

Neonatal pericardial effusion: case report and review of the literature

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Abstract

Pericardial effusion (PCE) is a rare condition in neonates. The most common cause is iatrogenic due to central venous catheters (CVCs) and symptoms vary from asymptomatic to more severe presentations, such as cardiac tamponade. Treatment of this condition in neonates remains controversial.

The authors present a case report of a preterm neonate with a PCE and a review of the literature. A preterm infant was born at 26 weeks of gestation and with a birth weight of 690 grams. A peripherally inserted central catheter (PICC) was inserted on day 4, which was uneventful. Due to a hemodynamically significant patent ductus arteriosus with no response to two cycles of treatment with ibuprofen, she was submitted to surgical ligation on day 38. In the postoperative echocardiogram, the tip of the PICC was seen in the right ventricle and the catheter was retracted. An echocardiogram was performed on day 55, showing a PCE with a slight diastolic compromise of the right atrium. The catheter was withdrawn and diuretic therapy with furosemide was initiated. PCE presented a gradual reduction until complete resolution within 3 weeks.

A review of the literature about postnatal PCE was performed. A final sample of 34 articles was included.

The main PCE causes were iatrogenic (due to CVCs, and postoperative of major cardiac surgery) and infection.

Management of this condition was variable between cases ranging from clinical surveillance in asymptomatic newborns with small effusions to pericardiocentesis in large effusions with signs of hemodynamic instability.

In conclusion, PCE is a condition that is often underdiagnosed in neonates. The most common cause, as occurred in the case presented above, is a

mispositioned CVC. Management of this condition is still controversial and further studies are needed to establish therapeutic protocols in neonates.

Keywords

Pericardial effusion, neonate, preterm, central venous catheter.

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Introduction

The pericardium is a membrane composed of two layers, parietal and visceral, separated by fluid. In neonates, its volume is usually inferior to 5 milliliters. A pericardial effusion (PCE) is the abnormal accumulation of fluid between the parietal and visceral layers. The clinical presentation of PCE varies according to the speed of pericardial fluid accumulation, with acute effusions being more symptomatic at lower volumes when compared to slow accumulation of pericardial fluid. The major complication of PCE is cardiac tamponade, which results in a restriction of heart contractility and decreased cardiac output [1].

PCE can be classified in terms of size (mild < 10 mm; moderate 10-20 mm and large > 20 mm), composition (transudate or exudate, blood or rarely air), onset (acute < 4-6 weeks, subacute and chronic > 3 months), distribution (localized or circumferential) and hemodynamic impact (none, cardiac tamponade or constrictive). This classification is based on adult patients, but it has been used in pediatric and neonatal age [2].

The main etiologies of PCE described in neonates are iatrogenic (postoperative, central venous catheter [CVC]-related), infection, congenital anomalies, tumors (pericardial or cardiac tumors), thyroid dysfunction and autoimmune diseases or idiopathic [1, 3, 4].

CVCs have been increasingly used in Neonatal Intensive Care Units (NICU) as they are the most

secure way to provide long-term access, especially in extremely low birth weight (ELBW) preterm neonates. PCE associated with CVCs has been described in the literature as a complication of both umbilical venous catheters (UVC) and peripherally inserted central catheters (PICC) [5, 6].

Most PCEs are incidental radiologic findings in asymptomatic newborns. When symptoms are present, they are usually nonspecific, such as hemodynamic instability, hypotension, brady- or tachycardia and sudden cardiorespiratory collapse. More specific findings such as raised jugular venous pressure or muffled heart sounds can occur, as well as pulsus paradoxus, which is considered the most specific sign of cardiac tamponade [1, 7].

Diagnosis is established through transthoracic echocardiogram. The size of the effusion is based on a simple semiquantitative echocardiographic assessment and is defined as the maximum perpendicular distance between the two layers at end-diastole, usually measured in subxiphoid incidence. The signs of tamponade can be identified by echocardiography: swinging of the heart, early diastolic collapse of the right ventricle, late diastolic collapse of the right atrium, abnormal ventricular septal motion, exaggerated respiratory variability (> 25%) in mitral inflow velocity, respiratory variation in ventricular chamber size, aortic outflow velocity (echocardiographic pulsus paradoxus) and inferior vena cava plethora [1].

When a specific cause for PCE is found, treatment of the underlying condition leads to resolution of the effusion. In moderate to large effusions with signs of hemodynamic instability, pericardiocentesis is recommended. The role of non-steroid anti-inflammatory, corticosteroid or diuretic therapy is still unclear in neonates [2, 8, 9].

The goal of this paper is to present a clinical case of PCE in a neonate and to conduct a review of the literature about PCE to identify and describe the main causes and management.

Case report

A preterm female infant was born from spontaneous vaginal delivery at 26 weeks of gestation, with a birth weight of 690 grams (appropriate for gestational age). Born to a healthy mother gravida 2 para 1, with unremarkable serologies and prenatal ultrasounds described as normal. She had an Apgar score of 3 and 7 at 1 and 5 minutes, respectively. Due to the lack

of efficient respiratory movements, she was intubated and received two doses of therapeutic surfactant for respiratory distress syndrome with a gradual response. A PICC was inserted on day 4. On day 27, the first PICC was removed and a second catheter was inserted in the right upper limb. The insertion was uneventful and its position was verified by chest X-ray. Due to a hemodynamically significant patent ductus arteriosus with no response to two cycles of treatment with ibuprofen, she was submitted to surgical ligation on day 38. In the postoperative echocardiogram, the tip of the PICC was seen in the right ventricle and the catheter was retracted (**Fig. 1**). An echocardiogram was performed on day 55, showing a PCE with 6.5 mm of diameter and diastolic compromise of the right atrium, with preserved biventricular function (**Fig. 2**). The neonate was asymptomatic, with no signs of hemodynamical instability and no abnormalities found in physical examination.

The main causes considered for the PCE were infection, surgical complication and mispositioned PICC. In order to identify possible causes, complete blood count (CBC) and C-reactive protein (CRP) were executed with no signs of infection; polymerase chain reaction for Cytomegalovirus, Enterovirus and Epstein Barr virus were negative. Thyroid function test (TSH and free T4) was normal and thoracic and abdominal ultrasound excluded other effusions.

The CVC was immediately withdrawn and diuretic therapy with furosemide was initiated after a pediatric cardiology consultation (2 mg/kg/day for 14 days). Throughout the treatment, the patient remained hemodynamically stable. Serial echocardiograms confirmed PCE reduction until complete resolution within 3 weeks. The remaining hospital stay was uneventful, with the infant being discharged home at 41 weeks of post-menstrual age.

Methods

A literature search was performed in Pubmed database with the terms “neonatal pericardial effusion”.

All articles published from January 2000 up to February 2018, written in English or Portuguese, were included in the analysis. The study was limited to human subjects. Duplicate articles, comments, systematic reviews and metanalysis were excluded.

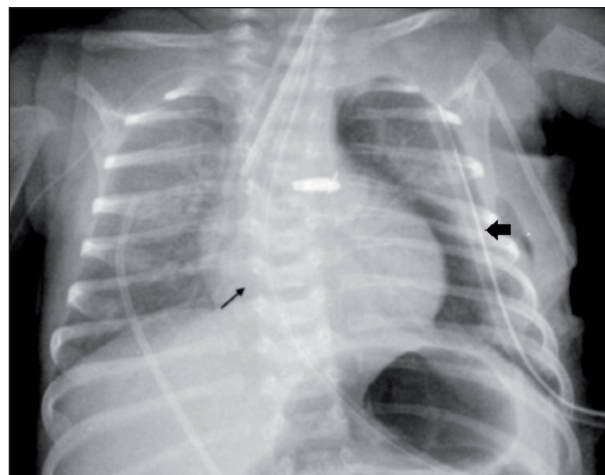


Figure 1. Chest X-ray showing the tip of the central venous catheter (CVC) in the right ventricle (thin arrow).

Thin arrow: CVC; thick arrow: chest drain.

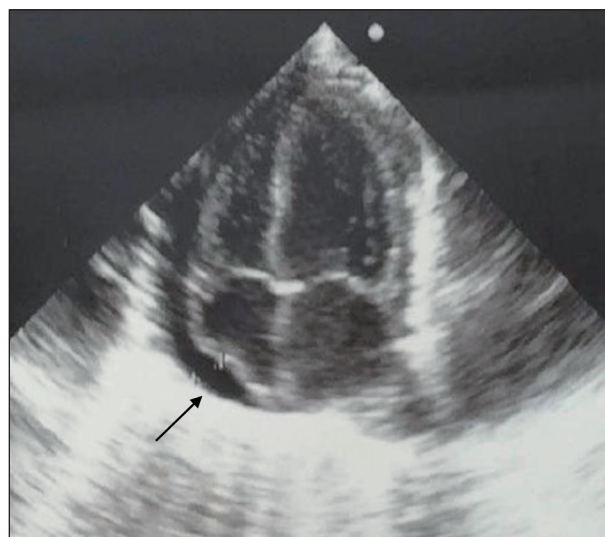


Figure 2. Echocardiogram showing the pericardial effusion (PCE) with systolic collapse of the right atrium (arrow).

PCEs with prenatal diagnosis, as well as cases in pediatric and adult patients, were not the purpose of this review.

Gestational age, birth weight, PCE causes, management and clinical course data were registered in an anonymous database.

Results

The initial search found 225 articles; the selection of the studies is specified in **Fig. 3**. The final sample of 34 articles included 27 clinical reports and 7 case series. The main causes of PCE are described in **Fig. 4**.

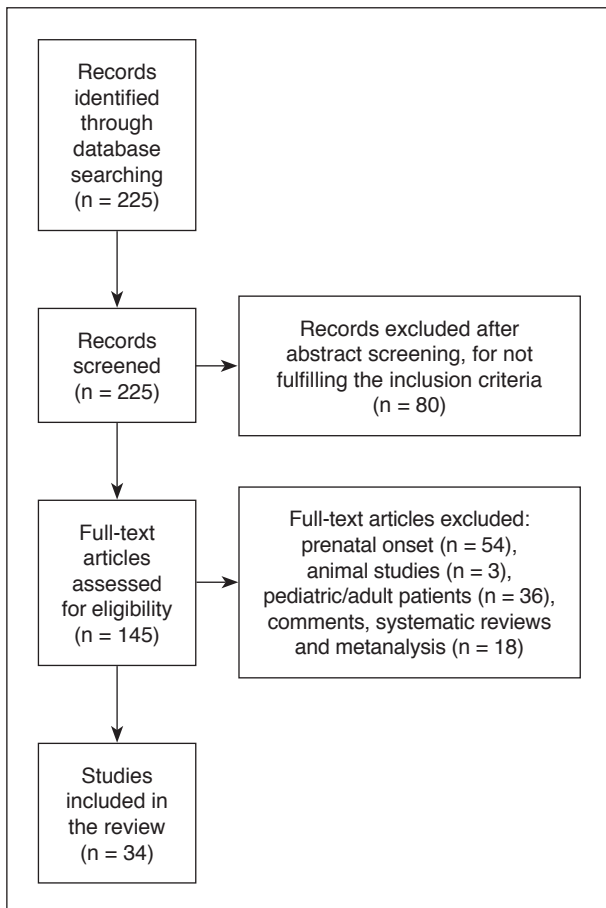


Figure 3. Selection of the articles.

PCE associated with infection (Tab. 1) [10-12]

Three cases associated with infection were found, two of them with pericarditis [10, 11]. Each case was caused by different pathogens and, in one case, identification in the pericardial fluid was achieved [10]. In two cases, drainage of the fluid was performed in association with diuretic and antibiotic therapy [10, 11].

Postoperative PCE (Tab. 2)

In two cases, PCE was detected after major corrective cardiac surgery, one of them needing pericardiocentesis [13]. A third case was a complication of an extracorporeal membrane oxygenation (ECMO) procedure with perforation of the intracardiac segment of inferior vena cava by the catheter and intraoperative death [14].

PCE associated with catheters (Tab. 3 and Tab. 4)

The authors found 21 case reports of PCE associated with catheters and 3 case series [4-7, 9, 15-30]. Most of the patients had a gestational age below 30 weeks (66.7%) and a birth weight inferior to 1,000 grams (52.4%).

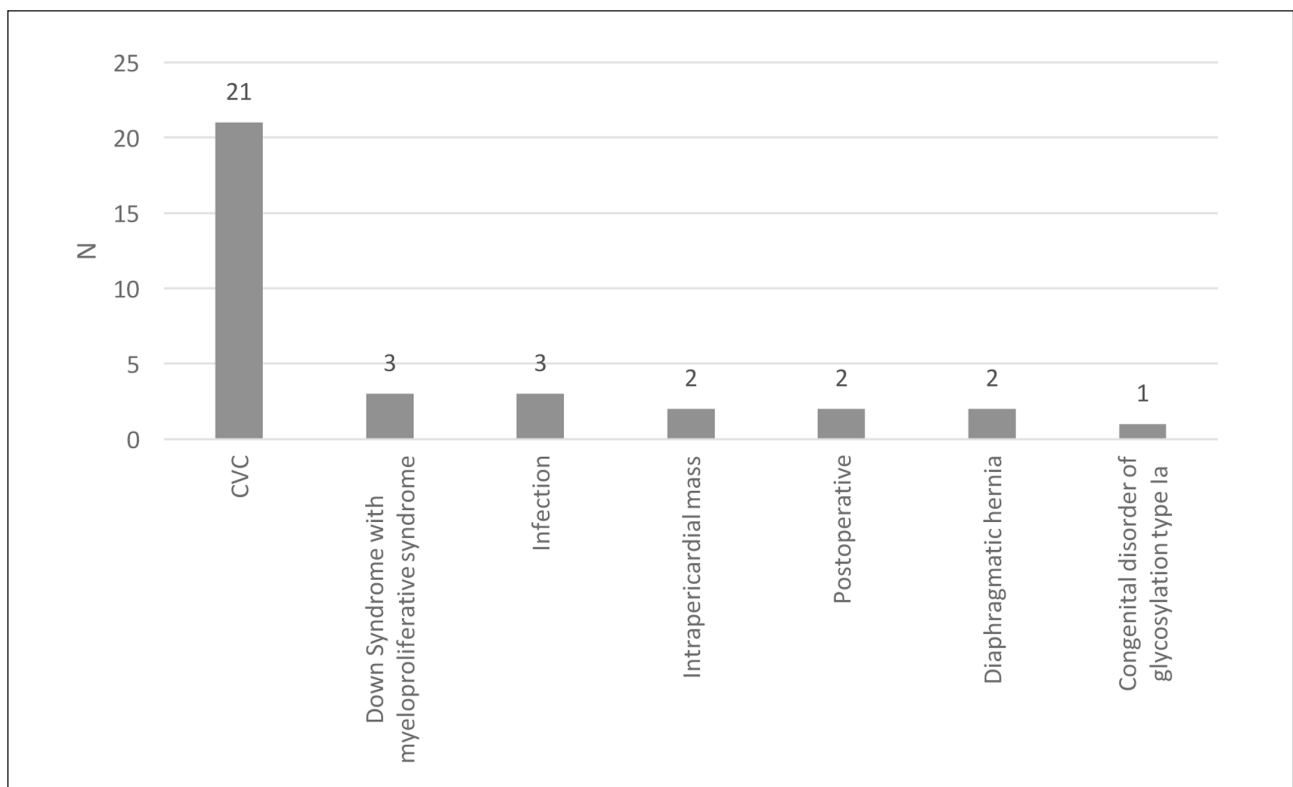


Figure 4. Main causes of pericardial effusion (PCE). CVC: central venous catheters; N: number of cases found.

Table 1. Pericardial effusion (PCE) associated with infection.

Article	Sex	GA	BW	D	Pathogen	Diagnosis	Treatment	Remission
Azhar, 2012 [10]	F	32 weeks	1,400 grams	14	<i>Candida albicans</i> (blood and pericardial fluid culture)	Chest X-ray Echocardiogram	Pericardiocentesis Furosemide Amphotericin B Fluconazole	10 days
Benjamin and Ebenroth, 2006 [11]	M	> 37 weeks	> 2,500 grams	10	<i>Escherichia coli</i> (blood culture)	Chest X-ray Echocardiogram	Pericardiocentesis Indomethacin Cefotaxime	3 weeks
Aranda Cazón et al., 2017 [12]	M	25 weeks	720 grams	30	Parainfluenza 3 (nasopharyngeal swab)	Chest X-ray Echocardiogram	Surveillance	5 days

BW: birth weight; D: day of life; F: female; GA: gestational age; M: male.

Table 2. Pericardial effusion (PCE) associated with surgical interventions.

Article	Condition	Intervention	Complication	Treatment	Recurrence	Death
Gardner and Cohen, 2017 [13]	Left ventricle hypoplasia	Norwood with Sano modification	PCE (large volume)	Pericardiocentesis	Yes – diuretic and corticosteroids	No
Gardner and Cohen, 2017 [13]	Left ventricle hypoplasia	Norwood with Sano modification	PCE (moderate volume)	Corticosteroids	No	No
Czerwonko et al., 2015 [14]	Respiratory infection (adenovirus)	ECMO	Perforation of IVC	-	-	Yes

IVC: inferior vena cava; PCE: pericardial effusion; ECMO: extracorporeal membrane oxygenation.

Table 3. Pericardial effusion (PCE) associated with central venous catheters (CVCs): outcomes from 21 case reports.

	UVC (n = 10)	PICC (n = 11)
Location	Umbilical vein	Left arm (3), right arm (5), right leg (1), non-specified (2)
Time after insertion (median)	4.00 days	3.64 days
Mispositioned catheter	4 cases	9 cases
Hemodynamic instability	6 cases	10 cases
Diagnosis	Chest X-ray (7) Echocardiogram (10)	Chest X-ray (5) Echocardiogram (9)
Treatment	Conservative approach (2) Pericardiocentesis (7) Pericardial drain (1)	Pericardiocentesis (6) Ibuprofen (1)
Pericardial fluid	Parenteral nutrition – 7 cases	Parenteral nutrition – 7 cases
Pleural effusion	4 cases	2 cases

PICC: peripherally inserted central catheter; UVC: umbilical venous catheter.

Table 4. Pericardial effusion (PCE) associated with central venous catheters (CVCs): outcomes from 3 case series.

Article	Study description	Population	Outcomes
Warren et al., 2013 [5]	Autopsies in cases with sudden death from PCE in neonates with CVCs	n = 5 GA: 22-41 weeks BW: 671-3,142 grams CVC: 3 UVC, 2 PICC	Time after insertion: 4-29 days 4 CVC in the right atrium 1 case of microperforation of right atrium
Beardsall et al., 2003 [29]	Questionnaire to 168 NICUs	82 cases of PCE associated with CVC	Incidence: 1.8/1,000 CVC Mortality rate: 0.7/1,000 Higher number in NICUs with < 50 CVC per year (p = 0.005)
Nowlen et al., 2002 [6]	Retrospective multicentric study (6 NICUs) and review of literature	PCE in newborns with CVC (n = 14) Review of literature (n = 47 case reports) Mean GA: 31 weeks Mean BW: 1,600 grams	Mean time after insertion: 3 days 82% with intracardiac CVC Mortality rate: 34%

BW: birth weight; CVC: central venous catheter; GA: gestational age; NICU: Neonatal Intensive Care Unit; PCE: pericardial effusion; PICC: peripherally inserted central catheter; UVC: umbilical venous catheter.

There were cases associated with UVC and PICC. The main outcomes of the case reports are described in **Tab. 3**. Despite what is described in the literature, most of the patients were identified due to hemodynamic instability. Management was variable, with the majority (13 cases) being treated with pericardiocentesis.

The fluid was analyzed in 15 cases, with 93% (14/15) being parenteral nutrition.

Pleural effusion was more commonly associated with UVC [15].

Data from the 3 case series are specified in **Tab. 4**.

Warren et al. described a series of 5 autopsies performed in cases with sudden death from PCE in neonates with CVCs. They state that PCE can occur even with appropriate CVC positioning and hypothesized that the hyperosmolarity of parenteral nutrition could damage myocardial wall leading to PCE [5].

Beardsall et al. made a retrospective study by sending questionnaires to 168 NICUs in the United Kingdom. They found 82 cases of PCE associated with CVCs and concluded that most cases occurred in centers with fewer than 50 CVCs per year ($p = 0.005$) [29].

A retrospective study determined that the median time between insertion and PCE detection was 3 days. Symptoms and signs leading to the diagnosis were variable, with increased cardiothoracic ratio being the only statistically significant finding ($p = 0.001$) [6].

PCE associated with other causes [31-34]

Two cases described PCE secondary to intrapericardial teratoma [31, 32], and two other cases were associated with diaphragmatic hernia [33, 34]. Most of the cases resolved with surgical repair/excision of the underlying cause.

All cases described in Down syndrome with myeloproliferative syndrome and congenital disorder of glycosylation type Ia needed pericardiocentesis [35-38].

Discussion

PCE is usually an underdiagnosed condition in neonates. The main differential diagnosis includes some prenatal conditions, such as immune or nonimmune hydrops fetalis, infections (TORCH, enterovirus) or iatrogenic causes (postoperative or CVC) [4].

In the present case, the three main causes considered for the PCE were: infection, which was not probable as the neonate was asymptomatic, CBC and CRP showed no signs of infection and polymerase chain reaction for the most common pathogens was negative; complication of surgical correction of patent ductus arteriosus, which was unlikely as the procedure had no direct contact with the pericardium; complication of mispositioned PICC, which was considered the most probable cause, as it was seen in the right ventricle before the onset of PCE.

The leading cause of new-onset PCE in neonates is CVCs, with an incidence of 0.5-3%. The median time between placement and diagnosis of PCE is 3 to 4 days. The risk factors that have been associated are lower gestational age and birth weight, intracardiac position or misplaced CVC, infusion of parenteral nutrition and vancomycin [29, 39, 40].

In the case reported by the authors, the neonate presented all the main risk factors: ELBW, gestational age inferior to 28 weeks, CVC in intracardiac position and parenteral nutrition infusion. The diagnosis of PCE was made 28 days after the introduction of the PICC, which could indicate either migration of the catheter or a delay in the diagnosis due to the lack of symptoms.

International recommendations state that the tip of the catheter should be located outside the cardiac outline. There have been cases described with correct positioned CVC, which could indicate that arm movements may affect the position of the catheter. Srinivasan et al. concluded that migration of the catheter was frequent and recommended a follow-up X-ray 24 hours after the insertion [41]. To avoid this complication, some NICUs adopted the policy to regularly verify the position of the PICC. Another possible reason is that measurement methods used (Dunn and Shukla) may not be valid for premature infants, especially those with ELBW [16, 17, 30, 42, 43].

In our NICU, the number of CVCs (> 50 per year) and the control of catheter position after placement with X-ray or ultrasound contribute to a lower complication rate. Functional echocardiography has been increasingly used in NICUs, as it enables a non-invasive bedside assessment of cardiac function and hemodynamic changes. The use of this tool in numerous procedures such as PICC placement leads to improved success rates. Compared to the use of X-ray, ultrasound

was shown to be a more accurate and faster tool with lower radiation exposure [44-46].

CVCs have considerable benefits in preterm neonates, but complications may arise such as infection, thromboembolism, malposition, displacement and, in rare cases, pericardial or pleural effusions. In our case, the tip of the catheter was visualized in the right ventricle after correct initial positioning, which suggests migration of the PICC. There have been numerous mechanisms described for the onset of PCE, such as direct lesion of the myocardium (rare), transmural necrosis due to repeated contact of the catheter tip with the myocardium and superior vena cava wall or osmotic lesion due to the infusion of parenteral nutrition [39, 42, 47].

Treatment of PCE in neonates remains controversial. In asymptomatic newborns with small effusions, clinical surveillance is advised with spontaneous resolution over 2 to 3 weeks in most cases. The effect of medical treatment is unclear and based on adult and pediatric patients. When pericarditis is present, ibuprofen has been used in newborns, but its efficiency remains unproven. In large effusions with signs of hemodynamic instability, pericardiocentesis is recommended [2, 8-10].

In conclusion, PCE is a condition often underdiagnosed in neonates. The most common cause is a mispositioned CVC. Management of this condition is still controversial and further studies are needed to establish therapeutic protocols in neonates. Regular verification of the position of the CVC by chest X-ray or echocardiography during its use could lead to a lower risk of complications.

Declaration of interest

The Authors declare that there is no conflict of interest.

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