Korean Journal of Pediatrics Vol. 49, No. 8, 2006

□ Case Report □

A case of constrictive pericarditis presenting with protein-losing enteropathy

**Jeong Mi Hong, M.D.*, Jae Young Lee, M.D., Soo Jin Kim, M.D.
Gi Young Jang, M.D. and Woo Sup Shim, M.D.**

Department of Pediatrics, College of Medicine, Kyunghee University, Seoul,
Department of Pediatric Cardiology, Sejong Heart Institute, Sejong General Hospital, Bucheon, Korea*

Constrictive pericarditis represents a rare cause of protein-losing enteropathy in children. Reported is an 11-year-old girl with protein-losing enteropathy (PLE) as the principal manifestations of constrictive pericarditis. After total pericardiectomy, symptoms and signs of PLE disappeared. Doppler echocardiography including tissue Doppler imaging is a useful noninvasive initial diagnostic tool for differential diagnosis of diastolic heart failure. **(Korean J Pediatr 2006;49:898-901)**

Key Words : Constrictive pericarditis, Protein-losing enteropathy, Doppler echocardiography, Children

Introduction

Protein losing enteropathy (PLE), uncommon in children, can be primary or result from various disease states as a consequence of either abnormal protein leakage across the gut mucosa or diminished protein uptake by intestinal lymphatics. Constrictive pericarditis (CP) is also rare in children and represents the end stage of an inflammatory process involving the pericardium caused by idiopathic cause, infection, post-surgery or radiation injury. The end result is a fibrotic, thickened, and adherent pericardium, which restricts diastolic filling of the heart.

Since Davidson et al.[1] first identified the association of PLE with heart disease in 1961, other authors have reported enteric protein loss in patients with structural heart disease, constrictive pericarditis, and cardiomyopathy[2-4]. However, PLE as the principal manifestations of CP is rare in children. Here, we described a patient with PLE and CP, and discussed the diagnostic issues of CP in comparison to restrictive cardiomyopathy.

접수 : 2006년 2월 24일, 승인 : 2006년 5월 12일
책임저자 : 이재영, 부천세종병원 소아심장과
Correspondence : Jae Young Lee, M.D.
Tel : 032)340-1123 Fax : 032)340-1236
E-mail : dire7613@chollian.net

Case Report

An 11-year-old girl was transferred to our hospital from China. She had been suffering from dyspnea on exertion, generalized edema, abdominal distension, and chronic diarrhea for 4 years. She was diagnosed as having pulmonary tuberculosis and took anti-tuberculous medications four years ago. Then a few months after the diagnosis of tuberculosis, generalized edema and dyspnea developed. Without definitive diagnosis in China, diuretics were added to the treatment regimen, but the symptoms aggravated.

On admission, she looked chronically ill and could not walk well. Her blood pressure was 100/70 mmHg with a pulse rate of 90 beats/min. Jugular veins were distended and were pulsating. The chest examination showed mild intercostal retraction and intermittent crackles in the both lower lung fields. Heart beats were regular without significant murmur. Her abdomen was severely distended and showed fluid wave and shifting dullness. Pitting edema was noticed in both lower extremities.

The chest radiograph showed bilateral pleural effusion and bilaterally elevated diaphragm but normal heart contour without pericardial calcification. An electrocardiogram revealed generalized low voltages in the limb leads and nonspecific T-wave changes. Laboratory findings indicated remarkable hypoproteinemia (total serum protein 3.7 g/dL, serum albumin 2.1 g/dL). The peripheral blood white blood

cell count was 7,540/mm^2 with a significant lymphocytopenia (9.8%). Stool alpha-1-antitrypsin concentration was 236 mg/dL (normal range <54 mg/dL), suggesting PLE.

Transthoracic echocardiogram demonstrated no intracardiac structural abnormalities, except for mild dilatations of both atria. Both ventricular systolic functions were within normal limits. The inferior vena cava and hepatic veins were dilated. Pericardial thickening was not definite. Transmitral Doppler echocardiography demonstrated an increased ratio of early (E) to late (A) filling velocities (E/A 2.43) with exaggerated normal respiratory variation patterns (>25 %) of E wave velocities; a significant decrease in the peak velocity of E wave during inspiration (0.98 m/sec during expiration to 0.64 m/s during inspiration) (Fig. 1). The peak diastolic flow velocity of the pulmonary veins also decreased during inspiration. Also we could find a reciprocal change of respiratory variation in the peak velocity of early filling of tricuspid inflow, and expiratory augmentation of diastolic flow reversal in the hepatic vein flow pattern. The tissue Doppler echocardiography showed normal mitral annular velocity patterns (Fig. 2).

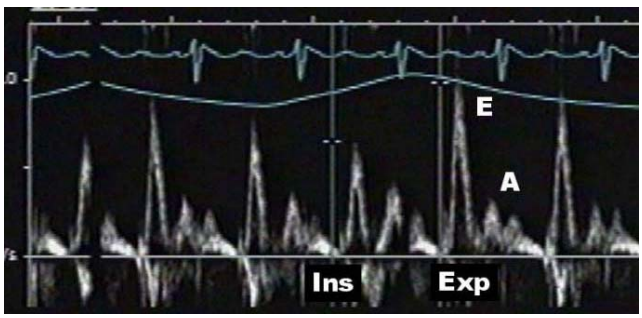

Fig. 1. Transmitral pulsed Doppler indicating short early filling (E) deceleration time and increased ratio of early to late filling (A) velocities with exaggerated respiratory variability. The INS and EXP indicate inspiration and expiration, respectively.

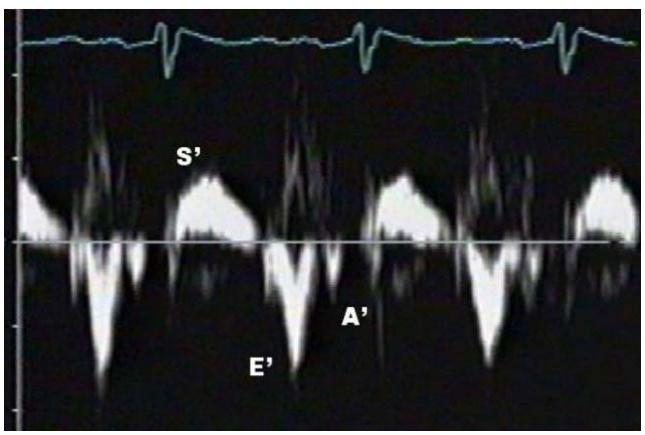

Fig. 2. Tissue Doppler velocities obtained from the lateral wall of the left ventricle. Early diastolic myocardial velocity (E′) is normal (30 cm/s). The S′ and A′ indicate systolic and late diastolic myocardial velocity, respectively.

Computed tomography showed suspicious pericardial thickening without calcification, minimal pericardial effusion, and pleural effusion.

On cardiac catheterization, the right atrial pressure was 28/22 mmHg, right ventricular pressure 37/24 mmHg, pulmonary capillary wedge pressure 38/28 mmHg, and left ventricular pressure 91/28 mmHg. The aortic pressure tracing showed a typical paradoxic pulse pattern. The characteristic dip and plateau pattern in the ventricular pressure curves was noticed.

The patient underwent surgical exploration and radical pericardiectomy. Intraoperative findings demonstrated thickened and inflamed pericardium. The pathologic finding showed dense fibrosis with fibrin deposition but no evidence of granuloma. The staining and culture for acid-fast bacilli was negative. After pericardiectomy, all symptoms disappeared. Total protein and albumin, and lymphocyte fractions were normalized. She was discharged from hospital without any complications on the 12th post-operative day. Follow-up echocardiography done 3 months after the operation showed normal systolic and diastolic functions.

Discussion

PLE is a syndrome characterized by hypoproteinemia, hypoalbuminemia, systemic edema, and diarrhea, caused by excessive loss of serum protein from the gastrointestinal tract, and leads to chronic malabsorption and immunodeficiency. PLE can be primary or secondary to other disorders causing obstruction of lymphatic drainage, such as congestive heart failure and retroperitoneal fibrosis. Supportive treatment has been the major therapy of choice, such as dietary modification, although few therapeutic trials with limited success have been reported[5].

The association of PLE with heart diseases has been reported[1-4]. Recently, PLE in patients with Fontan type palliation for complex congenital heart diseases with significant morbidity and mortality has drawn the attention of many clinicians[6]. The exact mechanism of the development of PLE in heart disease is controversial. It has been postulated that increased venous pressure may inhibit thoracic and intestinal lymphatic drainage and produce small bowel

changes such as lymphangiectasia, resulting in the loss of protein-rich lymph and immunoglobulin into the gastrointestinal tract[7, 8]. Although CP represents a rare cause of PLE and is rare in children, clinical suspicion is crucial because it can be cured surgically.

However, as in this case, the diagnosis of CP remains difficult in the absence of definite pericardial thickening or calcification, which has been considered an essential diagnostic feature of CP, on chest radiography or computed tomography. Actually, around 20% of patients with CP have normal pericardial thickness in computed tomography and pathologic examination[9, 10]. Moreover it is often mimicked by or can co-exist with restrictive cardiomyopathy, in which no curative treatment exists.

Invasive cardiac catheterization has been used to yield findings that are classic for CP in comparison to restrictive cardiomypathy. The traditional hemodynamic criteria for constrictive pericarditis differentiated from restrictive cardiomyopathy have included that left ventricular end-diastolic pressure usually does not exceed right ventricular end-diastolic pressure by more than 5 mmHg, right ventricular systolic pressure usually does not exceed 50 mmHg and right ventricular diastolic pressure is more than one-third of right ventricular systolic pressure in constrictive pericarditis[9, 11]. Vaitkus et al[11] found that, of the 70 patients meeting all three criteria, 91% had constrictive pericarditis rather than restrictive cardiomyopathy.

Doppler echocardiographic findings in the flow through the atrioventricular valves, and systemic and pulmonary veins may help to differentiate CP from restrictive cardiomyopathy. Exaggerated normal respiratory variation of the mitral early filling velocity and the reciprocal change of tricuspid early filling velocity[12], augmented diastolic flow reversal (≥25% of forward flow) in the central venous flow velocities[13], and the pulmonary venous systolic/diastolic flow velocity ratio <0.65 and the peak diastolic flow velocity fall ≥40% during inspiration[14] are useful signs in distinguishing CP from restrictive cardiomyopathy. However, these techniques may have limitations in the presence of lung disease and altered loading conditions that may mask these findings[15, 16].

Recently, a new echocardiographic modality called Doppler tissue imaging allows direct assessment of instantaneous changes in myocardial velocities throughout the cardiac cycle. Because the rate of left ventricular relaxation is affected by primary myocardial disease but not by CP, direct determination of myocardial wall expansion velocities may be useful in differentiating restrictive cardiomyopathy from CP. Several studies showed that early diastolic mitral annular velocities recorded by tissue doppler echocardiography decreased in patients with restrictive cardiomyopathy, but were relatively normal or even accentuated in those who had constrictive pericarditis[17, 18].

Therefore, a single approach to diagnose CP is not enough. After fully understanding the pathophysiology of this disease, judicious application of non-invasive and invasive methods would be more helpful in diagnosis of this disease. Tissue Doppler imaging is a useful noninvasive initial diagnostic tool for differential diagnosis of diastolic heart failure. Moreover, when clinical, echocardiographic, or invasive hemodynamic features indicate constriction in patients with heart failure, pericardiectomy should not be denied on the basis of normal thickness as demonstrated by noninvasive imaging.

한 글 요 약

단백 소실성 장병증을 동반한 교착성 심낭염 1례

경희대학교 의과대학 소아과학교실*, 부천세종병원 소아과

홍정미* · 이재영 · 김수진 · 장기영 · 심우섭

소아에서 교착성 심낭염은 매우 드문 질환으로 이에 의하여 단백 소실성 장병증이 동반되는 경우는 더욱 드물다. 저자들은 교착성 심낭염의 주요 증상의 하나로 단백 소실성 장병증을 보인 여아 1례를 경험하였기에 문헌고찰과 함께 보고하는 바이다.

References

1) Davidson JD, Waldmann TA, Goodman DS, Gordon RS. Protein-losing gastroenteropathy in congestive heart failure. Lancet 1961;1:899-902.
2) Jeejeebhoy KN. Cause of hypoalbuminemia in patients with gastrointestinal and cardiac disease. Lancet 1962;1:343-8.
3) Petersen VP, Mastrup J. Protein-losing enteropathy in constrictive pericarditis. Acta Med Scand 1963;173:401-3.
4) Valberg LS, Corbett WEN, McCorriston JR. Excessive loss of plasma protein into the gastrointestinal tract associated with primary myocardial disease. Am J Med 1965;39:668-73.
5) Takahashi H, Imai K. What are the objectives of treatment for intestinal lymphangiectasia? J Gastroenterol 2001;36:137-8.
6) Mertens L, Hagler DJ, Sauer U, Somerville J, Gewillig M. Protein-losing enteropathy after the Fontan operation : an international multicenter study. PLE study group. J Thorac

Cardiovasc Surg 1998;115:1063-73.
7) Nelson DL, Blaese RM, Strober W, Bruce R, Waldmann TA. Constrictive pericarditis, intestinal lymphangiectasia, and reversible immunologic deficiency. J Pediatr 1975;86:548-54.
8) Koch A, Hofbeck M, Feistel H, Buheitel G, Singer H. Circumscribed intestinal protein loss with deficiency in CD4+ lymphocytes after the Fontan procedure. Eur J Pediatr 1999;158:847-50.
9) Fowler NO. Constrictive pericarditis : its history and current status. Clin Cardiol 1995;18:341-50.
10) Talreja DR, Edward WD, Danielson GK, Schaff HV. Constrictive pericarditis in 26 patients with histologically normal pericardial thickness. Circulation 2003;108:1852-57.
11) Vaitkus PT, Kussmaul WG. Constrictive pericarditis versus restrictive cardiomyopathy : a reappraisal and update of diagnostic criteria. Am Heart J 1991;122:1431-41.
12) Hatle LK, Appleton CP, Popp RL. Differentiation of constrictive pericarditisve and restrictive cardiomyopathy by Doppler echocardiography. Circulation 1989;79:357-70.
13) Oh JK, Hatle LK, Seward JB, Danielson GK, Schaff HV, Reeder GS, et al. Diagnostic role of Doppler echocardiography in constrictive pericarditis. J Am Coll Cardiol 1994;23:154-62.
14) Klein AL, Cohen GI, Pietrolungo JF, White RD, Bailey A, Pearce GL, Stewart WJ, Salcedo EE. Differentiation of constrictive pericarditis from restrictive cardiomyopathy by Doppler transesophageal echocardiographic measurements of respiratory variations in pulmonary venous flow. J Am Coll Cardiol 1993;22:1935-43.
15) Oh JK, Tajik AJ, Appleton CP, Hatle LK, Nishimura RA, Seward JB. Preload reduction to unmask the characteristic Doppler features of constrictive pericarditis : a new observation. Circulation 1997;95:796-99.
16) Shabetai R. Controversial issues in restrictive cardiomyopathy. Postgrad Med J 1992;68 suppl 1:47-51.
17) Garcia MJ, Rodriguez L, Ares M, Griffin BP, Thomas JD, Klein AL. Differentiation of constrictive pericarditis from restrictive cardiomyopathy : assessment of left ventricular diastolic velocities in longitudinal axis by Doppler tissue imaging. J Am Coll Cardiol 1996;27:108-14.
18) Ha JW, Ommen SR, Tajik AJ, Barnes ME, Ammash NM, Gertz MA, Seward JB, Oh JK. Differentiation of constrictive pericarditis from restrictive cardiomyopathy using mitral annular velocity by tissue Doppler echocardiography. Am J Cardiol 2004;94:316-9.