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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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34

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

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57 **Case report**

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59 A 10 month-old baby boy weighing 9 kilograms with unremarkable past medical history was
60 admitted into our establishment following recovery from sudden cardiac arrest. He had been
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
64 ambulance. When the emergency services arrived, they administered care with external
65 cardiac massage and ventilation. Electrocardiography showed ventricular fibrillation.
66 Defibrillation was carried out and one shock restored sinus rhythm. On route to the hospital,
67 three further episodes of ventricular arrhythmia occurred, each requiring electrical
68 cardioversion. On admission into Intensive Care, the child was intubated and given general
69 anaesthetic. The child was afebrile and hemodynamically stable. Echocardiography showed a
70 normal-sized left ventricle with an ejection fraction of 35%. The remainder of the evaluation
71 was unremarkable. The coronary arteries were visible and in a normal configuration.
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),
74 hepatic cytolysis (AST 222 IU/L (<50 IU/L) and AST 70 IU/L (<50 IU/L)), very high BNP at 3,143
75 ng/L (<100.0 ng/L) and troponin Ic at 2.651 ng/mL (<0.35 ng/mL). Electrolytes were normal.
76 In the hour following admission, he experienced a series of rapid VT episodes, relatively
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
79 of amiodarone (5 mg/kg over 30 minutes then 20 mg/kg/day) and a beta-blocker (Esmolol,
80 200 µg/Kg/min). Lidocaine was transiently used without effect. All episodes began with

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).

83 Over the following few hours, there were numerous recurrences of ventricular arrhythmia.
84 The baby's hemodynamic condition deteriorated and his left ventricular ejection fraction
85 (LVEF) dropped further down to 25%. The clinical picture incited emergency circulatory
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
89 persisted. These were monomorphic and slower but were practically incessant. Some of
90 them continued to progress to ventricular fibrillation, requiring electrical cardioversion
91 (figure 2). Several electric shocks were required every day. In all, more than 50 shocks were
92 delivered over 7 days in Intensive Care on ECMO, despite intensive pharmacological
93 treatment. Given the incessant recalcitrant nature of the ventricular arrhythmia without any
94 clear aetiology, it was decided to attempt life-saving catheter ablation.

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
98 Jude Medical). We first used a standard 4 mm radiofrequency ablation catheter (5F, small
99 curve, St Jude Medical). This catheter was advanced through a short, small curve Agilis
100 sheath (St Jude Medical). Manipulating the catheter was difficult because the small curve
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).
106 Pace mapping at this site revealed a near identical QRS morphology to the clinical
107 arrhythmia (Figure 3). Radiofrequency application was limited at 5W because maximal
108 temperature was reached, without any effect on the arrhythmia. Then we decided to change
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
113 administered with a contact force of between 15 and 20 grams. The whole procedure took
114 188 minutes with 12 minutes of fluoroscopy.

115 No recurrence occurred after the procedure despite stopping all anti arrhythmic treatment.
116 Post-ablation echocardiography showed moderate, non-compressive pericardial effusion
117 opposite the LV. Although this was non-compressive, this serosanguinous fluid was drained
118 because of the need for intensive anticoagulant therapy related to the ECMO. The origin of
119 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.

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

129 Before discharge, a Linq ECG monitor (Medtronic) was implanted for remote monitoring.
130 After 30 months of follow-up, no recurrence of the arrhythmia has been observed. Global LV
131 systolic function has normalised although some highly localised segmental hypokinesia
132 persists in the ablated region. Psychomotor progress has been satisfactory with full recovery
133 of motor function on the left hand side of the body. Motor and intellectual development
134 have been normal and the child goes to regular school.
135 Electrocardiography in sinus rhythm has never detected any abnormality, in particular no
136 abnormality suggesting channelopathy. A family investigation including electrocardiography
137 and echocardiography on siblings and parents revealed nothing. Nor did a genetic analysis
138 focusing on all the genes known to be associated with channelopathy reveal any
139 abnormality.
140 In the end, the aetiology of this malignant arrhythmia remains unknown.

141

142 **Discussion**

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

145 The incidence of ventricular tachycardia is low in paediatric patients without any underlying
146 heart disease (5). Most cases concern idiopathic VT, commonly arising from the right
147 ventricular outflow tract (5, 6, 7, 8). Three cases of VT ablation via a transapical approach
148 have been reported in the literature (2, 3, 4). In all these three cases, the VT involved the
149 posterior mitral annulus. The children's ages were 10, 11 and 14 months. It should be noted
150 that in two of the three cases, transapical access was only attempted secondarily after
151 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.

156 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.

160 Despite decreasing prevalence, sudden infant death syndrome remains the leading cause of
161 death in babies of 1-12 months in the developed world, affecting some 1/2,000 births in the
162 United States (9). Various pathogenic mechanisms are suspected and certain risk factors
163 have been identified. The role of arrhythmia may be underestimated because autopsies
164 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.

169 The overall clinical picture did not indicate myocarditis. Moderate rises in CRP and troponin
170 Ic were attributed to the ventricular arrhythmia as well as repeated shocks. There was never
171 any fever and both CRP and troponin levels soon returned to normal. ECG findings remained
172 normal between episodes of ventricular arrhythmia. Unfortunately, cardiac MRI was not
173 performed before the ablation procedure. The MRI abnormalities observed following
174 ablation were probably associated with the delivery of radiofrequency energy. No
175 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**

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

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Pseudodiaptomus annandalei

Nauplii

