Dental Management of a Child with CLOVES Syndrome

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Introduction

CLOVES syndrome is a rare congenital disorder characterized by Congenital Lipomatous Overgrowth, Vascular malformations, Epidermal nevi, and Skeletal anomalies resulting from somatic, mosaic PIK3CA mutation, located on chromosome 3q26.32. This gene encodes the p110α subunit of phosphatidylinositol 3-kinase (PI3K), a key regulator of cellular growth, proliferation, migration, and survival. Overactivation of the PI3K-AKT signaling pathway leads to the hallmark features of the condition, including asymmetric overgrowth, complex vascular malformations, lipomatous masses, and skeletal abnormalities. The condition is associated with progressive overgrowth and multisystem involvement that can significantly increase anesthetic and surgical risk and complicate access to routine dental care. As a result, affected patients are at increased risk for untreated dental disease, pain,
and infection, necessitating individualized and multidisciplinary dental management.

Case Description

A 5-year 3-month-old African American female presented to the dental clinic at Jamaica Hospital Medical Center (JHMC), Queens, New York, with a chief compliant of (as presented by her mother) that “she has a lot of cavities that need to be filled when she’s asleep”. However, the significance of this case lies primarily in her extensive and complex medical history associated with CLOVES syndrome. Prenatally, the patient was diagnosed with a cystic hygroma and initially tested positive for Noonan syndrome with an **SOS1** mutation. However, postnatal evaluation and clinical progression revealed findings more consistent with CLOVES syndrome. Early workup included a head ultrasound, echocardiogram, and treatment of an infection with clindamycin.

- Initial Presentation:
  - 5-year 3-month-old African American female presented to JHMC (Queens, NY)
  - Chief complaint (per mother): “She has a lot of cavities that need to be filled when she’s asleep”
- Prenatal & Early History:
  - Prenatal diagnosis: cystic hygroma
  - Initially tested positive for Noonan syndrome (SOS1 mutation)
  - Postnatal findings more consistent with CLOVES syndrome
  - Early workup included head ultrasound, echocardiogram, and infection treated with clindamycin
- Cardiac Findings:
  - Small interatrial communication (PFO vs. ASD)
  - Requires monitoring due to potential anesthetic and procedural risks
- Major Medical Complications:
  - Extensive lymphatic and vascular malformations
  - Two life-threatening hemorrhages into lymphatic cysts:
    - First: treated with doxycycline sclerotherapy → anemia, hemodynamic instability, transfer to tertiary care
    - Second: complicated by consumptive coagulopathy → multiple transfusions
  - Recurrent cellulitis (right trunk, axilla, shoulder) → treated with IV clindamycin, discharged on Augmentin
- Chronic Medical Status:
  - G-tube dependent for feeding
  - Double-lumen Broviac catheter for long-term access
  - Immunocompromised with chronic anemia and coagulopathy
  - Increased thrombotic risk due to vascular malformations (may require anticoagulation such as enoxaparin)
- Surgical History & Prognosis:
  - Two major debulking surgeries (axillary/thoracic malformations)
  - Progressive overgrowth with functional impairment
  - Planned future surgery: right lower extremity amputation

Outpatient dental management was therefore pursued using a conservative, staged approach focused on minimizing physiologic stress and avoiding invasive procedures. Caries control was achieved using silver diamine fluoride, stainless steel crowns, and extractions of non-restorable teeth, with treatment delivered over multiple short visits. Care was coordinated closely with the patient’s medical team to ensure safety, with an emphasis on prevention and maintenance to reduce the need for future high-risk interventions.

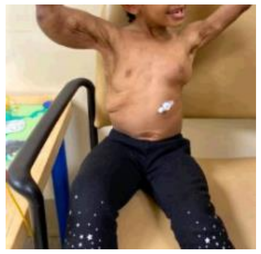

Figure 1: Trunk & R Arm (2024).

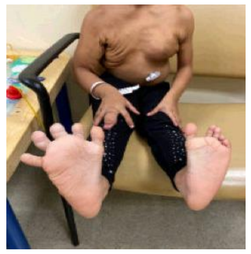

Figure 2: R vs L foot (2024).

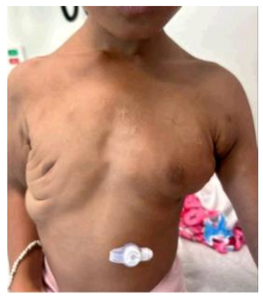

Figure 3: R vs L thorax (2024).

Figure 4: R vs L back (2024).

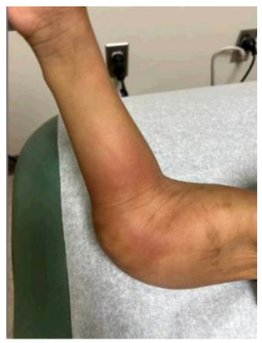

Figure 5: R elbow (2024).

Figure 6: L shoulder & chest (2024).

Figure 7: R brachium (2024).

Figure 8: R hand & fingers (2024).

Discussion

CLOVES syndrome represents a rare but severe manifestation within the PIK3CA-related overgrowth spectrum (PROS), characterized by progressive, disproportionate tissue overgrowth and complex vascular anomalies. The somatic mosaic nature of the mutation results in highly variable clinical presentations, often requiring lifelong multidisciplinary management. This case illustrates the significant morbidity associated with CLOVES syndrome, including recurrent hemorrhage, coagulopathy, infection, and progressive functional impairment. Vascular malformations, particularly lymphatic and venous anomalies, pose substantial risks, including bleeding into malformations, thrombosis, and localized or systemic infection. These complications are further exacerbated by the fragile hemodynamic balance in affected patients.

Management is largely supportive and procedural, often involving repeated surgical debulking, sclerotherapy, and careful monitoring of hematologic and vascular status. Despite intervention, disease progression is common, as demonstrated by this patient’s need for limb amputation due to severe overgrowth. Importantly, patients with CLOVES syndrome often require central venous access and nutritional support, reflecting the systemic burden of disease. These factors, combined with immunocompromise and coagulopathy, significantly increase the risk associated with anesthesia and surgical interventions.

While dental disease may not be life-threatening in comparison, it can be easily overlooked in the context of complex medical care. However, untreated oral disease may contribute to systemic infection risk, particularly in immunocompromised patients, underscoring the importance of integrating dental care into the broader medical management plan.

Conclusions

This case highlights the profound medical complexity associated with CLOVES syndrome and the challenges it presents across all aspects of patient care. The patient’s clinical course demonstrates the severe complications of vascular malformations, including life-threatening hemorrhage, coagulopathy, recurrent infection, and progressive overgrowth requiring surgical intervention.

CLOVES syndrome requires comprehensive, multidisciplinary management focused on minimizing complications and maintaining quality of life. In medically fragile patients such as this, even routine procedures must be carefully evaluated in the context of systemic risk. This case emphasizes the importance of coordinated care and individualized treatment planning, with recognition that non-urgent conditions, including dental disease, must often be managed within the constraints imposed by significant underlying medical pathology.

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