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SHORT COMMUNICATION

Giant Intracardiac Thrombus Secondary to Central Venous Catheter in Neonates: About Two Case Reports

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Abstract

Catheter-related thrombosis is the leading cause of thrombotic events in the neonatal period, with an increasing prevalence due to the routine use of central venous access. We present two clinical cases of intracardiac thrombosis associated with the use of central venous catheters in newborns, treated with different therapeutic approaches according to individual risk factors and clinical course. The first case, with a large intracardiac thrombus secondary to an umbilical catheter, was successfully resolved with low-molecular-weight heparin and antiplatelet therapy. In contrast, the second case, initially treated with alteplase and heparin infusion, presented a recurrence despite catheter replacement and sustained anticoagulation. These cases illustrate the variability in presentation and response to treatment and highlight the absence of standardized clinical guidelines for the management of neonatal thrombosis, underscoring the need to report clinical experiences to guide

Keywords: Central Venous Catheter (CVC), Thrombosis, Preterm Neonate

1. Introduction

Coagulation in newborns is a complex and dynamic process that requires the interaction of platelets, vascular endothelium, and coagulation factors to achieve adequate hemostasis. In the neonatal stage, this system is immature and evolves considerably during the first six months of life, resulting in increased susceptibility to both hemorrhagic and thrombotic events[1].Vascular catheter placement is the most significant risk factor for thrombosis in neonates, being implicated in 85–90% of thromboembolic events[1]. It is estimated that approximately 1% of newborns with catheters develop thrombotic complications, of which up to 30% may be asymptomatic [2]. This condition occurs approximately 40 times more frequently during the neonatal period than later in life. Additional factors such as perinatal asphyxia, hypovolemia, sepsis, dehydration, polycythemia or congenital heart disease can intensify this prothrombotic state [3]. Early detection and timely treatment of catheter-associated thrombosis are essential to prevent serious complications such as pulmonary embolism, portal hypertension, infections, and even death. However, therapeutic management in neonates faces multiple challenges: the optimal dosage, efficacy, and safety of anticoagulant and thrombolytic agents have not been clearly established in this population [4].

Despite the potential severity of these events, there are currently no robust, standardized clinical guidelines specifically addressing the treatment of neonatal thrombosis. Most available recommendations are based on expert consensus and data extrapolated from older pediatric or adult populations, leaving a critical gap in neonatal clinical decision-making. This lack of direct evidence requires tailoring treatment on a case-by-case basis, carefully assessing risks and benefits.

In this context, we present two cases of neonatal intracardiac thrombi associated with the use of central venous catheters, each with a distinct therapeutic approach based on individual clinical risk factors, as a contribution to the clinical discussion on personalized management in the absence of specific guidelines.

2. Case Presentation

Clinical Case One

We present the case of a full-term neonate (39 weeks) born to a 30-year-old mother (G5, P3, A1) with no history of substance use or chronic diseases. The maternal blood type was A Rh positive, with negative serologies for HIV and VDRL. Prenatal care was adequate, starting hematinic therapy from the second month of pregnancy. During the last month of gestation, gestational diabetes was diagnosed and treated with metformin. The birth occurred by elective cesarean section in a private hospital. The birth weight was 4370 g, and Apgar scores of 8 and 9 at 1 and 5 minutes, respectively.

The newborn was referred to the Cancún General Hospital for persistent tachypnea, and helmet-type oxygen therapy was initiated, along with the placement of a 5-Fr umbilical catheter without complications. A cardiological evaluation was requested due to a history of gestational diabetes, which revealed asymmetric septal hypertrophy and a non-obstructive thrombus in the right atrium (0.94 × 0.83 cm) (as shown in Figure 1).

Treatment with enoxaparin (1.7 mg/kg/day) was initiated, and after three days, the umbilical catheter was removed. However, anticoagulation was temporarily suspended due to thrombocytopenia and was subsequently resumed, completing 19 days of treatment. During his hospital stay, the thrombus remained stable, well adhered, and without obstruction of the inferior vena cava. The patient received supplemental oxygen for two days and treatment with ampicillin and amikacin. On day five of life, he presented with septic shock, leading to escalation of antibiotic treatment to cefotaxime and subsequently imipenem, following a positive stool culture for Klebsiella. Vancomycin was added to the regimen due to the detection of Staphylococcus haemolyticus. The initial transfontanellar ultrasound was normal, but a follow-up performed one month later revealed grade II intraventricular hemorrhage, with no evidence of active bleeding.

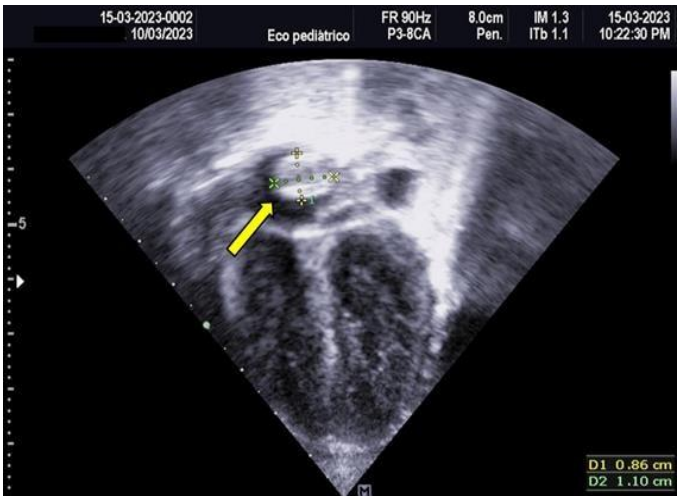

Figure 1. Transthoracic echocardiogram, Apical 4-chamber view. A hyperechoic image with defined edges is observed, compatible with an intracardiac thrombus measuring 1.1 × 0.86 cm, attached to the roof of the right atrium, with no evidence of obstruction to venous flow. This finding was incidental during the cardiological evaluation indicated by a maternal history of gestational diabetes, and conditioned the initiation of anticoagulation in the newborn.

Throughout the course of the thrombus, it showed no changes in size or ultrasound characteristics; it remained non-pendular and firmly adherent. Given the absence of indications for fibrinolysis, coupled with the risk of reinfection and hemorrhage associated with prolonged hospitalization, the decision was made to discharge the patient from the hospital with outpatient management, starting aspirin (ASA) and close follow-up by pediatric cardiology. Follow-ups were performed weekly for two months, and then monthly thereafter. Complete resolution of the thrombus was documented echocardiographically at six months of age (Figure 2), with no associated complications.

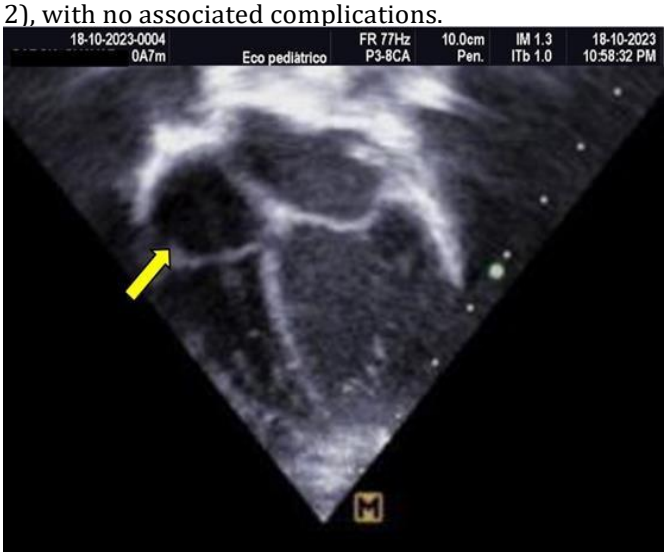

Figure 2. Transthoracic Echocardiogram, Apical 4-Chamber View: Complete resolution of the interatrial thrombus.

Clinical Case Two

This is a 37-week gestational age newborn, born to a 19-year-old mother (G1), with no relevant

personal history or substance use. The maternal blood type was O Rh positive, and serology tests for HIV and VDRL were negative. The pregnancy proceeded without apparent complications, and the patient received adequate prenatal care (eight visits). At 20 weeks of gestation, fetal gastroschisis was diagnosed, and although attempts were made to delay delivery with uterosuppressants, spontaneous labor occurred at 35.4 weeks. The delivery was by cesarean section with early cord clamping.

After adequate initial resuscitation, the newborn was preemptively intubated due to the exposed abdominal malformation, and a 3.5 Fr cannula was placed. The birth weight was 2765 grams, with a length of 45 cm and Apgar scores of 7 and 8 at 1 and 5 minutes, respectively. The gestational age was 37 weeks according to Capurro. Pediatric surgery placed a silo without complications, and empirical antibiotic treatment with ampicillin and amikacin was initiated, which was escalated to meropenem due to clinical signs of shock and inadequate response to initial treatment.

During hospitalization, a 4-Fr central venous catheter was placed in the left subclavian vein, with adequate radiological verification and subsequent adjustment. Pediatric cardiology was consulted for persistent hemodynamic abnormalities, which revealed a large intracardiac thrombus (1.5 × 0.7 cm) in the right atrium, highly mobile and pendulous, with a clear risk of embolization (see Figures 3 and 4). Initially, the use of alteplase was contraindicated due to significant alterations in coagulation times, so fresh frozen plasma (10 mL/kg) was administered to correct plasminogen levels. Enoxaparin was subsequently started at 1.7 mg/kg/day. A hematology consultation was requested, but this could not be performed due to a lack of availability at the institution, which hampered specialized decision-making.

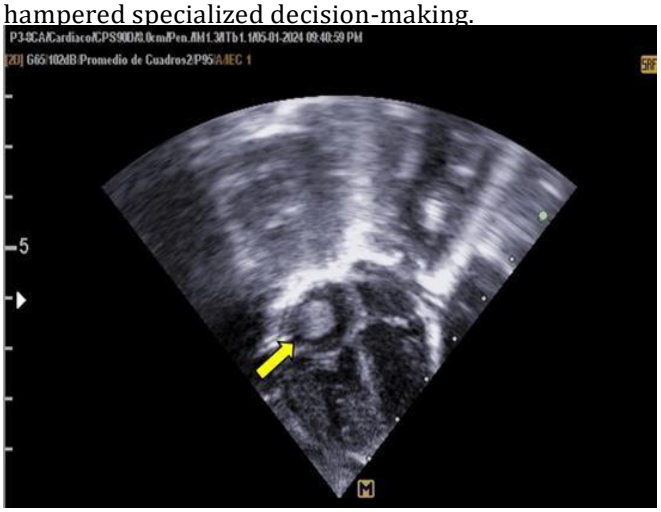

Figure 3. Transthoracic echocardiogram, apical 4-chamber view. A hyperechoic, mobile, and pendulous image is observed, corresponding to a 1.5 × 0.7 cm thrombus in the right atrium, visible during systole. Its morphology and mobility suggest a high risk of embolization, which prompted the initiation of fibrinolysis in a critically ill neonatal patient.

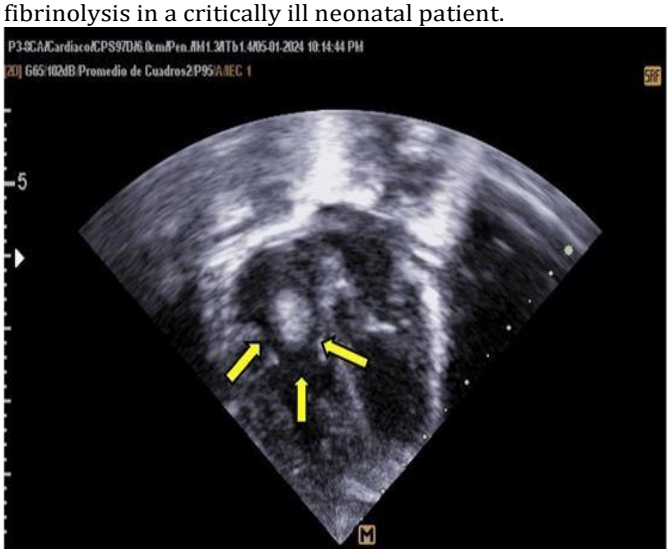

Figure 4. Transthoracic echocardiogram, apical 4-chamber view. The same pendulous intracardiac thrombus, 1.5 × 0.7 cm, is seen descending through the tricuspid valve into the right ventricle during diastole. This dynamic pattern reinforces its embolic potential and justifies an aggressive therapeutic approach.

The patient's initial course was favorable; however, the case is particularly relevant due to the subsequent development of thrombotic recurrence, a rare and clinically challenging complication in the neonatal population, which will be analyzed below. After 72 hours of support, and with partial improvement in the coagulation profile, fibrinolysis was initiated with low-dose alteplase (0.1 mcg/kg/h), along with heparin infusion at 10 U/kg/h and a new dose of fresh frozen plasma (10 mL/kg). Twice-daily echocardiogram monitoring demonstrated a rapid and favorable response, with a 90% reduction in thrombus size in the first 48 hours (see Figure 5).

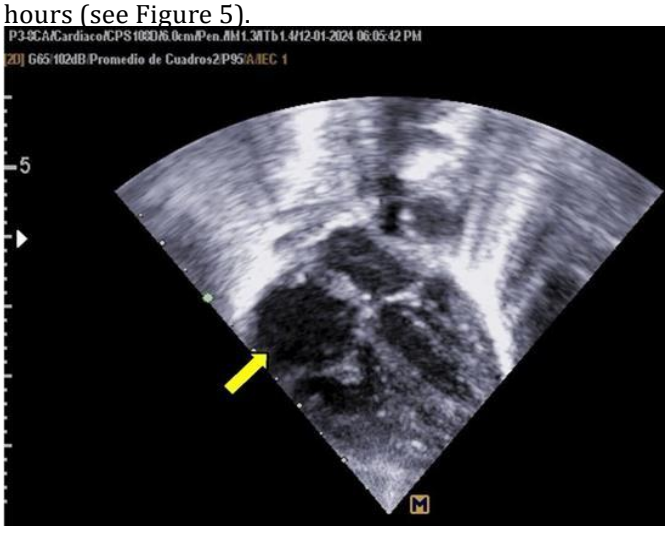

Figure 5. Transthoracic echocardiogram, apical 4-chamber view. Image corresponded to the first 48 hours after the start of fibrinolysis. A significant reduction (90%) of the previously identified intracardiac thrombus in the right atrium is observed, demonstrating an initial response favorable to treatment with alteplase and heparin.

However, despite anticoagulant therapy and adequate initial progress, a few days later, a new ultrasound image compatible with a recurrent thrombus was documented, now larger (1.5 × 1.8 cm), adhered to the interatrial septum, with marked mobility during systole (see Figure 6).

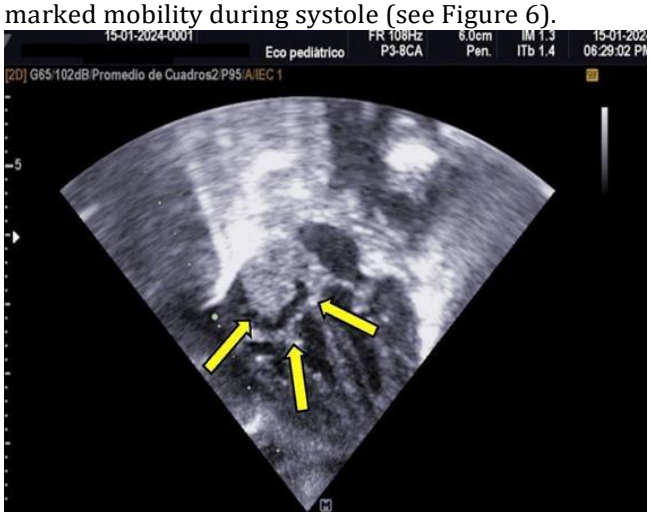

Figure 6. Transthoracic echocardiogram, apical 4-chamber view. Appearance of a recurrent thrombus, 1.5 × 1.8 cm, adhered to the interatrial septum, with a hyperechoic appearance and systolic mobility, detected days after the initial resolution. This finding suggests an early recurrence despite the ongoing anticoagulant treatment.

This recurrence occurred despite continued anticoagulant therapy and prior central venous catheter replacement, highlighting the aggressive and complex nature of neonatal thrombosis in this case. The new thrombus displayed similar characteristics to the initial one: pendulous, mobile, and at risk of embolization, even being seen descending through the tricuspid valve into the right ventricle during diastole (see Figure 7).

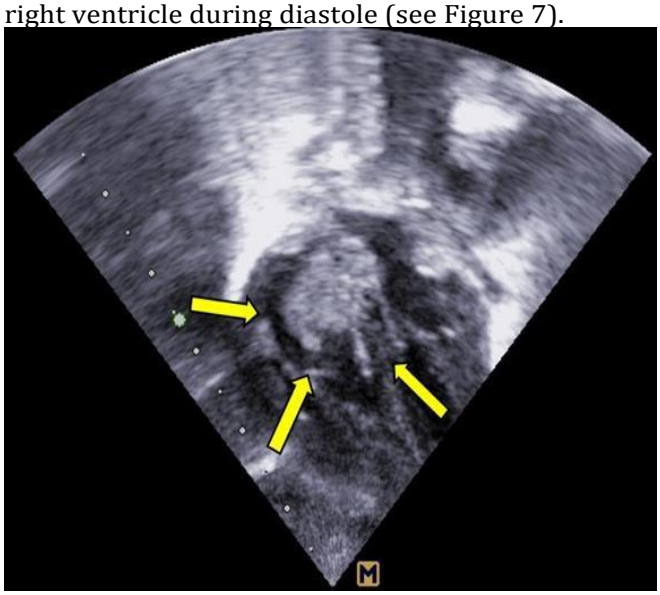

Figure 7. Transthoracic echocardiogram, apical 4-chamber view. The recurrent thrombus is observed descending through the tricuspid valve toward the right ventricle during diastole, with pendulous mobility. This dynamic behavior confirms its high embolic potential and the complexity of clinical management in the neonatal context.

Clinically, the newborn's condition progressively deteriorated. Bilateral pleural effusions developed, requiring thoracentesis. Despite intensive treatment, the patient progressed to refractory shock and died 15 days after birth.

Neurological monitoring was performed throughout the hospitalization using transfontanelar ultrasound, with no findings of intracranial hemorrhage.

However, the severity of the clinical picture, coupled with the lack of access to specialized hematological evaluation, limited the ability to identify underlying prothrombotic factors.

3. Discussion

In neonates, the physiological process that controls bleeding and maintains blood vessel integrity (hemostasis) is immature and undergoes significant changes during the first six months of life [5]. Several factors contribute to the increased susceptibility of neonates to thrombotic events:

Lower levels of anticoagulant proteins, such as protein C, protein S, and antithrombin III, which are essential for inhibiting coagulation; Limited capacity of the fibrinolytic system, responsible for clot dissolution; Reduced platelet adhesion and aggregation; and Lower levels of immunoglobulins, particularly IgG, which affect both the immune response and hemostasis [6].

Additionally, conditions such as sepsis, inflammation, hypoxia, and the presence of invasive devices or catheters further increase the risk of thrombosis. This is exacerbated by the small vessel diameter, high-osmolarity solutions, and impaired regulation of thrombopoiesis in neonates [7].

Despite these vulnerabilities, certain aspects of the neonatal hemostatic system are compensatory, facilitating the maintenance of a dynamic equilibrium between coagulation and fibrinolysis in normal conditions. However, under stress, the limited reserves of the neonatal hemostatic system may fail, significantly increasing the risk of thrombosis in critically ill neonates [7].

When using central venous catheters, several risk factors should be considered: the catheter's location, the use of multilumen catheters, prolonged catheter duration (over 14 days, although some guidelines suggest durations exceeding six days also pose a risk), improper placement, the administration of parenteral nutrition, and the infusion of blood products [7,8].

Catheter insertion can damage the vascular endothelium, especially in neonates with small-caliber vessels, triggering inflammatory responses and activating the coagulation cascade. Endothelial injury increases the likelihood of clot formation at the insertion site. Additional contributing factors include vascular occlusion, turbulent or slowed blood flow, the nature of infusions, and the catheter material. The diameter of the catheter relative to the vessel lumen is critical; an oversized catheter

can hinder blood flow around it, promoting stasis and thrombosis, particularly if the catheter remains in place for over 14 days [8].

In neonates, thrombopoietin levels, which regulate platelet production, are elevated. Once a thrombus forms, treatment depends on its location and clinical severity [9].

If necessary, central catheters should be removed after at least 3–5 days of anticoagulation, unless access to the vena cava is critical and the catheter remains functional [7]. For a first thrombosis episode involving the vena cava, prophylactic enoxaparin is recommended, with dosing adjusted to prolong the partial thromboplastin time (PTT) and achieve anti-Xa levels between 0.5 and 1.0 U/mL [8].

Anticoagulant therapy should continue at therapeutic doses until catheter removal. Thrombolytic therapy is reserved for cases of major vessel occlusion where organ or limb function is critically compromised, given the high risk of complications. In our patient, fibrinolytic therapy was chosen due to the significant embolization risk associated with the thrombus [9].

The recommended management approach includes: Central catheter removal: Performed following clinical and ultrasound evaluation.

Anticoagulation: Administration of low-molecular-weight heparin (LMWH) at 1.5–2 mg/kg every 12 hours, adjusting the dose to achieve anti-Xa levels of 0.5–1 U/mL. Enoxaparin is the most commonly used LMWH in neonatology.

Thrombolysis: Indicated when anticoagulation fails or urgent reestablishment of flow is necessary. Thrombolytic agents can be administered intravenously or locally via intra-arterial or intrathrombus catheters. Recombinant tissue plasminogen activator (rtPA), such as alteplase, is preferred in neonates due to fewer side effects compared to urokinase or streptokinase, although conclusive studies on dosing and duration are lacking. Typical doses range from 0.25–1 mg/kg/day, with intracerebral hemorrhage as the primary adverse reaction [9].

Surgical thrombectomy: Considered a last resort due to the low body weight and high mortality risk in neonates, it is only employed when all other options fail [10].

LMWH acts by inhibiting coagulation factors and platelet function, enhancing fibrinolysis, and promoting antithrombin activation. It specifically targets thrombin and factor Xa, though the optimal dosing, efficacy, and side effects of thrombolytic therapy in neonates remain unclear [11].

In neonatal thrombolysis, daily cranial ultrasounds are essential, along with thrombus imaging every 12–24 hours. Thrombolytic infusion should be stopped once the clot dissolves or complications arise. Reocclusion remains a potential issue following fibrinolytic therapy [9]. There is no consensus regarding the concurrent or subsequent use of heparin during rtPA infusion or the duration of administration. A median infusion dose of 0.2 mg/kg/h (range 0.15–0.3 mg/kg/h) has been shown to be effective and safe. Although the indications and dosing for thrombolytic therapy in neonates are not standardized, it may reduce long-term complications in selected patients [11].

Careful catheter placement, appropriate site selection, and vigilant monitoring of neonates are critical for the early detection of thrombosis. Understanding neonatal hemostatic physiology is key to minimizing risks [10]. Preventive strategies, such as anticoagulation during catheter placement, positioning the catheter tip outside the atrium, and ongoing medical education, may reduce the incidence and complications of thrombosis [12].

The current approach to neonatal thrombosis treatment remains challenging, as no specific therapeutic protocol exists for this population due to the high risk of complications.

The use of enoxaparin in low-risk thrombi appears safe in neonates, although thrombolysis may require more time. Outpatient management with aspirin (ASA) is a viable option until resolution. Recombinant tissue plasminogen activator should be reserved for thrombi with a high embolization risk due to its associated complications. Treatment safety and efficacy depend on the patient's clinical condition, guided by clinical and ultrasound findings [13].

Thrombi, depending on their size and location, can cause severe complications, including death, although most do not lead to significant long-term repercussions [13]. A conservative approach may be justified for thrombi with benign characteristics. Enoxaparin and ASA are safe with proper monitoring, while fibrinolytics are indicated when thrombosis poses a threat to life or organ function, provided no absolute contraindications exist [14].

The decision-making process in treating the first and second patients highlights the importance of individualized care in managing neonatal thrombotic conditions. An outpatient approach was chosen for the first patient due to the low risk of complications, resulting in satisfactory outcomes. In contrast, fibrinolytic therapy was employed in the second case due to the thrombus location and high embolization risk. Despite the potential for coagulopathy requiring hematological evaluation, the immediate risk of embolization necessitated fibrinolysis.

This review includes two cases of neonatal intracardiac thrombosis with contrasting outcomes. The first, a full-term newborn born to a mother with gestational diabetes, presented a non-obstructive thrombus in the right atrium associated with the use of an umbilical catheter. He was treated with enoxaparin and followed up as an outpatient, achieving complete resolution without complications. The second case, a newborn with gastroschisis and a central venous catheter, developed a high-risk, mobile intracardiac

thrombus. Despite anticoagulant and fibrinolytic therapy, the patient experienced thrombotic recurrence and an unfavorable outcome, dying from refractory shock. Both cases demonstrate the diagnostic and therapeutic challenge posed by this entity, underscoring the importance of the clinical context and the need for a timely multidisciplinary approach. While the first case showed a benign course, the second highlights the possibility of recurrence and fatal outcome, even with advanced treatment, reinforcing the need for clear protocols and access to specialized hematological evaluation.

4. Conclusions

Neonatal thrombosis, although rare, has become an entity of increasing clinical relevance due to its rising incidence and the potential complications it can cause. Beyond early detection, the real challenge lies in therapeutic decision-making in an environment where guidelines are still limited and the approach often depends on institutional experience. The variability in clinical presentation and the complexity of management require a comprehensive approach that combines active surveillance, timely diagnosis, and individualized treatment.

The lack of specific guidelines makes standardization of management difficult, highlighting the need to develop evidence-based protocols to guide medical personnel in critical situations. Furthermore, it is essential to guarantee access to specialized studies and promote ongoing training for healthcare professionals to recognize this condition early and respond effectively.

Advancing knowledge, systematic case registration, and interdisciplinary collaboration will be essential to reducing associated morbidity and mortality. Recognizing neonatal thrombosis as a silent but significant clinical emergency is the first step toward safer, more equitable, and evidence-based neonatal care.

DECLARATIONS

1- Authors' contributions (CRediT Taxonomy)

Contributor Role	Degree of Contribution		
	Lead	Equal	Supporting
Conceptualization	MFP	MVJ	IGV
Data curation	MVJ	IGV	MFP
Formal analysis	IGV	MFP	MVJ
Funding acquisition	MFP	MVJ	IGV
Investigation	MVJ	MFP	MVJ
Methodology	IGV	MFP	MVJ
Project administration	MFP	MVJ	IGV
Resources	IGV	MFP	MVJ
Software	MFP	MFP	IGV
Supervision	MFP	MFP	IGV
Validation	IGV	IGV	MEP
Visualization	MFP	MVJ	MVJ
Writing-original draft	MVJ	IGV	MEP
Writing-review & editing	IGV	IGV	MEP

2- Ethical approval: The study was conducted by the ethical principles established in the Declaration of Helsinki. It was approved by the Ethics Committee of the Cancún General Hospital, with approval number 20240928, issued on February 2, 2024. The confidentiality and anonymity of patients were guaranteed at all times, omitting any personal data that could allow their direct or indirect identification.

3- Funding resources: No funding resources.

4- Conflict of interest: The authors declare no conflict of interest with other previous studies.

5- Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

6- Data Availability Statement: Data is unavailable due to privacy or ethical restrictions.

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