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Short communication

Sudden death in transposition of the great arteries with atrial switch surgery: Autopsy evidence of acute myocardial ischemia despite normal coronary arteries

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ABSTRACT

Background: Sudden death is the leading cause of mortality in patients with transposition of the great arteries (TGA) and atrial switch surgery. Understanding underlying mechanisms could contribute to identifying high-risk patients and preventing such catastrophic deaths.
Methods: A total of 144 adults (≥18 years) with TGA and atrial switch surgery were followed at our adult congenital center since 1989. Four patients were excluded: two with double-outlet right ventricles and two with subsequent arterial switch surgery in childhood.
Results: Of the remaining 140 patients, age 37.6 ± 7.8 years, 37.1% female, 8 (6%) had a cardiac arrest of presumed arrhythmic etiology of whom 3 were resuscitated. The arrests occurred in 3 women and 5 men at age 30.5 ± 8.6 (range 22 to 50) years. None had established coronary artery disease, sustained ventricular arrhythmias, or syncope. Four (50%) had atrial arrhythmias and 6 (75%) had at least moderate systemic right ventricular dysfunction. For 5 patients in whom circumstances surrounding the arrests were documented, 3 occurred on exertion, 1 after consuming recreational methamphetamine, and 1 in the context of an atrial tachyarrhythmia. Autopsies were performed in 2 of 5 patients. Both revealed acute massive myocardial infarction of the hypertrophied systemic right ventricle with normal coronary arteries and chronic subendocardial ischemic lesions.
Conclusion: This is the first report to provide histopathological evidence in support of a myocardial ischemia hypothesis as a cause of sudden death in this patient population, despite the absence of coronary atherosclerosis.

1. Introduction

Sudden cardiac death is the leading cause of mortality in patients with transposition of the great arteries (TGA) and atrial switch surgery by means of a Mustard or Senning procedure. Attempts to reliably identify a high-risk subgroup have been disappointing, such that there is little evidence to guide the selection of suitable candidates for primary prevention implantable cardioverter-defibrillators (ICD) [1]. It has recently been hypothesized that a myocardial oxygen-supply mismatch of the systemic right ventricle can occur during rapid heart rates and provoke ischemia-related ventricular arrhythmias leading to sudden death [2]. Herein, we provide histopathological evidence in support of the myocardial-ischemia hypothesis as a cause of sudden death in this patient population.

2. Methods

A retrospective cohort study was conducted on all adults (≥18 years) with TGA and atrial switch surgery followed at the Montreal Heart Institute Adult Congenital Center since 1989. Patients with double-outlet right ventricles or arterial switch surgery during childhood (i.e., following a Mustard or Senning procedure) were excluded. Follow-up was performed according to the center's standardized assessment plan, which includes outpatient visits at least once per year (with cardiac imaging and a 12-lead electrocardiogram) and exercise tests and Holter monitoring every 2–3 years. Continuous variables are summarized as mean ± standard deviation and categorical variables by frequencies and percentages. Inferential statistics were not performed. The study was approved by our local institutional review board, with waiver of informed consent.

3. Results

A total of 144 adults (≥18 years) with TGA and atrial switch surgery were identified of whom 4 were excluded: two with double-outlet right ventricles and two with subsequent arterial switch surgery in

Abbreviations: ICD, implantable cardioverter-defibrillator; NYHA, New York Heart Association; TGA, transposition of the great arteries.

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childhood. Of the remaining 140 patients, age 37.6 ± 7.8 years, 37.1% female, 8 (6%) had a cardiac arrest of presumed arrhythmic etiology, 3 of whom were successfully resuscitated. The arrests occurred in 3 women and 5 men at age 30.5 ± 8.6 (range 22 to 50) years. None had a prior diagnosis of coronary artery disease, sustained ventricular arrhythmia, or syncope. Four (50%) had atrial arrhythmias, 1 (13%) had asymptomatic non-sustained ventricular tachycardia on Holter monitoring, 2 (25%) had pacemakers (for sinus node dysfunction and tachy/brady syndrome), 6 (75%) had at least moderate systemic right ventricular dysfunction, and 4 (50%) had more than mild systemic atrioventricular valve (tricuspid) regurgitation. The New York Heart Association (NYHA) functional class was I in 5 (63%), II in 2 (25%), and III in 1 (13%) patient. Only one patient had received a beta-blocker (bisoprolol 5 mg PO qday) prior to the arrest. For 5 patients in whom circumstances surrounding the cardiac arrest were documented, 3 occurred on exertion, 1 after consuming recreational methamphetamine, and 1 at rest in the context of an atrial tachyarrhythmia.

Autopsies were performed in 2 of 5 patients. The first had simple TGA with Mustard surgery at age 12. She presented with atrial tachyarrhythmias at age 21, with both atrial fibrillation and, later, intra-atrial re-entrant tachycardia, managed pharmacologically. At age 27, she underwent mechanical tricuspid valve replacement in the context of severe regurgitation with moderate to severe systemic right ventricular dysfunction despite NYHA class I symptoms. She was extubated the following day and died suddenly out-of-hospital 7 days post-operatively. Circumstances surrounding her death were not recorded. The second patient had a concomitant patent ductus arteriosus and underwent Mustard surgery at 1 year of age. She also had moderate to severe systemic right ventricular dysfunction, moderate tricuspid regurgitation, and NYHA class I symptoms following 4 uneventful term pregnancies. She had no history of arrhythmias but experienced atypical chest pain on exertion since the age of 29 years. Serial testing revealed no electrocardiographic or ischemic changes during exercise by myocardial perfusion scintigraphy. She died suddenly at 38 years of age while walking at work, with documented ventricular fibrillation. Autopsies for both patients showed acute massive myocardial infarction of the hypertrophied systemic right ventricle with normal coronary arteries and chronic subendocardial ischemic lesions. The acute myocardial infarction involved the postero-septal systemic right ventricle in the first patient. In the second patient, acute ischemic changes in the postero-lateral wall were associated with chronic subendocardial lesions in the same territory (Fig. 1).

4. Discussion

This report provides histopathological evidence in support of the myocardial ischemia hypothesis leading to sudden death in patients with TGA and Mustard or Senning baffles despite the absence of coronary atherosclerosis. The proposed pathophysiological mechanism invokes an impaired stroke volume response due to poor atrial transport, which is exacerbated by rapid heart rates [2]. The reduction in stroke volume combined with the increased myocardial oxygen demand of the hypertrophied systemic right ventricle, decreased perfusion pressure, and inefficient coronary circulation (i.e., systemic ventricle predominantly irrigated by a single right coronary artery) is thought to provoke ischemic ventricular arrhythmias. It has previously been

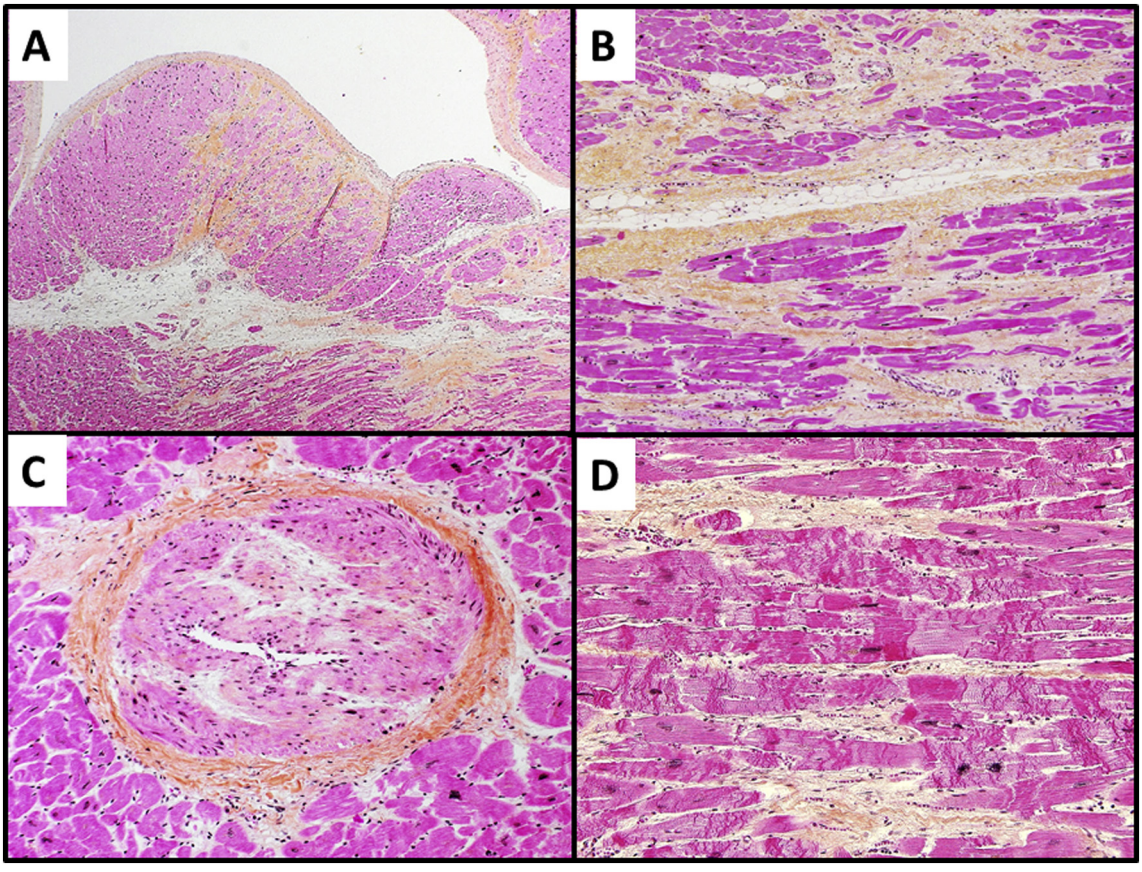

Fig. 1. Shown are histological hematoxylin phloxine saffron stains of the systemic right ventricle. Characteristic chronic subendocardial ischemic changes are seen at (A) low power (20×) and (B) medium power (100×), with subendocardial pericellular and replacement-type interstitial fibrosis and foci of fatty replacement. In Panel (C), marked medial hypertrophy of an intramural coronary artery is shown in the absence of atherosclerosis (100×). Panel (D) depicts multifocal acute ischemia in the form of contraction band necrosis superimposed on chronic ischemic changes (200×).

shown that patients with TGA and atrial switch have a lower coronary flow reserve during exercise [3], with evidence of perfusion defects predominantly in the systemic right ventricle's inferior and septal walls [4]. We also observed medial hypertrophy of the intramural coronary arteries, which has been described in patients with hypertrophic cardiomyopathy who died suddenly [5].

5. Conclusion

In conclusion, this is the first report to provide histopathological evidence in support of a myocardial oxygen supply-demand mismatch despite the absence of coronary atherosclerosis as a cause of sudden death in this patient population. These findings have important clinical implications and could inform efforts to identify and protect high-risk subgroups. For example, a case could be made for aggressive management of atrial tachyarrhythmias and counselling to avoid the use of stimulants and high intensity exercise, since these factors can potentially provoke subendocardial ischemia and trigger malignant ventricular arrhythmias. Consideration could also be given to liberalizing the use of beta-blocker therapy to prevent atrial arrhythmias from conducting rapidly, improve the stroke volume response, and increase the threshold for ischemic ventricular arrhythmias [1].

Conflict of interest

The authors report no relationships that could be construed as a conflict of interest.

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