

Differential gene expression profile of male and female copepods in response to cadmium exposure

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1	Percutaneous catheter ablation of malignant, recurrent
2	ventricular arrhythmia in a 10 month-old toddler
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7	Short title: Ventricular tachycardia ablation in a 10 month-old baby
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 membrane oxygenation.
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35 Abbreviations:

- 36 ECMO Extracorporeal membrane oxygenation
- 37 LV Left ventricle
- 38 LVEF Left ventricular ejection fraction
- 39 PVS Premature ventricular contraction
- 40 VT Ventricular tachycardia
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44 Introduction

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Catheter ablation is a safe and effective treatment modality for ventricular arrhythmia. The 46 procedure is routine at many electrophysiology centres and is being undertaken ever earlier 47 in patient care (1). However, the great majority of these procedures involve adults suffering 48 49 from ischaemic heart disease. Only three cases of transapical access catheter ablation of 50 ventricular tachycardia (VT) have been reported in children of under 15 months of age (2, 3, 4). Such procedures are technically difficult because the catheters available are ill-suited to 51 the small-sized heart of a child. We report a case of a 10 month-old toddler in whom life-52 53 saving ablation of VT was performed via a percutaneous femoral approach with trans-septal access to the left ventricle. 54

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57 Case report

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A 10 month-old baby boy weighing 9 kilograms with unremarkable past medical history was 59 admitted into our establishment following recovery from sudden cardiac arrest. He had been 60 61 at the house of his grandmother who is a nurse. About 30 minutes after bed-time at about 9 62 p.m., she noticed abnormal breathing sounds. In the bedroom, she found him cyanotic and 63 appearing lifeless. In the absence of a pulse, she started cardiac massage and called an ambulance. When the emergency services arrived, they administered care with external 64 cardiac massage and ventilation. Electrocardiography showed ventricular fibrillation. 65 Defibrillation was carried out and one shock restored sinus rhythm. On route to the hospital, 66 three further episodes of ventricular arrhythmia occurred, each requiring electrical 67 cardioversion. On admission into Intensive Care, the child was intubated and given general 68 anaesthetic. The child was afebrile and hemodynamically stable. Echocardiography showed a 69 70 normal-sized left ventricle with an ejection fraction of 35%. The remainder of the evaluation was unremarkable. The coronary arteries were visible and in a normal configuration. 71 72 Electrocardiography findings were normal between the episodes of ventricular arrhythmia. 73 Tests showed normal blood counts, moderately elevated CRP at 14.1 mg/L (<5.0 mg/L), hepatic cytolysis (AST 222 IU/L (<50 IU/L) and AST 70 IU/L (<50 IU/L)), very high BNP at 3,143 74 ng/L (<100.0 ng/L) and troponin Ic at 2.651 ng/mL (<0.35 ng/mL). Electrolytes were normal. 75 In the hour following admission, he experienced a series of rapid VT episodes, relatively 76 77 monomorphic at 280 bpm with most episodes progressing to ventricular fibrillation (figure 1 78 and 2). About 20 electric shocks had to be delivered despite the intravenous administration

80 200 μg/Kg/min). Lidocaine was transiently used without effect. All episodes began with

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of amiodarone (5 mg/kg over 30 minutes then 20 mg/kg/day) and a beta-blocker (Esmolol,

81 monomorphic ventricular extrasystole, identical to the VT with an origin at the median 82 posterolateral part of the left ventricle (Figure 1 and 2).

Over the following few hours, there were numerous recurrences of ventricular arrhythmia. 83 The baby's hemodynamic condition deteriorated and his left ventricular ejection fraction 84 (LVEF) dropped further down to 25%. The clinical picture incited emergency circulatory 85 86 assistance with extracorporeal membrane oxygenation (ECMO) via right jugulocarotid 87 cannulation. Although haemodynamics improved and BNP and troponin levels returned to 88 normal on sustained intravenous amiodarone plus esmolol, recurrent episodes of VT persisted. These were monomorphic and slower but were practically incessant. Some of 89 them continued to progress to ventricular fibrillation, requiring electrical cardioversion 90 (figure 2). Several electric shocks were required every day. In all, more than 50 shocks were 91 92 delivered over 7 days in Intensive Care on ECMO, despite intensive pharmacological treatment. Given the incessant recalcitrant nature of the ventricular arrhythmia without any 93 clear aetiology, it was decided to attempt life-saving catheter ablation. 94

95 The approach strategy chosen to access the left ventricle was the right femoral vein 96 combined with trans-septal puncture guided by a trans-oesophageal echocardiography 97 (figure 3). We mapped left ventricular activation using a 3D Velocity navigation system (St Jude Medical). We first used a standard 4 mm radiofrequency ablation catheter (5F, small 98 99 curve, St Jude Medical). This catheter was advanced through a short, small curve Agilis sheath (St Jude Medical). Manipulating the catheter was difficult because the small curve 100 101 was large relative to the small heart. The Agilis sheath proved ineffective and was therefore 102 left in the right atrium. When the catheter was in place in the left ventricle (LV), amiodarone 103 and esmolol were stopped. Subsequently, the ventricular arrhythmia got worse very quickly. 104 The voltage map did not show any scar. The tachycardia activation map showed primary

105 activation in the posterolateral wall of the middle part of the LV (maximum precocity 19 ms). Pace mapping at this site revealed a near identical QRS morphology to the clinical 106 arrhythmia (Figure 3). Radiofrequency application was limited at 5W because maximal 107 temperature was reached, without any effect on the arrhythmia. Then we decided to change 108 109 for an irrigated ablation catheter with contact force measurement (Tacticath, 4 mm, 8F, 110 small curve, St Jude Medical). As soon as radiofrequency application was begun at this site 111 with the irrigated catheter, the ventricular arrhythmia slowed down and then stopped 112 entirely after 11 seconds (Figure 3). In all, four 60-second, 25 Watts applications were administered with a contact force of between 15 and 20 grams. The whole procedure took 113 188 minutes with 12 minutes of fluoroscopy. 114

No recurrence occurred after the procedure despite stopping all anti arrhythmic treatment.
Post-ablation echocardiography showed moderate, non-compressive pericardial effusion
opposite the LV. Although this was non-compressive, this serosanguinous fluid was drained
because of the need for intensive anticoagulant therapy related to the ECMO. The origin of
the pericardial effusion remains unknown.

120 ECMO could be discontinued 48 hours after the ablation procedure.

121 Cardiac MRI a week after the procedure showed a LVEF of 50% with hypokinesia of the 122 posterolateral wall of the LV, a T2 hyposignal and contrast medium uptake after injection of 123 gadolinium into the sub-endocardial portion of the middle, inferolateral segment. It was 124 concluded that this was probably related to the delivery of radiofrequency energy.

The child's recovery was complicated by symptoms of withdrawal from the sedative regimen. A physical examination showed left hemiparesis. The stroke may have been due to the ablation procedure itself being on the left side of the heart that or to the jugulocarotid circulatory assistance.

129 Before discharge, a Linq ECG monitor (Medtronic) was implanted for remote monitoring.

After 30 months of follow-up, no recurrence of the arrhythmia has been observed. Global LV systolic function has normalised although some highly localised segmental hypokinesia persists in the ablated region. Psychomotor progress has been satisfactory with full recovery of motor function on the left hand side of the body. Motor and intellectual development have been normal and the child goes to regular school.

Electrocardiography in sinus rhythm has never detected any abnormality, in particular no abnormality suggesting channelopathy. A family investigation including electrocardiography and echocardiography on siblings and parents revealed nothing. Nor did a genetic analysis focusing on all the genes known to be associated with channelopathy reveal any abnormality.

140 In the end, the aetiology of this malignant arrhythmia remains unknown.

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142 **Discussion**

To our knowledge, this is the first report of successful catheter ablation of left VT achieved
by trans-septal access in a child of under one year of age.

The incidence of ventricular tachycardia is low in paediatric patients without any underlying heart disease (5). Most cases concern idiopathic VT, commonly arising from the right ventricular outflow tract (5, 6, 7, 8). Three cases of VT ablation via a transapical approach have been reported in the literature (2, 3, 4). In all these three cases, the VT involved the posterior mitral annulus. The children's ages were 10, 11 and 14 months. It should be noted that in two of the three cases, transapical access was only attempted secondarily after failure of trans-septal and retro-aortic approach.

152 In our procedure, the main technical difficulties were associated with the trans-septal 153 approach and manipulation of the ablation catheter. Despite using the smallest curve 154 available, it was still far too big for use in such a small heart. The steerable sheath proved 155 entirely ineffective.

For the mapping, primary activation was localised fairly quickly even though it was limited (-157 19 ms) compared with what is usually seen in adults. This was probably not a re-entry 158 because no mid-diastolic potential was recorded and the tachycardia did not respond to 159 ventricular stimulation.

Despite decreasing prevalence, sudden infant death syndrome remains the leading cause of death in babies of 1-12 months in the developed world, affecting some 1/2,000 births in the United States (9). Various pathogenic mechanisms are suspected and certain risk factors have been identified. The role of arrhythmia may be underestimated because autopsies often find nothing and genetic analyses uninformative.

165 In the case reported here, the initial cardiological investigations did not find any abnormality 166 or establish the aetiology. In particular, electrocardiography findings did not point to 167 channelopathy. Explorations in first-degree relatives found nothing: all findings were 168 perfectly normal.

The overall clinical picture did not indicate myocarditis. Moderate rises in CRP and troponin lc were attributed to the ventricular arrhythmia as well as repeated shocks. There was never any fever and both CRP and troponin levels soon returned to normal. ECG findings remained normal between episodes of ventricular arrhythmia. Unfortunately, cardiac MRI was not performed before the ablation procedure. The MRI abnormalities observed following ablation were probably associated with the delivery of radiofrequency energy. No subepicardial uptake of contrast medium—classically seen in myocarditis—was observed. In

176 contrast, there was delayed subendocardial enhancement associated with hypokinesia,177 corresponding to the tissue targeted for ablation.

178 Conclusion

We have reported the first catheter ablation of left ventricular tachycardia via a percutaneous, trans-septal approach in a 10 month-old baby on ECMO suffering from malignant arrhythmia refractory to pharmacological treatment. The cause of this massive arrhythmia was not determined. After 30 months of follow-up, no recurrence of the arrhythmia has been observed.

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