ECMO support in a child with cardiogenic shock due to *Kingella Kingae* endocarditis

ECMO en un lactante con shock cardiogénico secundario a endocarditis por *Kingella Kingae*

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**Abstract**

**Introduction:** Endocarditis is a rare disease in children, especially in those without previous heart disease, and *Kingella Kingae* (*KK*) is rarely identified as the cause. Extracorporeal membrane oxygenation (ECMO) is a support for both heart and respiratory failure. **Objective:** To report the first case of infectious endocarditis (IE) due to *KK* which required ECMO support secondary to refractory cardiogenic shock. **Clinical case:** 19-months-old previously healthy female patient, with a 2-day history of fever, and diagnosed with hand-foot-and-mouth disease. The patient developed refractory cardiogenic shock, multiorgan failure, acute respiratory distress syndrome, and deep hemodynamic compromise that required veno-arterial ECMO support. The echography showed an image compatible with mitral valve vegetation, confirming IE with transthoracic echocardiography. Blood culture was positive for *KK*. She had an ischemic stroke and required two heart surgeries, the first one for the mass resection and the second one for mitral valve repair, which had a posterior ring pseudoaneurysm. The patient had a favorable evolution and was discharged 73 days after admission. At one year of follow-up, she had no cardiological symptoms, but a mild right brachial-crural hemiparesis persisted. **Conclusion:** This is the first reported case of IE due to *KK* that required extracorporeal life support. *KK* endocarditis is an uncommon pathology that can cause multiorgan failure, which can be successfully supported with ECMO.
**Introduction**

ECMO is a cardiorespiratory support procedure that has been developed since the 1970s in children and adults\(^1\). Its use has been expanding, especially over the last decade, with increasingly better results in different age groups\(^2\).

Infectious endocarditis (IE) is a serious disease, and is rare in people who have no previous heart disease. Risk factors for its occurrence include valve pathology, prolonged use of intravenous catheters, and immunosuppression. Hand-foot-and-mouth disease has recently been described as a risk factor for *Kingella Kingae* (KK)\(^3\).

Out of the causative germs, the HACEK group (*Haemophilus parainfluenzae*, *Aggregatibacter actinomycetemcomitans*, *Aggregatibacter aphrophilus*, *Cardiobacterium hominis*, *Eikenella corrrodens*, *Kingella kingae*), particularly KK, is one of the less frequent and is difficult to diagnose, considering that they are ‘fastidious’ organisms difficult to identify microbiologically, as they require special means for their growth\(^4\)\(^-\)\(^7\).

KK is a gram-negative microorganism – hemolytic anaerobic facultative, which is difficult to isolate and identify in fluids, with up to 90% false negatives described. This has led to the development of new diagnostic techniques, such as nucleic acid amplification assays, this increases the sensitivity and reduce the time to diagnosis from days to hours. The usual treatment is penicillin, ampicillin or cephalosporins of second and third generation\(^7\). Increased resistance to beta-lactams has been reported\(^8\). The germ usually colonizes the upper respiratory tract in children\(^9\), so overcrowding, is the main risk factor for carrying it\(^10\). The pathogenesis of invasive disease is unclear, but viral co-infection has been identified as a risk factor\(^11\), in particular, hand-foot-and-mouth disease\(^3\). The most common invasive KK disease is osteoarticular infection, but the most severe is infectious endocarditis\(^9\).

Patients with IE may progress to cardiogenic shock, and, as with other conditions, when routine medical therapy (consisting of volume management, vasoactive drugs, and general support in addition to baseline disease) is not enough, ECMO may support if there is an acute cardiorespiratory failure.

The objective of this study is to report the first case of IE due to KK that required ECMO support due to a refractory cardiogenic shock.

**Clinical case**

A 19-month-old infant, previously healthy and eutrophic, who consulted due to 2-days history of fever and general condition involvement. The initial diagnosis was a probable herpetic gingivostomatitis or hand-foot-and-mouth disease, with initial symptomatic treatment, and after a second consultation, acyclovir.

Due to the symptoms persistence, she consulted again after three days. She was admitted to the emergency service in good general condition, with laboratory tests compatible with bacterial infectious disease, evolving with hemodynamic instability, therefore she received two boluses of crystalloids and was transferred to the intensive care unit (Tables 1 and 2).

She was admitted to the intensive care unit three hours after her emergency consultation, with rapid...

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**Table 1. First Lab Values (Emergency Department)**

<table>
<thead>
<tr>
<th>Lab Values</th>
<th>Normal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>7.9 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>33000/cc</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>23500/cc</td>
</tr>
<tr>
<td>Bacilliformes</td>
<td>7%</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.28 mg/dL</td>
</tr>
<tr>
<td>Ureic nitrogen</td>
<td>15 mg/dL</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>130 mg/L</td>
</tr>
<tr>
<td>Venous Blood Gases</td>
<td>Normal Values</td>
</tr>
<tr>
<td>pH</td>
<td>7.35</td>
</tr>
<tr>
<td>pCO(_2)</td>
<td>41 mmHg</td>
</tr>
<tr>
<td>pO(_2)</td>
<td>34 mmHg</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>22 mmol/L</td>
</tr>
<tr>
<td>BE</td>
<td>-3.4 mmol/L</td>
</tr>
<tr>
<td>Saturation</td>
<td>62%</td>
</tr>
</tbody>
</table>

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*Figure 1. Chest X Ray after Veno Arterial ECMO cannulation, consolidation in both lower lobes is shown.*
Table 2. Vital Signs Evolution

<table>
<thead>
<tr>
<th>Vital Sign</th>
<th>ER admission</th>
<th>1 hour post admission</th>
<th>2 hours after admission</th>
<th>3 hours (transfer to ICU)</th>
<th>4 hours (pre-Intubation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (bpm)</td>
<td>199</td>
<td>158</td>
<td>177</td>
<td>165</td>
<td>192</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>AP (mmHg)</td>
<td>-</td>
<td>-</td>
<td>78/41</td>
<td>126/110</td>
<td>-</td>
</tr>
<tr>
<td>Sat O₂ (%)</td>
<td>97</td>
<td>98</td>
<td>98</td>
<td>95</td>
<td>-</td>
</tr>
<tr>
<td>Axillary Temp (ºC)</td>
<td>37,3</td>
<td>37,7</td>
<td>36</td>
<td>35,8</td>
<td>35,6</td>
</tr>
<tr>
<td>GCS</td>
<td>15</td>
<td>15</td>
<td>15</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>


Table 3. Arterial Blood Gases (FiO2 100%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Post Intubation</th>
<th>PostECMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.06</td>
<td>7.24</td>
</tr>
<tr>
<td>pCO₂</td>
<td>75.9</td>
<td>34.4</td>
</tr>
<tr>
<td>pO₂</td>
<td>40</td>
<td>79.2</td>
</tr>
<tr>
<td>HCO₃</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>BD</td>
<td>-10</td>
<td>-3.4</td>
</tr>
<tr>
<td>Sat</td>
<td>60%</td>
<td>62%</td>
</tr>
</tbody>
</table>

ECMO: Extracorporeal Membrane Oxygenation; pCO₂: CO₂ partial pressure; pO₂: O₂ partial pressure; HCO₃: Sodium bicarbonate; BD: base excess; Sat: O₂ saturation.

progression to shock (Table 2), thus she was intubated and empirical antimicrobials were initiated (cefofaxime, vancomycin, and acyclovir), as vasoactive drugs, and transfusions (240cc red blood cells, 120cc fresh frozen plasma, 1 platelet concentrate, and 1 cryoprecipitate). Within a few hours, she developed acute respiratory distress syndrome (ARDS), requiring increased support with invasive mechanical ventilation (IMV), bag-mask ventilation, and then high-frequency oscillatory ventilation (HFOV): mean airway pressure 30mmH₂O, delta pressure 40, respiratory rate 10Hz, inspired oxygen fraction (FiO₂) 100%, all under deep sedation, neuromuscular blockade and prone position. In spite of the above, she did not achieve adequate saturation or perfusion: pH 6.96 PaO₂ 97mmHg and PaCO₂ 102mmHg HCO₃ 22.5 BE -11 Saturation 92.8%, with lactic 17.21 mmol/L, requiring occasionally ventilation by bag mask. This was associated with acute hemodynamic compromise despite maximum vasoactive support (epinephrine 0.4mcg/Kg/min, norepinephrine 0.4mcg/Kg/min plus dobutamine 15mcg/Kg/min) (Table 2). Due to hemodynamic reasons, she did not tolerate high-volume continuous venovenous hemofiltration. The x-ray showed both lung fields with bilateral shadows. In the echography, an image compatible with mitral valve vegetation was observed. In the presence of catastrophic shock progression and ARDS, ECMO was requested.

She was evaluated by our mobile ECMO team and then cannulated on site to the cervical veno-arterial ECMO, with rapid blood gases improvement (Tables 2 and 3). She was transferred by ambulance connected to ECMO to our center. The cannula position was checked with ultrasound and radiography (Figure 1).

Upon admission, transthoracic echocardiography was performed, which confirmed mitral valve endocarditis and acute heart failure (accentuated mitral insufficiency, Jet area 40% of the left atrial area, left-ventricular ejection fraction (LVEF) of 35% (Figure 2). Brain CT scan showed left parietal infarction, with small hemorrhagic foci (Figure 3), so prophylactic anticonvulsants were initiated. That same day, the mass was resected and the mitral valve repaired.

Her initial evolution was satisfactory and without complications, with progressive improvement of cardiac function, shown by decreased vasoactive drug re-
quirements and echocardiographic monitoring. Volume depletion and sepsis control were achieved. ECMO support was removed after nine days, with low-dose support of epinephrine and milrinone, LVEF 65%. Protective ventilation was used (tidal volume 6mL/Kg, FiO₂ 40%, breathing rate (BR) 20 breaths per minute and end-expiratory pressure of 8mmHg). Three days after ECMO removal, VMI was removed, requiring reintubation 24 hour after due to acute pulmonary edema, attributed to increased post-load and moderate mitral insufficiency demonstrated in a new monitoring echocardiography. Post-loading was optimized and was extubated within ten days of this event.

In a control echocardiogram, on the 24th day after admission and already extubated, an undefined image of the mitral valve ring was detected. Due to the impossibility of performing a complimentary MRI due to pacemaker wires, Angio-CT was performed which showed mitral valve posterior ring pseudoaneurysm, with flow from the ventricular cavity (Figure 4). Repair of the mitral valve in extracorporeal circulation was performed, after which the patient required IMV for four days.

The initial standard aerobic blood culture was positive for KK, however, the culture of pericardial effusion and vegetation was negative - no special isolation techniques such as C-reactive protein (CRP) were applied. No lumbar puncture was considered necessary. Given the sensitivity of the germ, she was treated with ceftriaxone for 42 days. Secondary to the cerebral infarction diagnosed at admission, the patient developed right hemiparesis and promptly started physical therapy and multimodal rehabilitation.

The discharge was 73 days after the admission, in good general condition, with mild mitral insufficiency and recovering hemiparesis; on drug therapy with captopril, furosemide, aspirin, levetiracetam, and phenobarbital, as well as physical rehabilitation and occupational therapy. No immunological study was considered necessary. Follow-up one year after, the patient returned to normal activities for a girl of her age, with no symptoms of heart failure, and mild right brachial-crural hemiparesis.

Discussion

ECMO is a respiratory and/or cardiorespiratory support procedure that has been used since the 1970s to support patients with both respiratory and heart failure. In childhood heart failure has allowed a survival of 43%2,12. 269 ECMOs procedures have been performed at our center, 59 of them have been pediatric and 14 neonatal. During the past two years, eight cardiac ECMOs have been performed in pediatric patients, two of them have died (data not reported).

Out of the etiologies of acute heart failure in pediatrics, IE is one of the diagnoses that should be ruled out, even if the patient has no previous heart disease. The increasing use of intravascular devices - whether indwelling or temporary catheters - has been described as a major risk factor in patients without prior heart disease13. Another risk factor is immunosuppression14,15.

33% of patients with IE due to HACEK group have no risk factors15. KK is demonstrated in 4% of all cases of IE, being one of the most uncommon13,16. In our literature review, there are only 43 cases reported (in
both adults and children) with IE to this germ. Given the difficulty of diagnosis and its low frequency, a targeted study should be conducted in selected patients in order to provide specific antimicrobial therapy.

Out of the complications of IE, embolic stroke is one of the most feared and frequent ones, occurring in 24% of cases of IE due to *K. kingae*. In the presented case, an embolic stroke was observed at the time of the diagnosis of IE. This, together with catastrophic heart failure, required urgent heart surgery.

ECMO support in cardiorespiratory failure provides full support to let the patient stabilizes and get to surgery in better condition. In the experience of our center, it is a feasible and safe technique that can be used for a long time. As of February 2018, 92 ECMO mobile procedures have been performed, with 62% of survival at discharge (unpublished data). An adequate multidisciplinary support allows optimizing the evolution and improvement of the patient. Our patient had no complications out of ECMO, although she had a severe and torpid evolution, the ECMO provided time to make decisions in the most complex moment of her disease.

**Conclusions**

IE due to *Kingella kingae* is rare but it has a specific treatment. The diagnostic suspicion should be high, and not limited to children with classic risk factors for IE. To our knowledge, this is the only reported case of IE due to *KK* patient requiring ECMO support. In patients with heart failure or multiple organ failure resulting from an IE, an adequate diagnosis and a comprehensive multidisciplinary management, including ECMO, allows for favorable results despite the severity of their presentation.

**Ethical Responsibilities**

**Human Beings and animals protection:** Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

**Data confidentiality:** The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

**Rights to privacy and informed consent:** The authors state that the information has been obtained anonymously from previous data, therefore, Research Ethics Committee, in its discretion, has exempted from obtaining an informed consent, which is recorded in the respective form.

**Financial Disclosure**

Authors state that no economic support has been associated with the present study.

**Conflicts of Interest**

Authors declare no conflict of interest regarding the present study.

**References**

14. Foster MA, Walls T. High rates of complications following Kingella kingae
infective endocarditis in children: a case
series and review of the literature. Pediatr
15. Feder H, Roberts J, Salazar JC. HACEK
endocarditis in infants and children:
two cases and a literature review. Pediatr
16. Stockheim JA, Chadwick EG, Kessler S.
Are the Duke criteria superior to the Beth
Israel criteria for the diagnosis of infective
17. Le Bourgeois F, Germanaud D, Bendavid
M, et al. Kingella kingae Sequence Type
25 Causing Endocarditis with Multiple
and Severe Cerebral Complications. J
18. Noyes AM, Ramu B, Parker MW,
Underhill D, Gluck JA. Extracorporeal
Membrane Oxygenation as a Bridge
to Surgery for Infective Endocarditis
Complicated by Aorto-Atrial Fistula and
Cardiopulmonary Collapse. Tex Heart