



CASE REPORTS

Anesthetic management in an infant with a rare disease: the ectrodactyly-ectodermal dysplasia-clefting (EEC) syndrome

Manejo anestésico em lactente com rara doença: Síndrome Ectrodactilia, displasia ectodérmica e fissura labiopalatina (EEC)

Alberto Freaza Lobão Bastos¹

orcid.org/0000-0001-6412-1221
albertolobao@gmail.com

Lilian Satie Ykeizumi¹

orcid.org/0009-0003-7334-0612
lilian.satie.y@gmail.com

Paula Cristina Leitão de Assunção¹

orcid.org/0000-0002-0533-9121
paulaclassuncao@gmail.com

Cláudia Regina Machado²

orcid.org/0000-0002-9709-7958
claudia.r.machado1107@gmail.com

Bruno Vítor Martins Santiago²

orcid.org/0000-0002-2712-6311
bruno.santiago@hupe.uerj.br

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Abstract: Ectrodactyly, ectodermal dysplasia and cleft lip and palate syndrome (EEC), is a rare congenital genetic disease with autosomal dominant inheritance. This report is the first in the literature from the perspective of the anesthesiologist in relation to the perioperative care of a child with EEC syndrome, undergoing surgical corrections in different sites, at the same surgical time, which makes the conduction of anesthesia challenging, which must enable adequate control of pain and postoperative nausea and vomiting, without delaying hospital discharge. In these cases, pre-operative planning and interdisciplinary integration are essential to anticipate critical steps, in addition to allowing an individualized and comprehensive approach to achieve better results. The use of total intravenous anesthesia, associated with regional anesthesia, can be a systemic opioid-sparing strategy, decreasing emergency delirium and accelerating pediatric recovery.

Keywords: Infant, EEC syndrome, Pediatric anesthesia, Perioperative management.

Resumo: A síndrome ectrodactilia, displasia ectodérmica e fissura labiopalatina (EEC), é uma doença genética congênita rara com herança autossômica dominante. Este relato é o primeiro na literatura sob a perspectiva do anestesiolegista em relação aos cuidados perioperatórios de uma criança com síndrome EEC, submetida a correções cirúrgicas em diferentes sítios, no mesmo tempo cirúrgico, o que torna desafiadora a condução da anestesia, que deve possibilitar o controle adequado da dor e das náuseas e vômitos pós-operatórios, sem retardar a alta hospitalar. Nestes casos, o planejamento pré-operatório e a integração interdisciplinar são essenciais para antecipar etapas críticas, além de permitir uma abordagem individualizada e abrangente para atingir melhores resultados. O uso de anestesia venosa total, associada à anestesia regional, pode ser uma estratégia sistêmica poupadora de opioides, diminuindo o delírio de emergência e acelerando a recuperação pediátrica.

Palavras-chave: Lactente, Síndrome EEC, Anestesia pediátrica, Manejo perioperatório.

Introduction

Ectrodactyly-ectodermal dysplasia-cleft (EEC) syndrome is a rare genetic disorder with multiple congenital anomalies characterized by triad of ectrodactyly-ectodermal dysplasia, and facial clefting (1-2). The EEC syndrome was first described in 1936 by Cockayne (3). The term was first coined by Rüdiger *et al.* (4) in 1970. The inheritance is autosomal dominant, but sporadic and autosomal recessive traits have also been

¹ Hospital Universitário Pedro Ernesto. Universidade do Estado do Rio de Janeiro (UERJ), RJ, Brazil.

² Faculdade de Ciências Médicas. Hospital Universitário Pedro Ernesto. Universidade do Estado do Rio de Janeiro (UERJ), RJ, Brazil.

reported. Genetic studies have revealed that mutation in the TP63 or TP73L genes occur in these cases (5). Celli *et al.* (1) reported that a mutation in p63 gene a homolog of p53 gene-is found to be associated with EEC syndrome.

More than 300 cases have been described in the literature, affects both males and females but the prevalence and incidence is not known (6). Although these patients undergo surgical procedures for anatomical deformities; there are no articles, to date, that propose to study anesthetic care in patients with this syndrome, with the aim of proposing a line of care.

The main clinical findings in EEC syndrome are varying degrees of mesoaxial and longitudinal defects in the distal part of the limbs, cleft lip and palate, and abnormal development of ectodermal derivatives, such as malformed or missing teeth, dystrophic nails, tear duct stenosis, thin underdeveloped nipples, and absent or hypopigmented hair. Other signs include hearing loss and urinary tract disorders (7-8). These anatomical changes can interfere with anesthesia, making it a real challenge, as shown in **Figure 1**, which summarizes the main implications, which must be included in the line of care.

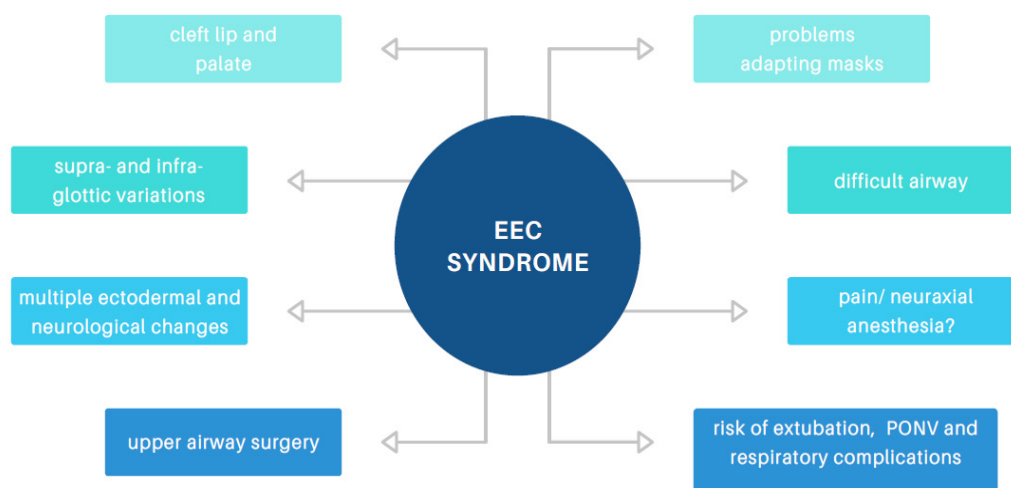


Figure 1 – Anatomical changes and their implications for anesthesia

This report is the first to discuss the perioperative care of a pediatric patient with EEC syndrome undergoing surgical corrections at different sites from the anesthesiologist's perspective. Furthermore, it addresses the safety aspects and good clinical practices focusing on early discharge.

The case report was approved by the Human Research Ethics Committee of the Rio de Janeiro State University, N°. 6.600.413. Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information and image to be published in this article. This report follows the CARE guidelines (<https://www.care-statement.org/checklist>) and adheres to the recommendations of the Society for Pediatric Anesthesia (SPA) guidelines (9-10).

Case Report

A male pediatric patient aged 1 year and 7 months, weighing 10 kg, with EEC syndrome and a history of cow's milk protein allergy was eligible for the surgical correction of anomalies in the toes, cheiloplasty, palatoplasty, and implantation of an ear ventilation tube under general anesthesia (**Figure 2**).

Dexmedetomidine $2 \mu\text{g}\cdot\text{kg}^{-1}$ was administered intranasally as the premedication 40 min before entering the operating room, with satisfactory effect and mild sedation classified as -2 on the Richmond Agitation-Sedation Scale (11).

Cardiography, noninvasive blood pressure measurement, pulse oximetry, consciousness level assessment using the bispectral index (BIS),

temperature measurement, capnography, and neuromuscular transmission were performed to monitor the patient. A mixture of 8% sevoflurane and 100% oxygen was used to induce anesthesia via inhalation until the appropriate anesthetic plane was reached. Spontaneous ventilation was maintained to obtain peripheral venous access in the left upper limb using a 24-gauge catheter. Following this, fentanyl 20 µg, rocuronium 10 mg, and ketamine 3 mg were administered intravenously (IV).

Initially, a thermal blanket was placed under the patient, and a facemask was used for ventilation for 3 min until the peak action of the drugs was achieved, followed by orotracheal intubation using a 4.5 mm tube with a cuff and a Mcgrath Mac® 3.0 video laryngoscope.

A caudal epidural block with 0.25% ropivacaine 5 mL and bilateral maxillary sinus blocks with 0.3% ropivacaine 2.5 mL were administered. Anesthesia was maintained based on the consciousness le-

vel using continuous IV target-control infusion of propofol 2–2.5 µg.mL⁻¹ and remifentanyl 0.05–0.3 µg.kg.min⁻¹. Cefazolin 500 mg IV was administered for antibiotic prophylaxis. Metamizole 500 mg, ketoprofen 10 mg, dexamethasone 4 mg, and ondansetron 2 mg IV were administered as adjuvants. Finally, the neuromuscular block was reversed by administering sugammadex 20 mg (2 mg.kg.⁻¹) IV, obtaining a train-of-four ratio >0.9 before extubation.

The entire procedure lasted approximately 5 h and was uneventful. The patient awoke easily and had no pain or postoperative nausea or vomiting. In total, 400 mL of heated balanced crystalloid solution was infused.

The patient was discharged from the hospital the following day with care guidelines and a prescription for symptomatic drugs. After 3 weeks he returns to the outpatient clinic for a follow-up consultation, which is within the expected evolution.



Figure 2 – Intraoperative image showing cleft palate correction

Discussion

The surgical approach for this patient involved correcting multiple malformations at different sites during a single surgical session, which posed significant challenges for anesthesia management. This case demanded thorough interdisciplinary planning to anticipate and address various risks. Key concerns included the possibility of an unexpected difficult airway, accidental extubation during the procedure, and effective control of pain and postoperative nausea or vomiting. Additional challenges were maintaining normothermia and managing fluid replacement due to the prolonged surgical time. There was also an increased risk of respiratory complications, autonomic reflexes, and laryngospasm, either from surgical manipulation or the presence of secretions in the upper airway.

Garrocho-Rangel et al., in their study, include a recent review with 15 studies on patients with EEC syndrome. Despite mentioning the importance of general anesthesia for oral rehabilitation and correction of deformities, none of the studies discussed the role of the best anesthetic strategy for the recovery of these patients (12).

Recent studies evaluated the impact of pre-, peri-, and postoperative measures altogether in accelerating the recovery of pediatric patients based on the Enhanced Recovery after Surgery protocol and reported significantly improved clinical outcomes, patient recovery, family satisfaction, and health costs (13).

Premedication may be advisable in this population to enable peaceful separation from the parents before surgery. We decided to use intranasal dexmedetomidine, a more selective alpha-2-agonist, which has been recently supported by several publications for better sedation profile, reduced airway secretions, facilitating orotracheal intubation and allowing for a more peaceful awakening. This route and dosage were chosen within the commonly recommended pediatric range of 1–4 $\mu\text{g}\cdot\text{kg}^{-1}$, with 2–3 $\mu\text{g}\cdot\text{kg}^{-1}$ being the most frequently reported for premedication. Evidence supports intranasal dexmedetomidine as a safe and effective anxiolytic and sedative

in children, providing adequate preoperative conditions while avoiding respiratory depression and maintaining hemodynamic stability (14–16).

Airway management can be critical due to the limited evaluation of difficulty predictors and the anatomical specificities inherent to the pediatric population, as well as this patient's malformations and possible supra- and infra-glottic variations. Thus, complementary methods, such as ultrasound (17), can help manage such cases, highlighting the need for advanced difficult airway devices and the presence of an experienced anesthesiologist.

Multimodal general anesthesia associated with maxillary sinus and caudal epidural blocks covers different surgical sites with satisfactory pain control and fewer adverse effects compared to opioid use, corroborating some recent findings. High opioid doses have been directly associated with increased incidence of postoperative nausea or vomiting, which can result in extremely unfavorable outcomes in orofacial surgery due to intense discomfort or the possibility of emergency surgical re-approach in case of emesis.

Maintaining anesthesia with the propofol target-control infusion system also reduces postoperative nausea or vomiting, and it has been reported as a safe technique in pediatric patients. Some pharmacokinetic models can improve the target-control infusion system in the pediatric population, such as the Paedfusor (age: 1–16 years; weight: 5–61 Kg) and Kataria (age: 3–16 years; weight: 15–61 Kg) systems. Total intravenous anesthesia has also been associated with decreased occurrence of emergence delirium, resulting in smoother awakening, which is an extremely relevant attribute in ear surgeries with the placement of ventilation tubes, as reported in this case. Choosing between deep or awake extubation is a challenge and must integrate multiple data and combine patient safety with surgical aspects and the expertise of the anesthesiologist (18).

Although no neurological changes were documented in this case, neuraxial anesthesia should be used cautiously in pediatric patient with EEC syndrome to avoid embryonic correlations be-

tween the ectoderm and neural tube formation. Imaging methods can complement and increase the safety of the procedures. Alternatively, peripheral nerve blocks are an excellent approach within the multimodal arsenal of analgesic therapy as an opioid-sparing strategy in the pediatric population.

In summary, managing patients with rare and complex syndromes in tertiary hospitals requires careful interdisciplinary planning to address potential risks. Anatomical changes in the airway may complicate mask adaptation and intubation, demanding specific anesthetic strategies and clear communication between teams to avoid intraoperative complications.

Total intravenous anesthesia combined with regional techniques offers an effective, opioid-sparing approach for multi-site surgeries, improving analgesia and reducing postoperative nausea. While neuraxial anesthesia may be an option, its safety should be assessed individually, often with imaging support. Agents like dexmedetomidine enhance multimodal anesthesia by improving sedation, reducing bleeding, and facilitating smoother recovery. Ultimately, adherence to good anesthetic practices and enhanced recovery protocols is essential for optimizing pediatric outcomes.

Notes

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Conflicts of interest disclosure

The authors declare no competing interests relevant to the content of this study.

Authors' contributions

All the authors declare to have made substantial contributions to the conception, or design, or acquisition, or analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content; and to approve

the version to be published.

Availability of data and responsibility for the results

All the authors declare to have had full access to the available data and they assume full responsibility for the integrity of these results.

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Alberto Freaza Lobão Bastos

Mestre em Ciências Médicas e Médico pela Universidade de Lisboa. Médico Anestesiologista do Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro e da Universidade Federal do Rio de Janeiro, RJ, Brasil.

Lilian Satie Ykeizumi

Especialista em Anestesiologia pela Sociedade Brasileira de Anestesiologia. Médica Anestesiologista do Instituto Fernandes Figueira e Hospital Estadual da Criança, RJ, Brasil.

Paula Cristina Leitão de Assunção

Especialista em Anestesiologia e Dor pela Sociedade Brasileira de Anestesiologia. Médica Anestesiologista do Hospital Universitário Pedro Ernesto, Universidade do Estado do Rio de Janeiro e do Hospital Federal do Andaraí, RJ, Brasil.

Cláudia Regina Machado

Doutora em Saúde Pública pelo Instituto de Medicina Social da Universidade do Estado do Rio de Janeiro (UERJ). Professora Adjunta da Faculdade de Ciências Médicas (FCM) – UERJ, RJ, Brasil.

Bruno Vitor Martins Santiago

Doutor em Medicina pela Pós-Graduação em Ciências Médicas PGCM/UERJ. Médico Anestesiologista do Hospital Universitário Clementino Fraga Filho – Universidade Federal do Rio de Janeiro (HUCFF-UFRJ); Professor da Disciplina de Anestesiologia da Faculdade de Ciências Médicas da UERJ (FCM-UERJ), RJ, Brasil.

Endereço para correspondência

Boulevard 28 de setembro, n. 77

Vila Isabel, 20550-900

Rio de Janeiro, RJ, Brasil

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