ABSTRACT: Duchenne muscular dystrophy (DMD) is the most common hereditary neuromuscular disease in children. It is an X-linked hereditary dystrophinopathy due to the absence of dystrophin. Its onset is often in early childhood and presents with proximal distribution of weakness and a progressive course. Cardiac involvement in DMD is common, and its onset is usually after the age of 10 years. The most common cardiac manifestations are a dilated cardiomyopathy and cardiac arrhythmia. However, pericardial effusion with cardiac tamponade is a very rare cardiac complication of DMD. We report a boy with DMD who initially presented with progressive dyspnea and an enlarged cardiac silhouette on chest radiography who subsequently developed a large pericardial effusion with cardiac tamponade. Early recognition of pericardial effusion with cardiac tamponade is important for institution appropriate therapy.

Muscle Nerve **40:** 476–480, 2009

PERICARDIAL EFFUSION WITH CARDIAC TAMPONADE AS A CARDIAC MANIFESTATION OF DUCHENNE MUSCULAR DYSTROPHY

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Accepted 9 February 2009

Duchenne muscular dystrophy (DMD) is the most common hereditary neuromuscular disease in children. Cardiac involvement in DMD is common. Its onset is usually after the age of 10 years and increases in incidence with age. It affects almost all patients beyond the age of 18.[11] They are usually free of cardiac symptoms (fatigue and reduced exercise tolerance), because they use a wheelchair full time and do not exercise vigorously.[1] Only a minority of patients in the advanced stage of DMD suffer severe cardiac manifestations. The most common cardiac manifestations are dilated cardiomyopathy and cardiac arrhythmia.[1] However, pericardial effusion with cardiac tamponade is a very rare cardiac complication of DMD.[12] We report a boy with DMD who developed a large pericardial effusion with cardiac tamponade, a previously rarely recognized complication of DMD.

Abbreviations: DMD: Duchenne muscular dystrophy; EKG: electrocardiogram; PSVT: paroxysmal supraventricular tachycardia

Key words: pericardial effusion; cardiac tamponade; Duchenne muscular dystrophy

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Published online 21 July 2009 in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/mus.21346

CASE REPORT

A 14-year-old boy with a history of DMD presented with worsening shortness of breath and dyspnea over 5 days. DMD was diagnosed by histological examination at the age of 5 years with the initial presentation of progressive proximal muscle weakness of the legs and pelvis. He became wheelchair-dependent at the age of 9 years and was bedridden since the age of 12 years. The last documented echocardiogram was reported about 1 year previously and showed no dilated cardiomyopathy, but the ejection fraction was decreased (49%). There was also no history of rapid heart rates in the past. He had a history of recurrent pneumonia in the past 2 years.

Approximately 5 days prior to admission, he developed paroxysmal dyspnea. No history of recent viral infection, chest pain, or fever had occurred, but

he had experienced a dry cough. Symptomatic drugs were prescribed at a local hospital. The patient did not improve and returned 4 days later to the same hospital. There, a chest x-ray revealed an enlarged cardiac silhouette and right pleural effusion (Fig. 1). Due to progressive dyspnea and an enlarged cardiac silhouette on chest radiography, acute heart failure secondary to dilated cardiomyopathy was suspected.

On arrival at our hospital he became increasingly tachycardic (sinus tachycardia, heart rate 110 beats/min) and hypotensive (88/40 mmHg). He required high levels of oxygen supplementation in addition to inotropic support (milrinone). On physical examination, heart sounds were distant. Laboratory examination revealed all values within normal limits, except a plasma creatine kinase of 2533 U/L. An electrocardiogram (EKG) showed a ventricular rate of 111 beats/min, normal PR/QRS/QTc intervals, and low voltages in all leads except high right precordial R-amplitudes. No significant pulsus paradoxus was apparent during bedside clinical examination (maximal inspiratory decline in peak systolic pressure of 6 mmHg). An echocardiogram obtained shortly after admission demonstrated a large circumferential pericardial effusion with collapse of the right atrium and ventricle during diastole suggestive of early cardiac tamponade physiology (Fig. 2). Moderate global left ventricular hypokinesis and left atrial and ventricular dilatation were also apparent. The ejection fraction was 36%. Pericardial effusion with cardiac tamponade and dilated cardiomyopathy were the impression. The patient underwent emergency pericardiocentesis via a subxyphoid approach under echocardiographic guidance. Approximately 300 ml of yellowish fluid was drained followed by placement of a pigtail catheter. Hemodynamics improved soon after pericardiocentesis with partial resolution of tachycardia and dyspnea. The pericardial fluid was examined, and it showed a pH of 8.3, 1,425 cells/μl of red blood cells, 86 cells/μl (76% lymphocyte) of white blood cells, total protein level of 2.9 g/dL, and glucose level of 118 mg/dL. Pericardial fluid bacterial, viral and tuberculosis cultures showed no organisms, and cytology showed no malignant cells. The pericardial drain was removed on day 14 after admission.

Two days after removal of the pericardial drain, a sudden episode of tachyarrhythmia (up to 200 beats/min) with hypotension (systolic arterial pressure fell from 110 to 85 mmHg) was noted. Hypovolemia, pneumothorax, and metabolic derangement were excluded by laboratory, x-ray, and clinical findings. An EKG showed paroxysmal supraventricular tachycardia (PSVT). The PSVT was ineffectively treated with adenosine followed by amiodarone. A follow-up echocardiogram showed a persistent large circumferential pericardial effusion without collapse of the right atrium and ventricle. Emergent pericardiocentesis with replacement of the pigtail catheter was performed, and he was weaned off amiodarone. He received surgical pericardiotomy on day 28 due to persistent large pericardial effusion on follow-up echocardiograms between day 16 to day 28 after admission. Finally, he received digoxin, captopril, and furosemide at discharge.

DISCUSSION

DMD is the most common hereditary neuromuscular disease in children. It results from a mutation in the gene located at Xp21, which encodes dystrophin, a sarcolemmal protein abundant in skeletal and cardiac muscle cells. Dystrophin plays an important role in the maintenance of the cellular architecture and permits signal transduction between the cytoskeleton and the extracellular matrix. Dystrophin is typically absent in DMD.[1] DMD is very often complicated by cardiac involvement that usually develops after the age of 10 years together with restrictive lung disease that will usually require respiratory support. Death secondary to cardiac or respiratory failure typically occurs in the second or third decade of life.[11]

The most common cardiac manifestations are dilated cardiomyopathy and cardiac arrhythmia.[1–4,6,10,11] Cardiac involvement in DMD manifests at varying ages. The cardiomyopathy is usually latent initially without symptoms or overt clinical signs. When all cardiac reserve has been eroded, symptoms and signs of heart failure emerge. However, early manifestations of heart failure often go unrecognized secondary to physical inactivity and a lack of classic signs and symptoms.[1,11] On investigation, dilated cardiomyopathy reveals an increased cardiothoracic ratio on chest x-ray. Echocardiogram shows left ventricular dilatation with normal or thinned walls and reduced ejection fraction.[5] However, classic features of cardiac tamponade are the Beck triad of elevated jugular venous pressure, muffled heart sounds, and hypotension. Classic echocardiographic findings of cardiac tamponade include right atrial and right ventricular diastolic collapse.[7] In our case, it initially presented with progressive dyspnea and an enlarged cardiac silhouette on chest radiography, and acute heart failure secondary to dilated cardiomyopathy was suggested. But physical examination showed muffled heart sounds without obvious pulsus paradoxus. An echocardiogram obtained shortly after

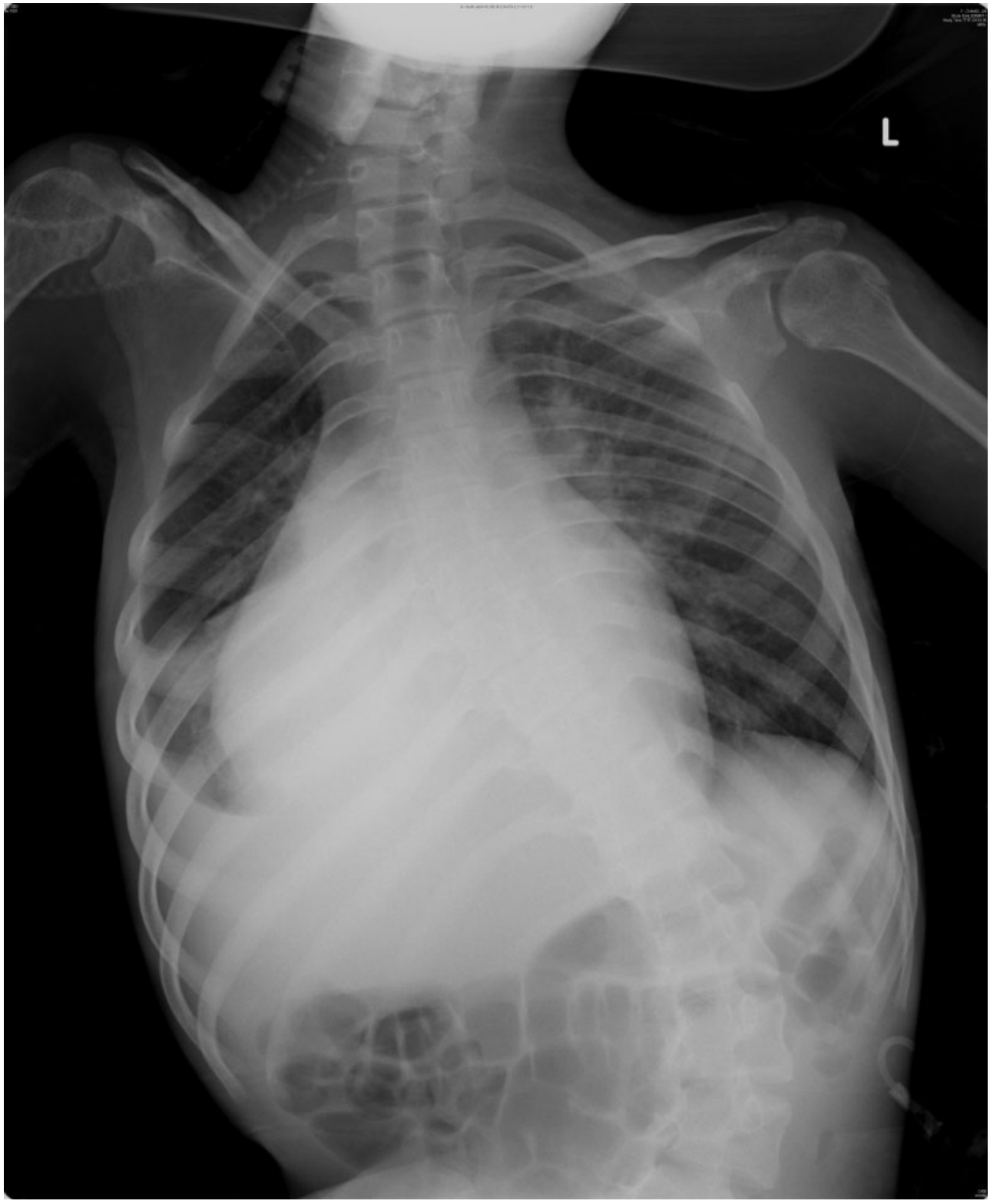

FIGURE 1. Chest x-ray at admission showed an enlarged cardiac silhouette and right pleural effusion.

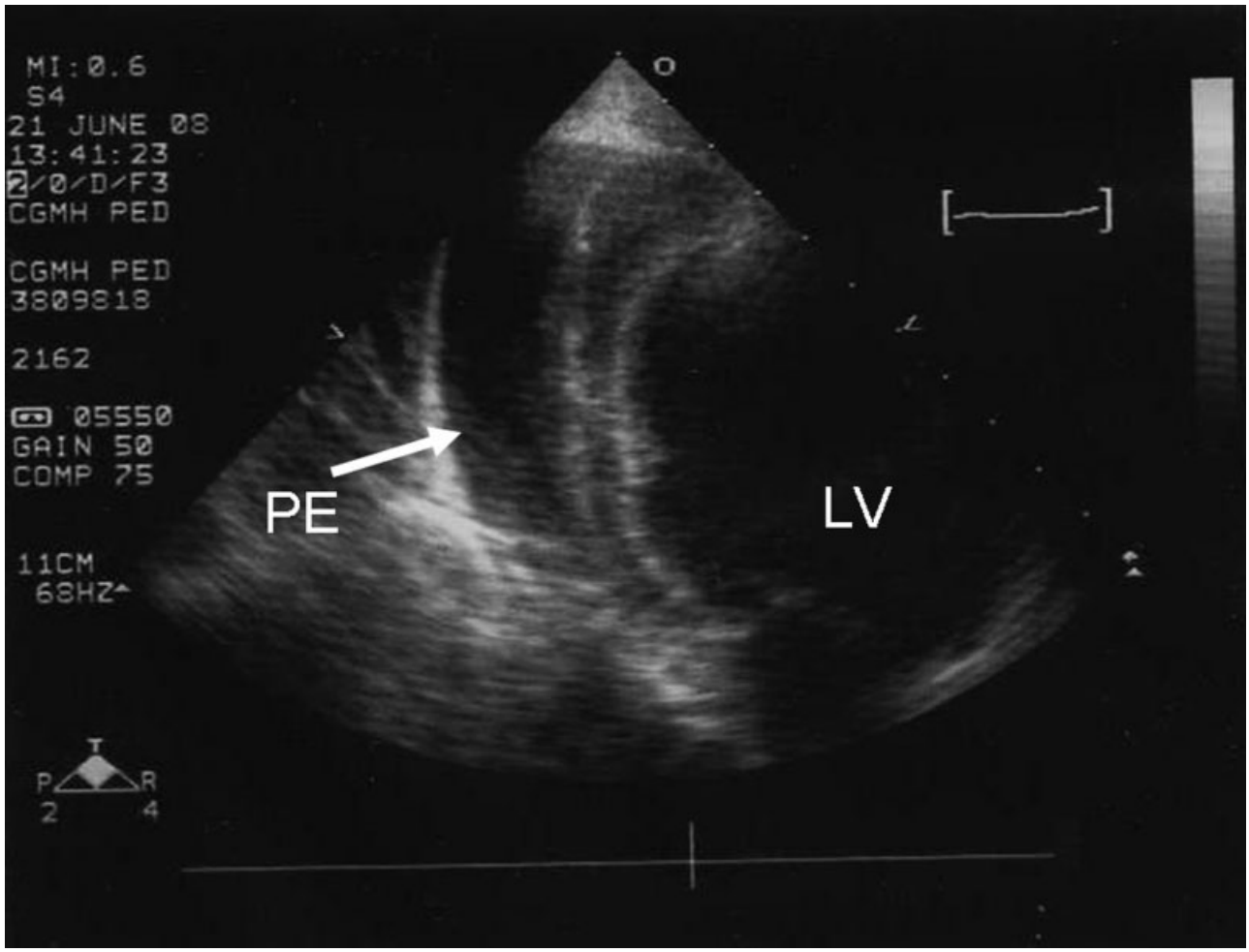

FIGURE 2. An echocardiogram obtained shortly after admission demonstrated a large circumferential pericardial effusion (PE, pericardial effusion, white arrow; LV, left ventricle).

admission demonstrated a large circumferential pericardial effusion with collapse of the right atrium and ventricle during diastole suggestive of early cardiac tamponade physiology. Moderate global left ventricular hypokinesis, left atrial, and ventricular dilatation were also apparent. The ejection fraction was 36%. Pericardial effusion with cardiac tamponade and dilated cardiomyopathy were impressive. However, pericardial effusion with tamponade is a rare presentation of cardiac failure secondary to DMD. The lack of dystrophin and pericardial effusion are not directly linked. To our knowledge, this is the second case of pericardial effusion with cardiac tamponade caused by DMD.[12]

Large pericardial effusions and cardiac tamponade are rare in childhood.[7,9] However, etiologies of pericardial effusions in the pediatric population are poorly characterized. Effusions may be transudative (congestive heart failure, myxedema, nephrotic syndrome), exudative (tuberculosis, spread from empyema), or hemorrhagic (trauma, rupture of aneurysms, malignant effusion). Kühn et al.[9] reviewed 116 children with moderate or large pericardial effusions during a period of 20 years at a tertiary children's hospital. The etiology was neoplastic disease (39%), idiopathic (37%), collagen vascular disease (9%), renal disease (8%), bacterial infection (3%), and human immunodeficiency virus infection (HIV) (2%).[9] Guven et al.[7] reported 10 children with a diagnosis of large pericardial effusion and cardiac tamponade requiring pericardiocentesis and pericardial drainage. The etiology was tuberculosis (30%), malignancy (20%), no identifiable etiology (20%), uremic pericarditis (10%), bacterial pericarditis (10%), and postpericardiotomy syndrome (10%).[7] In our case, pericardial fluid bacterial, viral, and tuberculosis cultures showed no organisms, and cytology showed no malignant cells. Renal function

was within normal limits. The pericardial fluid chemistries indicated a transudate. Presumably, the cause of pericardial effusion with cardiac tamponade in our case was related to congestive heart failure subsequent to dilated cardiomyopathy, the cardiac complication of DMD.

Once the diagnosis of pericardial effusion has been made, it is important to determine whether the effusion is creating significant hemodynamic compromise.[7–9] Asymptomatic patients without hemodynamic compromise, even with large pericardial effusions, do not need to be treated with pericardiocentesis unless there is a need for fluid analysis for diagnostic purposes (e.g., in acute bacterial pericarditis, tuberculosis, and neoplasias). Alternatively, when the diagnosis of cardiac tamponade is made there is a need for emergency drainage of pericardial fluid. Echocardiography-guided percutaneous pericardial puncture and pigtail catheter placement is safe and effective for initial treatment of patients with large pericardial effusion and cardiac tamponade in most cases.[7] The long-term management of symptomatic chronic pericardial effusions provides a greater challenge.[8] Pericardiocentesis with sclerosing agents, radiation therapy, percutaneous, and surgical pericardiotomy and other surgical techniques are particularly efficacious, depending on the underlying cause and the patient's prognosis. In similar cases, if the persistent pericardial effusion resolved at follow-up, we recommend referral to a cardiologist for a pragmatic evaluation for cardiac conditions (e.g., dilated cardiomyopathy and pericardial effusion). Actually, we believe pericardiotomy is a better treatment for recurrent pericardial effusion after subxyphoid drainage.[5]

In conclusion, we stress that this is a rare complication and address the fact that there are many DMD patients with mildly decreased ventricular function at baseline who do not develop effusions. Due to decreased function, this patient should have had more consistent cardiac follow-up, and the standard of care at this point would be to have the child on an ACE-inhibitor or beta-blocker or both. This case also highlights the need for clinicians to recognize that pericardial effusion with cardiac tamponade can occur in DMD. Early recognition of pericardial effusion with cardiac tamponade is important to institute appropriate therapy. Thus, pericardial effusion with cardiac tamponade must be considered in the differential diagnosis in the presentation of cardiac failure secondary to DMD.

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