Cardiac Tamponade-Associated Dense Deposit Disease: A Case Report and Review of the Literature

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Abstract
Pericardial effusion is an abnormal accumulation of fluid in the pericardial cavity. It can be associated with various cardiac and non-cardiac disorders. Dense deposit disease (DDD) is a rare kidney disease caused by uncontrolled activation of the alternative complement pathway. We are reporting a seven-year-old male child who was diagnosed to have DDD approved by renal biopsy and presented with shortness of breath, cough, and fever. Chest X-ray displayed cardiomegaly. Thereafter, echocardiography showed massive pericardial effusion and left ventricle compression with a risk for cardiac tamponade. He subsequently underwent pericardiocentesis with the removal of 450 ml of pericardial fluid. The patient’s edema was not correlated with the described amount of drained pericardial fluid. To the best of our knowledge, this is the first reported case of significant pericardial effusion carrying the risk of cardiac tamponade associated with DDD. With this report, we would like to highlight the importance of cardiac assessment in patients with DDD, in particular those with nephrotic range proteinuria who present with cardiac symptoms and cardiomegaly.

Introduction
C3 glomerulopathy (C3G) is a form of glomerulonephritis that results from abnormal regulation of the alternative complement pathway leading to C3 deposition in glomerular capillaries. C3G may be categorized into dense deposit disease (DDD) and C3 glomerulonephritis (C3GN) [1-3]. It is ultra-rare with an incidence of approximately one per million per year [2]. C3GN is driven by genetic and/or acquired defects, and dysregulation mostly occurs at the level of the C3 converge of the alternative pathway in the fluid phase [2]. The presentation is usually a slowly progressive disease with hematuria and non-nephrotic proteinuria, but nephrotic syndrome and more severe presentations have been described [4]. About 50% of patients with DDD progressed to end-stage renal disease (ESRD) within 10 years [5,6]. Cardiovascular complications are a leading cause of death in ESRD in pediatric and adult patients. The pericardial cavity is the potential space between the visceral and parietal components of the pericardium, which is normally lubricated by a very small amount of serous fluid. An abnormal increase in fluid volume leads to pericardial effusion, which could be a result of different etiology [7,8]. Pericardial effusion in renal diseases is usually caused by continuous volume overload as a result of salt and water retention or secondary to hypoalbuminemia leading to shifting of fluid from intravascular into the interstitial compartment [8,9]. Patients with ESRD, in particular, are more likely to develop chronic pericardial effusion due to continuous volume overload [9]. Pericardial effusion and tamponade are extremely rare but serious complications of nephrotic syndrome [10]. When pericardial effusion generates pericardial tamponade, the patient usually develops dyspnea, tachycardia, jugular venous distension, and pulsus paradoxus, and these symptoms lead to hypotension and shock [11].

Case Presentation
A previously healthy seven-year-old boy presented with mild facial puffiness, red-colored urine, and decreased urine output preceded two days by an upper respiratory tract infection. He was edematous with extensive peribital puffiness, bilateral pitting peripheral edema, and ascites. He presented with a picture of rapidly progressive glomerulonephritis (RPGN). The laboratory findings upon initial presentation are summarized in Table 1.
Laboratory tests | During initial presentation | One month later, during the presentation with cardiac tamponade
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Hemoglobin, g/dl | 8.8 | 9.8
WBC, 10⁹/L | 5.3 | 13.1
Platelets, 10⁹/L | 394 | 630
Creatinine, umol/L | 304 | 69
Urea, mmol/L | 19.4 | 3.5
Albumin, g/L | 25 | 26
Sodium, mmol/L | 138 mmol/L | 140
Potassium, mmol/L | 4 mmol/L | 4
Bicarbonate, mmol/L | 17 | 20
C3, g/L | 0.1 (0.9-1.8) | 0.4 (0.9-1.8)
C4, g/L | 0.23 (0.1-0.4) | 0.3 (0.1-0.4)
ASO titer, ANA, ANCA, anti-GBM | Negative | Not repeated
CFH | 20.1 (23.6-43.1 mg/dl) | Not repeated
CFB | 8.1 (15.2-42.3 mg/dl) | Not repeated
CFI | 65 (29.3-58.5 mg/l) | Not repeated
MAC | 479 (<251 ng/ml) | Not repeated
24-hour urine protein, g/day | 8.4 | 3.4 g/day
Genetic testing | Negative | Not repeated
Pericardial fluid analysis
Albumin, g/L | NA | 5.5
LDH, U/l | NA | 53
Glucose, mmol/L | NA | 6.3
Count | NA | 10/cumm
WBC count | NA | 1/cumm
PCR MTB DNA complex | NA | Target not detected
Mycobacterium examination | NA | Negative
Fungal examination | NA | Negative

TABLE 1: Laboratory findings upon initial presentation and during the presentation of cardiac tamponade

WBC: white blood cells; RBC: red blood cells; ASO: antistreptolysin O; ANA: antinuclear antibody; ANCA: antineutrophil cytoplasmic antibodies; anti-GBM: anti-glomerular basement membrane; CFH: complement factor H; CFB: complement factor B; CFI: complement factor I; MAC: membrane attack complex (C5b-C9); LDH: lactate dehydrogenase; PCR MTB DNA complex: Mycobacterium tuberculosis complex DNA.
presented with shortness of breath, edema, low-grade fever, and cough. His pulse rate was 102 beats/minute, blood pressure was 114/72 mmHg, respiratory rate was 26/minute, and weight was 24.5 kg. A chest X-ray showed huge cardiomegaly (Figure 1). Echocardiography showed massive pericardial effusion (Figures 2-4).
FIGURE 2: Initial echocardiography showing massive pericardial effusion and early diastolic right ventricular collapse

PE: pericardial effusion; RV: right ventricular.

FIGURE 3: Initial echocardiography showing the pre-systolic right atrial collapse

RA: right atrial.
His clinical parameters and echocardiography findings indicated a high risk for cardiac tamponade; thus, an urgent pericardiocentesis was performed, where 450 ml of serous fluid was drained. Laboratory testing including pericardial fluid analysis is shown in Table 1. A repeated echocardiography two weeks later showed minimal effusion (Figure 5). Up to the present, he is on regular eculizumab therapy.

**Discussion**

Patients with DDD can be presented with asymptomatic microhematuria and/or proteinuria to severe disease with nephritic or nephrotic syndrome and renal impairment [12]. Nephrotic syndrome has been
reported up to 38-43% in DDD [12]. Acute cardiac tamponade is a life-threatening condition, caused by pressure on the heart from fluid in the pericardial space that causes a severe decrease in ventricles diastolic filling. Thus, it requires a preemptive diagnosis and treatment [11,13]. The causes of pericardial effusion inducing pericardial tamponade are heart surgery, trauma, chest radiation, tumor, chest radiation, hypothyroidism, ESRD, invasive cardiac intervention, autoimmune disease, and acute inflammatory pericarditis [14]. Pericardial effusion can occur in idiopathic nephrotic syndrome and systemic lupus erythematosus (SLE) [15,8]. Pericardial tamponade is an extremely rare but serious complication of nephrotic syndrome with only a few documented cases in the literature [8,10,16,17]. Table 2 summarizes some cases reported for nephrotic syndrome patients with pericardial tamponade.
Our patient was presented with nephrotic range proteinuria as well as other presentations of DDD. Pericarditis caused by b-hemolytic Streptococcus has been reported in pediatric patients and adults with post-streptococcal glomerulonephritis, both complicated by cardiac tamponade and managed by pericardiocentesis [18,19]. We suggest that this complication in our patient occurred because of hypoalbuminemia that is secondary to significant proteinuria. Other causes such as hypothyroidism,
Conclusions
With this report, we would like to remind clinicians that pericardial tamponade is a possible and uncommon but serious complication of DDD with nephrotic range proteinuria, which requires prompt and lifesaving pericardiocentesis. Patient edema was not correlated with the amount of pericardial effusion, which might be due to the slow accumulation of pericardial fluid. A detailed cardiac assessment should be carried out when a child with nephrotic syndrome or nephrotic range proteinuria presents with chest pain, tachycardia, tachypnea, dyspnea, and cardiomegaly.

Additional Information
Disclosures
Human subjects: Consent was obtained or waived by all participants in this study. IRB Committee, King Fahad Medical City issued approval 17-594. I am pleased to inform you that your request for the study titled “Cardiac Tamponade–Associated Dense Deposit Disease: A Case Report and Review of the Literature” was reviewed and approved according to the ICH GCP guidelines. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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