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CLINICAL CASE

Neonatal sepsis by *Citrobacter Freundii* as a debut of cystic lymphatic malformation

Sepsis neonatal por *Citrobacter Freundii* como debut de malformación linfática quística

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What do we know about the subject matter of this study?

Citrobacter Freundii is a bacillus considered part of the normal flora of the gastrointestinal tract and can cause mainly urinary tract infections. Abdominal CLMs account for less than 5% of all lymphangiomas described in the literature.

What does this study contribute to what is already known?

Currently, there are no neonatal cases of Citrobacter Freundii as an infectious agent of abdominal origin described in the literature. The use of non-invasive approaches that could reduce the complications of surgery for CLMs should be considered.

Abstract

Cystic lymphatic malformation (CLM) is a rare and benign entity caused by alterations in the embryological development of lymphatic structures. Its typical location is in the head and neck, although it has also been described at the abdominal level. It may not be evident in the first stages of life and its first manifestation may be a complication such as abdominal distension, hemorrhage, or sepsis, which may put the patient's life at risk. Surgical treatment is increasingly discussed, and less invasive techniques are proposed. **Objective**: To describe an uncommon presentation of CLM, radiographic findings, complications, differential diagnosis, and both invasive and more conservative treatments. **Clinical Case:** Newborn female infant consulted for fever and irritability, without specific signs on physical examination, with suspicion of sepsis. Ultrasonography showed a complex septate mass with cysts of different sizes encompassing the mesenteric vessels, supravesical location. In its most anterior aspect, it presented a greater echogenicity that corresponded to the superinfected component. Magnetic resonance imaging identified a multitabulated cystic tumor corresponding to a complicated mesenteric lymphangioma with signs of infection. Due to its size, which compressed the vena cava and the associated signs of complication, complete resection was decided with good subsequent

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evolution. **Conclusion**: The treatment of CLM in pediatric age is increasingly individualized and can vary from surgical resection to less invasive approaches that could reduce acute intraoperative or postoperative complications and mortality. In our case, the infection acted as sclerotherapy, managing to delimit the CLM and helping to improve the prognosis.

Introduction

Although classically the name cystic lymphangioma has been used, since 1982 and based on histological studies, the term cystic lymphatic malformation (CLM) is considered more accurate to refer to those vascular lesions caused by embryological defects of the primordial lymphatic structures[1,2]. Histologically, they are composed of macro-, microcystic, and mixed dilatations combined with other usually venous malformations and thin and vascularized inner septa covered by endothelial cells and filled with protein fluid. Macroscopically, they can result in the formation of masses of different sizes that, depending on their location, can be identified through deep palpation as non-pulsatile and painless masses if they are not associated with bleeding or infection[3]. The overlying skin is usually normal, but it can also be bluish or contain pink vesicles, which can resemble capillary malformations, angiokeratomas, or angiomas[4].

The cervicofacial region is the most affected (48%) followed by the trunk, armpits, and limbs (42%) while mediastinal and abdominal locations are rare (< 10%)[1]. In the abdominal area, the clinical presentation can vary from an incidentally discovered mass to severe symptoms such as acute abdomen. In recent years, the diagnosis of neonatal CLMs has increased markedly with the widespread use of ultrasound during pregnancy, allowing prenatal diagnosis suspicion, and MRI can be performed to confirm the diagnosis.

Given the asymptomatic presentation and benign course, the diagnostic strategy should be as minimally invasive as possible. Due to the rarity of this location and the age at the onset, publications about neonatal abdominal CLMs are scarce and there is no consensus on its treatment.

The objective of this report is to present the clinical case of a newborn with sepsis due to *Citrobacter Freundii* as the onset of abdominal CLM, to describe the typical and atypical images of CLMs, its complications, and differential diagnosis, as well as to describe the most used therapeutic techniques in the management from less to more invasive.

Clinical Case

A 12-day-old newborn female infant presented to the pediatric emergency department due to low-grade fever and irritability. The patient is Caucasic, with delivery at 39 + 5 weeks of gestation, spontaneous, and without complications. Her weight was 3350g (p50) and Apgar score 10/10. The mother was 32 years old, primipara, with no remarkable history. The pregnancy had been monitored and there were no pathological ultrasound findings.

The physical examination was completely unremarkable, and the blood test showed an increase in acute phase reactants (CRP 126 mg/L) with leukocytosis (14.6 x109/L) and neutrophilia (8.1 x109/L). Given the suspicion of sepsis, it was decided to complete the study with a lumbar puncture and blood culture, and hospitalization with empirical treatment with ampicillin and gentamicin.

72 hours after admission, due to a positive blood culture for *Citrobacter Freundii*, it was decided to suspend ampicillin, adjust specific antibiotic treatment with gentamicin, and, due to the suspicion of a possible abdominal origin because of the characteristics of the bacteria, the study was completed with imaging tests.

The abdominal ultrasound showed a complex septated mass with cysts of different sizes. The mass encapsulated the mesenteric vessels, located at the supravesical level with intra-abdominal extension, and maximum diameters of 54mm x 45mm x 36mm. In its most anterior aspect, there was greater echogenicity corresponding to the superinfected component (figure 1). Given the suspicion of a complicated abdominal lymphatic malformation, the study was completed with an MRI which showed a multiseptated cystic tumor corresponding to a complicated mesenteric lymphangioma with signs of infection inside (figures 2 and 3).

With these findings, it was decided to broaden the antibiotic spectrum by changing the gentamicin for meropenem at 20mg/kg/dose every 12 hours and transfer the patient for surgical evaluation.

At the referral center, complementary ultrasound tests were repeated, and given the clinical stability of the patient, we took a wait-and-see approach until the antibiotic therapy was completed and surgery was scheduled at one month of life. The patient underwent surgery excising the mesenteric lymphatic malformation through a median laparotomy, respecting the vascular structures and the colon. The anatomopathological study determined that it was a micro-macrocystic

lymphatic malformation. During the procedure, despite respecting the vascular structures, a blood transfusion was required. In the postoperative period, there were no incidents.

Discussion

Citrobacter Freundii is an aerobic gram-negative bacterium, considered part of the normal flora of the gastrointestinal tract, and transient in skin and oropharynx[5-6].

Although upper intestinal tract and pulmonary infections are described in the literature, most of the reported cases are urinary tract infections in elderly and immunocompromised patients[7-8].

In pediatrics, it represents a microorganism very infrequently related to neonatal sepsis, presenting most frequently as an early infection of the central nervous system due to the production of a neurovirulent toxin[9-10]. Currently, there are no neonatal cases described in the literature of *Citrobacter Freundii* as an infectious agent of abdominal origin, hence the importance of our case. The route of transmission is usually vertical or nosocomial[10]. Most patients are newborns between 33 and 36+6 weeks of gestation and/or with low birth weight[10], and extreme prematurity is a predisposing factor for central nervous system infection[11].

The abdominal CLMs represent less than 5% of all lymphangiomas described in the literature[12]. In pediatrics, the most frequent location is the mesentery (45%) and in more than 80% of the cases, they are detected during the preschool period (< 5 years)[13].

Although the cause remains uncertain, hypotheses on congenital alteration of the lymphatic structures' development during the embryological phase, as well as theories about lymphatic obstruction secondary to bleeding or inflammation of the lymphatic vessels, are of greater importance.

In 88% of cases, abdominal CLMs present with variable symptomatology, with the appearance of complications as the most frequent clinical presentation (acute abdomen due to sepsis, pyelonephritis, hemoperitoneum, or jaundice), and only occasionally cause non-specific signs of abdominal distension[3].

Among the neonatal abdominal masses (table 1) that should be considered for differential diagnosis, the most frequent are those of genitourinary origin (50-75%)[14].

Among the complementary tests, ultrasound is the first line in early diagnosis and represents the most accessible examination[16-17]. The study was completed with an MRI to assess with greater precision the location, size, and possible complications.

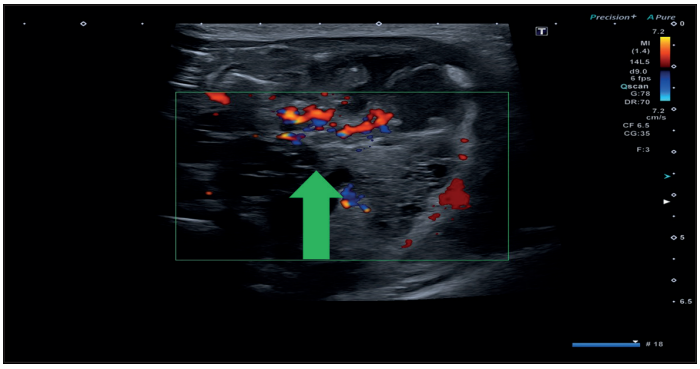
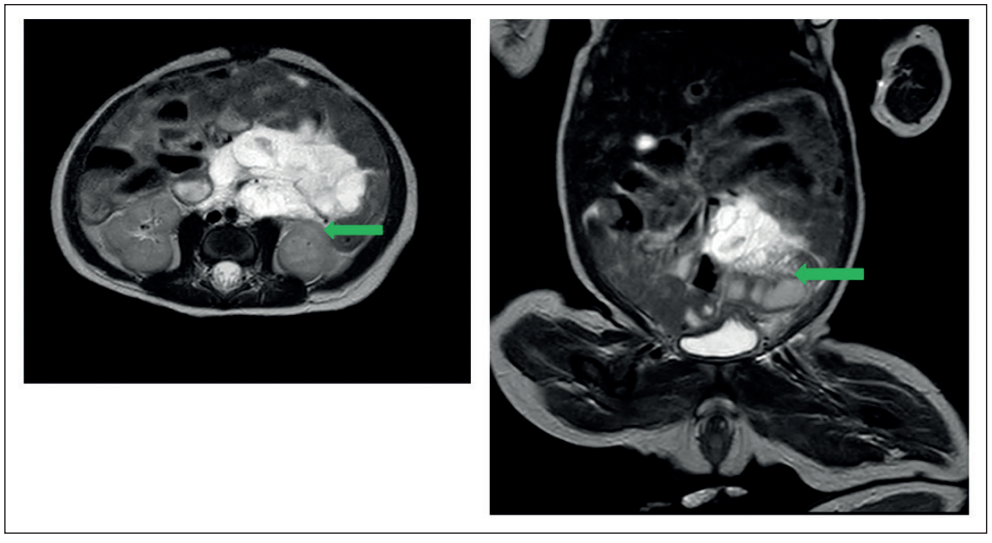


Figure 1. Abdominal color Doppler ultrasound where a multi-stage cystic mass is visualized. In its most anterior region it presents a component of greater echogenicity that corresponds to the infected slope (arrow).



Figures 2 and 3. Magnetic Resonance: Sequences enhanced in T2 in coronal and axial plane. A cystic mass located in mesentery is identified, of polylobed morphology with the presence of multiple fine septa inside, without evidence of solid poles. The mass previously displaces the intestinal package. In the caudal component of the mass, partial affectation of 35mm x 28 mm corresponding to superinfection (arrow) is observed.

Table 1. Table of abdominal masses in neonates[15]

Flank: Hydronephrosis	
	Multicystic kidney
	Wilms tumor
	Neuroblastoma
	Adrenal hemorrhage
	Renal vein thrombosis
	Extralobar pulmonary sequestration
Upper right quadrant:	
	Hemangioendothelioma
	Hamartoma
	Hepatoblastoma
	Choledochal cyst
Upper left quadrant:	
	Splenic cyst
Mesogastrium:	
	Hypertrophic pyloric stenosis
	Bowel duplication
	Lymphangioma (intestinal, mesenteric)
	Meconium ileus
	Wall defects
Pelvis:	
	Follicular cysts
	Solid tumors
	Urachal cyst
	Teratoma
	Hernia-hydrocele
	Hydrometrocolpos

Currently, the management of abdominal CLMs is controversial. According to some authors, expectant management is recommended generally in asymptomatic cases[18-19-20].

Historically, early and complete surgical resection has been considered the gold standard if the mass is symptomatic, large, complicated, or if it compresses and displaces vital tissues. The laparoscopic approach, as well as laparotomy, have practically the same results although open surgery is preferred as the method of choice when the resection is considered complex[6]. However, remission may not be achieved due to the recurrence rate which, according to some studies, is as high as 64% in situations of incomplete resection and 22% in resections that are considered to be complete[3-21]. For this reason and due to the high risk of surgery complications (33%), less invasive therapeutic options are usually considered, such as ultrasound-guided sclerotherapy with percutaneous aspiration and drugs administration (doxycycline, bleomycin, or OK-432/Picibanil). According to recent studies, this technique could be considered the technique of choice in pediatrics in selected cases[22-23]. At the same time, it represents an option that would considerably reduce complications secondary to surgery (such as bleeding) which occur in up to 33% of the procedures.

This clinical case confirms that if the mass is large, compresses, and displaces vital tissues and/or presents complications such as infection, the treatment of choice is complete surgical resection. However, we must consider the increasing use of non-invasive approaches that could reduce acute intra- or postoperative complications and long-term recurrences. Abdominal ultrasound performed by experienced professionals has a decisive role not only in detection but can also be a tool of choice after treatment for subsequent follow-up.

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 have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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