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Case Report

Biochemical Clue towards an Etiology of an Unusual Radiological Diagnosis in a Preterm Neonate

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Abstract

Background: Central venous catheter (CVC) extravasation remains the commonest cause of pericardial effusion in a neonate. The concurrent presence of both pericardial and pleural effusions is rare with CVC extravasation. This can present with diagnostic dilemma in very sick neonates with a positive bubble/agitated saline study on echocardiogram.

Case report: We report such a challenging case in a 30 weeks gestational age preterm neonate with a pre-existing cardiomegaly who had umbilical venous catheter placed few hours after birth that was confirmed central by both X-ray and a positive echocardiographic bubble study. The neonate developed progressive pericardial and right pleural effusions in this context, where the unifying etiology to the concurrent occurrence of the two effusions was provided by the glucose content in both the effusions compared to blood glucose level and parenteral solution. The other biochemical analytes of the fluid were different in comparison to parenteral solution.

Conclusion: This case emphasizes the importance of detailed scrutiny of all information in such cases and the limitation of echocardiographic confirmation using bubble study.

Keywords: Pericardial effusion, Pleural effusion, Central venous catheter, Umbilical venous catheter, Neonates

Introduction

Pericardial effusion can be fatal in neonates if unrecognized due to progression into cardiac tamponade secondary to limited and restricted pericardial cavity in them. Mispositioned CVC is the commonest cause of pericardial effusion in neonates [1,2]. Simultaneous development of both pericardial and pleural effusions secondary to CVC extravasation is extremely rare due to anatomical barriers [3]. Here, we report a case of preterm neonates with pre-existing cardiomegaly that was diagnosed to have large pericardial effusion by 16 hours of life along with a positive bubble study and had progressive development of right pleural effusion. The longitudinal assessment showed worsening pleural and pericardial effusions with development of cardiac tamponade. The unifying etiology for the development of both pericardial and pleural effusion, laid in the vigorous scrutiny of the glucose content in the biochemical analysis of both the pericardial and pleural fluid.

Case Report

We present a male neonate born at 30weeks of gestational age to a 26year old G3-1-0-1-1. This was spontaneously conceived pregnancy complicated by preterm rupture of membranes since 25weeks that was managed with betamethasone and Mercer protocol. There was progressive oligohydramnios with development of fetal heart rate abnormality resulting in preterm delivery via caesarean section at 30weeks. The neonate's birth weight was 1170grams (24th centile). His Apgar scores were 2, 2, 4, 5 and 7 at 1, 5, 10, 15, and 20 minutes respectively. Due to ongoing poor respiratory effort, he was successfully intubated by 12minutes of life.

He was transferred to Neonatal Intensive Care Unit and initiated on conventional mechanical ventilation. Enlarged cardiac silhouette was noted on chest x-ray done for assessing endotracheal tube position soon after birth (Figure 1). Surfactant was administered and umbilical venous catheter (UVC) and umbilical arterial catheter (UAC) were placed subsequent to this. X-ray post umbilical catheter placements showed UVC just at the right diaphragm level at T8 vertebrae and UAV at T10 vertebral level (Figure 2).

The cardiomegaly continued to persist on repeat x-rays. Total

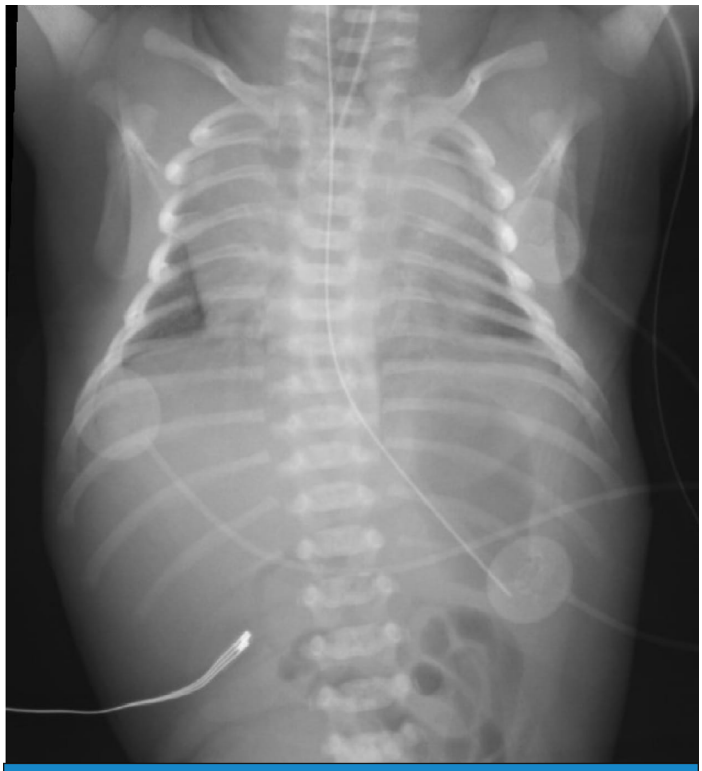

Figure 1: Chest X-ray done soon after birth to access endotracheal tube position. Anteroposterior view of the chest and abdomen showing low lung volume, enlarged cardiac shilloutte, orogastric tube in the distal stomach and an endotracheal tube at T2-T3 vertebral level.

parenteral nutrition (TPN) was initiated via the UVC and an empirical antibiotic was started for suspected sepsis. Given the persistence of cardiomegaly, cardiology was consulted upon which an echocardiogram was performed by 16hours of life. He was found to have a large circumferential pericardial effusion with deepest pocket of 9 mm (Figure 3A) with no tamponade physiology [Mitral Valve inflow variation 18%, no dilated IVC, no Right Atrium(RA)/Right Ventricle(RV) diastolic collapse], and a small right sided pleural effusion. The UVC tip position was not well seen. Furthermore, a bubble study using agitated saline showed bubbles entering the RA (Figure 3B) first then going into the RV and Left Atrium.

Over the subsequent 16hours, he had escalating ventilatory requirement to high frequency oscilatory ventilation and development of tachycardia with progressive metabolic acidosis. Rest of

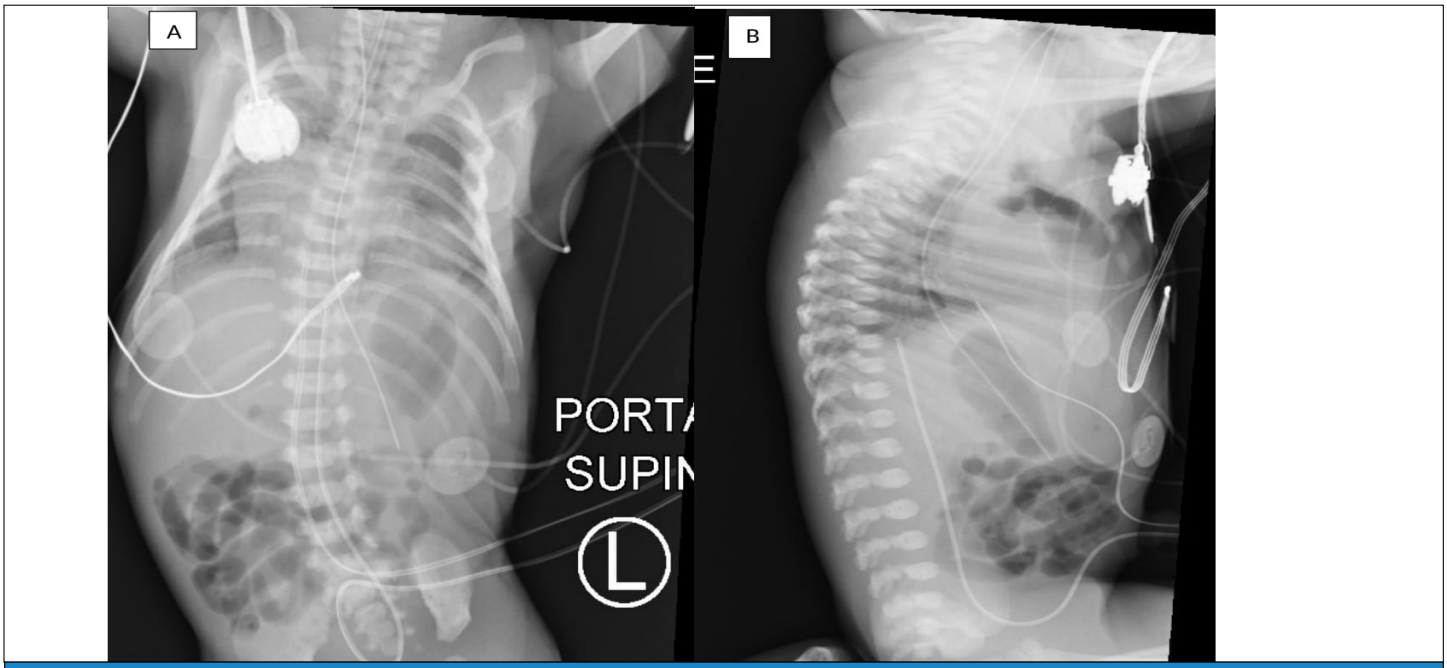

Figure 2: Chest and abdominal X-rays Anteroposterior and lateral views to access umbilical line position.: A: Anteroposterior view showing UVC at T8 vertebral level, enlarged cardiac shilloutte, orogastric tube in the distal stomach and an endotracheal tube at T2-T3 vertebral level. B: Lateral X-ray showing UVC tip at the level of the diaphgram.

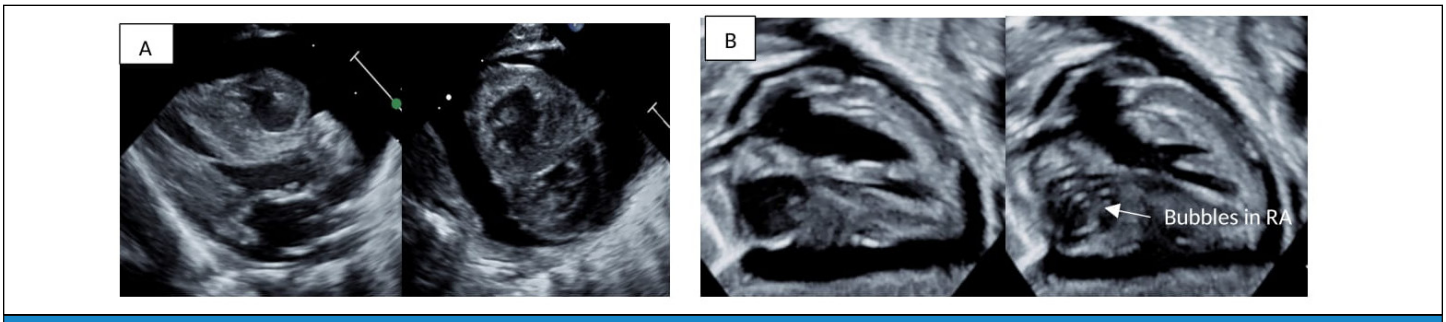

Figure 3: 3A-Echocardiogram showing parasternal long axis view (left) and parasternal short axis view (right) with large circumferencial pericardial effusion at 16hours of life (DOL1). 3B: Echocardiogram showing bubbles in the RA during bubble study.

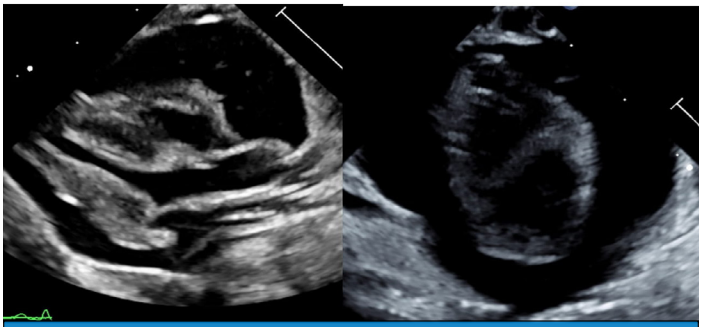

Figure 4: Echocardiogram showing parasternal long axis view (left) and parasternal short axis view (right) with worsening large circumferencial pericardial effusion on DOL2.

his hemodynamic parameters were within normal limits. Repeat echocardiogram on DOL2 showed increasing size of pericardial effusion with deepest pocket measuring 1.2cm along with mild RA collapse (Figure 4). There was also interval development of progressive right pleural effusion (Figure 5). Thus, a decision was made to proceed with pericardiocentesis and pleurocentesis. 32mls of pericardial fluid and 45mls of pleural fluid from right chest was drained under ultrasound (US) guided needle aspiration on DOL2, followed by insertion of right sided pleural chest tube. Both these fluids appeared milky (Figure 6) and samples

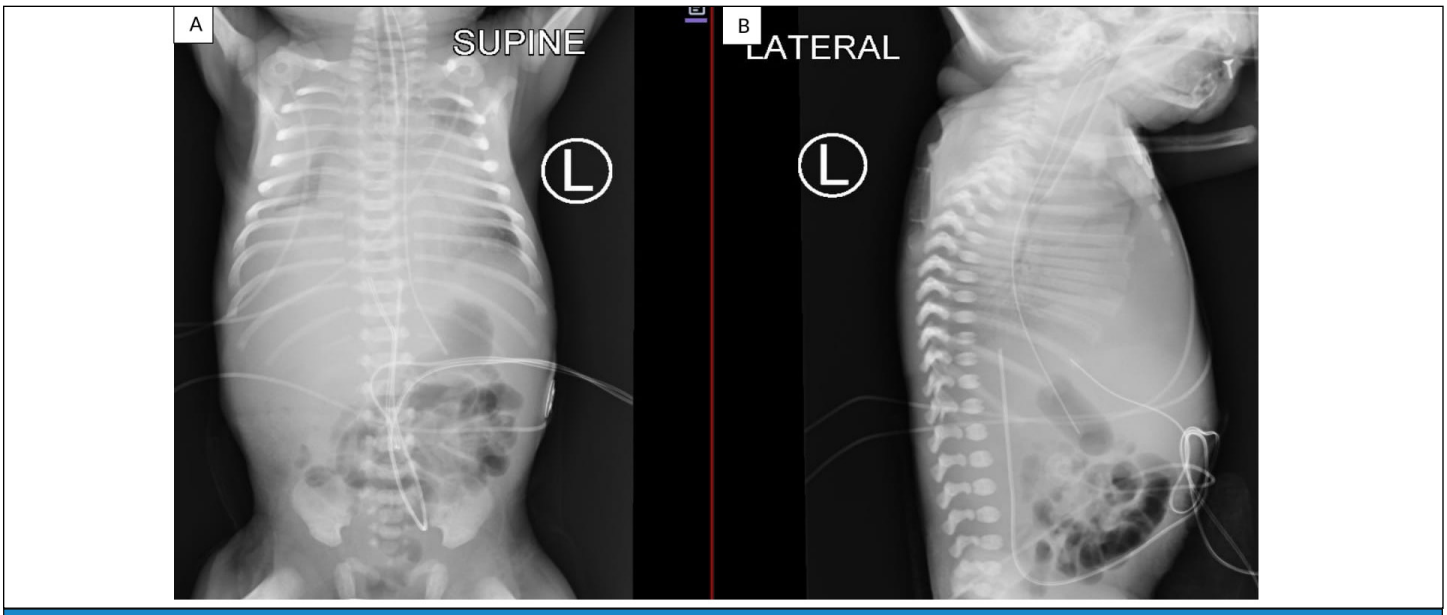

Figure 5: Chest and abdominal X-rays Anteroposterior and lateral views. A: Anteroposterior view showing moderate to large right pleural effusion, UVC pushed down to T9-10 vertebral level, UAV at T10 vertebral level, enlarged cardiac shilloutte, orogastric tube in the distal stomach and an endotracheal tube at T2-T3 vertebral level. B: Lateral X-ray showing UVC tip pushed below the diaphgram giving an impression to be in the liver.

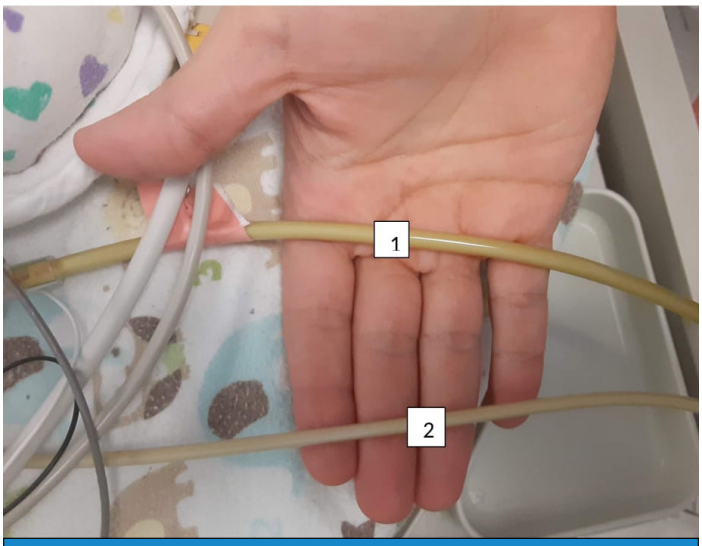

Figure 6: Picture showing milk coloured fluid in the pericardial drain (1) and pleural drain (2).

were sent for analysis.

Subsequent serial echocardiograms showed re-accumulation of pericardial effusion along with recurrence of tachycardia and onset of diastolic hypotension. Pericardial drain was hence inserted under US guidance. A large amount of milk colored fluid continued to drain from both cavities. Serial biochemical analysis showed presence of high triglyceride levels (Table 1). He was thus started on octreotide for possible congenital chylothorax/chylopericardium in consultation with pediatric gastroenterologist. He continued to have significant pericardial and pleural drainage for milky fluid and remained nil per os given his critical nature. However, by DOL6, following a careful scrutiny of the longitudinal biochemical and cellular analysis thus far, a trend in persistently high glucose levels (28-31mmol/dl) was noticed in both pericardial and pleural fluids in comparison to blood glucose level (2.6mmol/dl-5.6mmol/dl) while other parameters were very variable. This rose the suspicion for an external source for high glucose content in both pericardial and pleural fluids and possible UVC extravasation despite a pre-existing cardiomegaly and a positive bubble study.

UVC was thus discontinued upon which he had no further re-accumulation of pericardial or pleural effusions thereby confirming the diagnosis of UVC extravasation. He progressively improved in his clinical status with de-escalation of respiratory support and eventually extubated by DOL13 to non-invasive pressure support

Table 1: Comparison of biochemical and hematological analysis of pericardial, pleural fluid, parenteral nutrition solution and blood sample

Variables	Pericardial fluid		Pleural fluid		Parenteral nutrition solution		Blood
Days of Life	DOL2	DOL4	DOL2	DOL4	DOL2	DOL4	DOL2
Protein, g/l	2	12	2		50	50	
Albumin	<10	<10			-	-	28
Glucose, mmol/l	31.4	28.9	29.3	30.1	687	835	2.6- 5.6*
Cholesterol, mmol/l	<0.08	0.37	<0.08	0.21			
Triglyceride, mmol/l	8.42	31.03	11.66	1.6	6.77	6.77	2.09
LD, u/l	100	162	124	467	-	-	1799
Appearance	Yellow and cloudy	Milky	Yellow and cloudy	Yellow and cloudy	-	-	-
Nucleated cells, 10^9/l	0.134	3.86	0.223	0.761	-	-	15.4
Neutrophils, %	N/A	56	N/A	87	-	-	65.6
Lymphocytes, %	N/A	1	N/A	10	-	-	15
Monocytoid, %	N/A	39	N/A	3	-	-	15.6
Eosinophil, %	N/A	1	N/A		-	-	0.6

N/A- not applicable as total nucleated cells <0.3
*There were four blood sugars done on DOL2 in the range of 2.6-5.6mmol/l

and to low flow by DOL25. Octreotide was discontinued by DOL6 and enteral feeds were initiated with no concerns in clinical status. Given the need for multiple interventions, he received empiric antibiotics for 7days despite the negative 48hour blood culture result. He was eventually transferred to his home hospital by 36weeks and 4days corrected gestational age on low flow oxygen therapy to continue establishing oral feeds and for monitoring growth.

Discussion

Iatrogenic etiology is the commonest cause of pericardial effusion (PE) in neonates with CVC extravasation being the highest [4,5]. PE is a potential life-threatening complication of CVC extravasation which require prompt identification [1,6]. But concurrent occurrence of a progressive pericardial effusion along with pleural effusion is rare with one published case report in a preterm neonate [7]. Our case report highlights such an occurrence in a critically sick preterm infant with pre-existing cardiomegaly right from birth and a positive bubble study, making clinical judgement of a centrally placed UVC extravasation extremely challenging. Detailed scrutiny of a longitudinally performed biochemical component of the fluid analysis along with extremely high index of suspicion provided etiological clue in our case. While cardiomegaly at admission could be red herring, this case emphasizes the need for multimodal assessment and taking all the information into consideration inorder to make a causative diagnosis.

Pericardial cavity is a serious cavity located inside the middle mediastinum and bordered laterally by the mediastinal parietal pleura [8]. It has an external fibrous sac called the fibrous pericardium and an internal layer called serous pericardium which covers the heart as visceral pericardium as well as lines the inner part of fibrous pericardium as parietal pericardium [9]. Pericardial cavity is anatomically separated from pleural cavities by pleuro-pericardial membrane [3]. But there have been rare reports on partial or complete absence of pleuropericardial membranes in adults [10]. Furthermore, histopathological studies in animal models have shown “micro pores” on the surface of the parietal pericardium which directly connects it with mediastinal pleural cavities [11,12]. Though its significance is unknown, these pores have been shown to allow passage of red blood cells in experi-

mental animal models [13]. Its presence is human pericardium remains unreported and therefore pericardium in humans is considered not to have anatomical connections with pleural cavities.

In our case, there was presence of both pericardial and right pleural effusion which showed persistently high glucose content despite other biochemical contents not being comparable to TPN, suggestive of an external source for high glucose levels. Hence making it TPN secondary to UVC extravasation. Possible explanation includes puncture of pericardial cavity by UVC catheter which may have further traversed through the pleuropericardial membrane on the right side leading to UVC partially infusing both the pericardial cavity and the right pleural cavity. In addition, the misplaced UVC could have created a communication between pleural and pericardial cavities allowing passive diffusion of the TPN between the two cavities. Potential presence of micro pores or congenital defect in the pleuro-pericardial membrane could not be excluded in our case.

Risk factors for UVC extravasation include being preterm neonates, administration of TPN solution, manipulation during insertion of UVC like rail-roading or tunneling, sepsis causing fragile blood vessel, and line migration during handling of lines or movement of the neonate [14,15]. TPN makes fluid more hyperosmolar affecting vessel wall integrity leading to perforation particularly in preterm neonates where incidences of line migration are more frequent as well. Some of these risk factors existed in our case making our neonate more vulnerable to UVC extravasation. Presence of cardiomegaly on initial x-ray prior to placement of UVC was a red herring and could probably be explained by apparent cardiomegaly due to relative degree of pulmonary hypoplasia suggested by the low lung volumes. Hence high index of suspicious is required in any sick neonate with central UVC with a finding of unexplained pericardial effusion with or without pleural effusion.

Post procedural chest X-ray is the standard of care for assessing UVC placement location with tip at the level of diaphragm and outside of the cardiac shadow [16,17]. Numbers of studies have shown the poor accuracy of X-ray for this purpose [18-20]. There is increasing evidence suggesting ultrasound being more reliable method of assessment [18-25]. But migration of catheter tip is very common especially in preterm neonates [25]. Bubble study is increasing used in emergency department to confirm the tip of the CVC tip even by those with little or no ultrasound experience [26,27]. During the echocardiogram, a saline solution that has been rapidly mixed with air by agitation to produce tiny bubbles, is injected into the CVC. The bubbles circulate in the right side of the heart, showing up on the echocardiogram in case of an appropriately placed CVC. Bubble study has shown excellent sensitivity of 100% and specificity of 94% including when performed by residents with minimal training [27]. In our case, the bubble study using agitated saline showed bubbles entering the RA first then going into the RV and LA, falsely reassuring clinical team against UVC extravasation initially. There could be two reasons for this. First, given that this particular neonate's blood sugar was within normal range, the UVC might have been partially intravascular, thereby allowing the bubbles to reach the RA. Second, it may be possible that the bubbles were originating within RA due to some turbulence of venous return possibly secondary to restriction in RA chamber due to pericardial effusion.

Heightened attention to details on biochemical components of pericardial and pleural fluid analysis could help in delineating etiology in unusual presentation of pericardial effusion especially in a critically sick neonate. High glucose content of pericardial and or pleural fluid compared to blood glucose should suggest CVC extravasation in the presence of a CVC infusing TPN [28]. Glucose content in body cavities are usually similar or lower than blood glucose content. Normal range for pericardial glucose level in an adult is 6-8.8 mmol/dl [29] with mean fluid to serum glucose ratio of 1 (0.8-1.2 99% CI), which has been extrapolated to neonates given the lack of data in this population. A raised glucose content in effusions should raise suspicion for an external source for the pericardial or pleural effusions. Analysis of both pericardial and pleural fluid consistently showed 8-10fold increase in glucose concentration compared to blood glucose in our case. The other analytes were very variable in both the effusions on serial assessment compared to blood and TPN solution. This would confirm the iatrogenic etiology for both effusions as in our case following which UVC was discontinued leading to complete resolution of pericardial and pleural effusions.

Conclusion

While simultaneous presence of pericardial and pleural effusion in critically sick preterm neonates with a reassuring bubble study can make etiological differentiation challenging, glucose content of the fluid can provide a valuable clue to diagnosis and therapeutic decision making when other fluid analytes are variable in longitudinal biochemical analysis. CVC extravasation continues to remain the commonest cause of PE and should still be considered in unusual presentations.

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