 J defibrillation shock. No other pathological findings were documented. The RV was normal in size, shape, and function. Coronary arteries as well as right and left ventricular and atrial chamber pressures and resting cardiac output were normal.

Endomyocardial biopsies taken from the RV apex, outflow tract, and mid-septal region showed no signs of myocarditis, sarcoid disease, arrhythmogenic right ventricular cardiomyopathy, or storage disease. Biopsies obtained from the site of the LV aneurysm disclosed fibrotic and scar tissue (Figure 5) with compensatory hypertrophy of cardiomyocytes located on the borders. No signs of inflammation or fibrofatty replacement were observed.

Programmed ventricular stimulation reproducibly induced a fast polymorphic VT (cycle length 150–190 ms) with one extrastimulus during sinus rhythm (coupling interval 280 ms). The arrhythmia terminated spontaneously after 18 s or was terminated by a 200 J defibrillation shock.

18F-FDG-PET measuring myocardial glucose uptake detected a transmural defect located in the mid-lateral LV, matching with the location and extent of the aneurysm as depicted in MRI and LV angiography.
As no spontaneous or inducible sustained ventricular tachyarrhythmias were present, the implantation of an ICD on the basis of primary or secondary prevention of sudden cardiac death was not recommended. However, prophylactic and empiric treatment with amiodarone was advised. During a follow-up of more than 39 months, no episodes of syncope or other serious cardiac events occurred. The patient complained of sporadic palpitations, which were documented on Holter-ECG as ventricular couplets (no non-sustained or sustained VT). The medication with amiodarone was discontinued due to side effects and changed to an oral beta-blocker (bisoprolol).

**Discussion**

Three young patients with idiopathic LV aneurysms and life-threatening ventricular tachyarrhythmias underwent detailed evaluation by imaging techniques (echo, MRI). Additional radionuclide tests showed a transmural defect of myocardial glucose metabolism with concordant defects in MIBG uptake limited to the aneurysmal segment but without distal denervation.

**Pathogenesis of LV aneurysm**

LV aneurysms are usually classified as congenital or acquired, i.e. arising from a cardiac or non-cardiac disorder (Figure 6).

Acquired LV aneurysms mainly result from myocardial infarction or coronary artery malformations (i.e. fistula). However, they may also be present in arrhythmogenic right ventricular cardiomyopathy, hypertrophic cardiomyopathy, or myocarditis (Figure 6). Non-cardiac or systemic diseases include sarcoidosis, Chagas’ disease, lupus erythematosus, Behçet’s disease, tuberculosis, or HIV. As a rare complication, LV aneurysms were also observed in glycogen storage diseases and in the hyperimmunoglobulin E syndrome. Furthermore, blunt chest trauma may lead to the development of an LV aneurysm.

Congenital LV aneurysms, comprising the perinatal period, have been detected as early as the second trimester of gestation and were associated with severe co-morbidity (hydrops fetalis, ventricular arrhythmias, heart failure) and intra-uterine fetal death.

To investigate further the underlying pathophysiology of arrhythmogenic LV aneurysms in the reported three cases, we assessed myocardial morphology, function, metabolism, and sympathetic innervation by means of MRI, echo, angiography, and radionuclide imaging. Consistent defects of myocardial glucose metabolism and presynaptic adrenergic sympathetic innervation were displayed in the area of the LV aneurysm. However, the area of denervation did not exceed that of the LV aneurysm, as is usually the case in post-myocardial infarction scarring (distal denervation).

**LV aneurysm and malignant tachyarrhythmias**

In the present report as well as in previous studies, the tissue of the LV aneurysm was found to be inhomogeneous with viable, normal myocytes, fibrotic tissue, and/or hypertrophic myocytes. As non-transmural myocardial infarction, this may well represent an arrhythmogenic substrate due to local conduction delay and dispersion of excitability and refractoriness which may even be augmented by catecholamines during physical exercise and/or mental stress. These factors may increase the propensity to potentially lethal arrhythmias in idiopathic LV aneurysms.

**Case 3**

A 31-year-old male student was operated for a right-sided chromophobic grade II renal carcinoma in June 2001. Postoperatively, ventricular premature beats with left bundle branch block morphology were documented on a routine 12-lead surface ECG. A Holter-recording revealed multiple asymptomatic ventricular couplets and triplets that triggered further cardiovascular workup. The family history was unremarkable with regard to premature death, unexplained syncope, or ventricular tachyarrhythmias. He had no history of palpitations or arrhythmic events and no cardiovascular risk factors or allergies. Physical examination, 12-lead surface ECG, bicycle exercise test, and laboratory tests showed normal findings.

LV angiography confirmed an infero-basal aneurysm with polycyclic-bordered prolonged dye persistence, which had also been detected on transthoracic echocardiography and MRI. No other abnormalities were observed during right ventricular angiography, coronary angiography, and haemodynamic assessment, respectively.

Programmed ventricular stimulation reproducibly induced polymorphic, fast (cycle length 160–230 ms) non-sustained VT with three extrastimuli.

**Figure 5** Case 2. Histopathology of endomyocardial biopsies from the site of idiopathic LV aneurysm. Myocardial fibrosis (scarring) without signs of inflammation or active myocyte lysis is demonstrated 200-fold magnification with Haematoxylin–Eosin staining (A) and 400-fold magnification with van-Gieson staining (B).
Treatment options and treatment dilemma
Patients with LV aneurysms may present with a variety of symptoms, encompassing ventricular tachyarrhythmias and sudden cardiac death, angina pectoris,28 congestive heart failure,3 or recurrent arterial emboli.29,30 Treatment and prognosis of idiopathic LV aneurysms are dependent on their size, location, and degree of valvular involvement, functional class of congestive heart failure, and the presence of ventricular tachyarrhythmias. Therapeutic options therefore range from antiarrhythmic drug treatment31 to VT ablation,32 implantation of an ICD,25 or (less frequently) aneurysmectomy.33 However, prospective long-term follow-up studies comparing the different management strategies are not available.

Sympathetic denervation in LV aneurysm
This report describes for the first time a match between myocardial adrenergic innervation and metabolism in patients with idiopathic LV aneurysms. Regional sympathetic innervation itself can be influenced by factors such as ischaemia or local tissue destruction (e.g. infection, systemic metabolic disorders). It is generally accepted that a local sympathetic nerve destruction results in a distal denervation of non-affected myocardium because the sympathetic nerves travel epicardially from the base to the apex of the heart, parallel to the coronary arteries. Therefore, a ‘downstream sympathetic denervation’ was described after myocardial ischaemia34 as well as following epicardial application of phenol to proximal parts of the myocardium in experimental animal studies.34 A subsequent imbalance of denervated but viable myocardium results in dispersion of refractoriness and increased sensitivity toward catecholamines (‘supersensitivity’), thus providing a substrate for the high propensity of malignant ventricular tachyarrhythmias. However, such a ‘downstream sympathetic denervation’ was not present in the investigated patients, because the defect in $^{123}$I-MIBG-SPECT consistently matched the tissue defect displayed by the $^{18}$F-FDG PET scintigraphy and MRI. It is therefore hypothesized that these aneurysms may have occurred early in the evolution of the heart where nerve travel still has the chance to circumvent the structural defect or where re-innervation has already occurred.

The young age of the patients studied with no history of angina, no clinical event indicative of myocardial infarction, and normal coronary arteries and flow strongly argues against myocardial infarction as the underlying cause for the development of the described LV aneurysms, which cannot, however, be completely excluded.

It remains unclear why a congenital origin of the LV aneurysms should lead to ventricular tachyarrhythmias as late as in adolescence. However, this is in line with previous reports of non-acquired LV aneurysms,25,31,33,35,36 and has also been observed in other arrhythmogenic diseases with a congenital or genetic background (e.g. arrhythmogenic right ventricular cardiomyopathy, idiopathic VT, Brugada syndrome, hypertrophic cardiomyopathy, and others).

Study limitations
Although this report included only a small number of patients with a rare cardiac disease, the patients are well characterized and underwent detailed diagnostic evaluation to assess the morphological, functional, and pathophysiological characteristic features of this rare disorder.

Conclusions
Patients with an idiopathic LV aneurysm are at potential risk for life-threatening ventricular tachyarrhythmias and sudden death, which may sometimes occur as the first clinical presentation.

Transthoracic echocardiography, MRI, and cardiac catheterization can reliably detect the location, extent, and morphology of the aneurysm. Modern contrast-enhanced MR imaging provides additional information on myocardial tissue characteristics, perfusion, and viability. Radionuclide
imaging with analysis of viability (18F-FDG-PET) and sympathetic innervation (123I-MIBG-SPECT) can help to elucidate further the pathogenesis of idiopathic LV aneurysms. Management strategies should be individualized and are mainly directed toward prevention of sudden death and recurrent life-threatening arrhythmias by antiarrhythmic drug therapy,31 VT ablation,32 ICD implantation, or (less frequently) aneurysmectomy.33 In addition, treatment of heart failure may be required in selected cases.

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