Restrictive cardiomyopathy in a patient with primary hyperoxaluria type II

**Summary** This is the first report of a cardiac manifestation of a primary hyperoxaluria type II (PH II) with the hemodynamic characteristics of a severe restrictive cardiomyopathy. PH II is a rare inherited metabolic disease characterized by a deficiency of D-glycerate dehydrogenase, which has also glyoxylate reductase activity. This defect causes an accumulation of hydroxypyruvate the precursor of oxalate. The renal excretion of oxalate is impaired causing a deposition of oxalate mainly in the kidneys. To date, less than fifty cases have been reported. Systemic oxalosis in PH II is an occasional finding; thus far, myocardial oxalosis due to PH II has never been reported. Described is the case of a 41 year old male with renal failure and severe neuropathy of unknown cause, who underwent endomyocardial biopsy under the suspicion of cardiac amyloidosis. Echocardiography and cardiac catheterization showed a severe restrictive cardiomyopathy; endomyocardial biopsy established the diagnosis of oxalosis. Plasma oxalate levels were markedly increased, therefore a liver biopsy was performed. Immunoreactivity for D-glycerate dehydrogenase/glyoxylate reductase was absent and activity of the enzyme was <5% of normal. In summary, these findings established the diagnosis of a restrictive cardiomyopathy due to PH II.

**Key words** Cardiomyopathy – heart failure – endomyocardial biopsy – hyperoxaluria – storage disease

**Introduction**

Restrictive cardiomyopathy is defined as a heart-muscle disease that results in an impaired ventricular filling caused usually from an increased stiffness of the myocardium. Due to the increased stiffness there is a disproportional pressure rise within the ventricle with only small increases in volume. Because the disease can affect either or both ventricles, it may cause signs and symptoms of left or right heart failure. A restrictive cardiomyopathy may result from different local and systemic disorders. They are classified according to the cause in myocardial and endomyocardial (e.g., endomyocardial fibrosis, which is endemic in parts of India, Africa, South America, and Asia) affections [9]. Diseases affecting the myocardium are differentiated into noninfiltrative (e.g., idiopathic cardiomyopathy), infiltrative (e.g., amyloidosis, sarcoidosis), and storage diseases (e.g., hemochromatosis). A very frequent cause of a restrictive cardiomyopathy is a primary or secondary amyloidosis [9]. Besides these diseases, only few metabolic diseases have been identified on a molecular level to cause restrictive cardiomyopathy.
Primary hyperoxalurias are rare inherited metabolic diseases. They are differentiated into two types. Both types lead to end-stage renal failure and have due to their systemic oxalate deposits a deadly course. Primary hyperoxaluria type I (PH I) is more common than type II (PH II) and is characterized by a lack or defect of the liver enzyme alanine-glyoxylate aminotransferase (AGT) (Fig. 1), which is located inside the peroxisomes [3]. PH II was first described in 1968 [18]. As of 1997, only 24 cases had been reported [10], but its prevalence is likely underestimated [8]. PH II is characterized by a deficiency of the cytosolic enzyme D-glycerate dehydrogenase and glyoxylate reductase (D-GDH/GR) (Fig. 1), which is found in liver cells and leukocytes. The deficiency of glyoxylate reductase allows production of oxalate from glyoxylate by lactate dehydrogenase. The clinical course is usually more severe in PH I [14]. Systemic oxalosis in PH II is reported casually. Marangella reported a case with renal failure and systemic calcium oxalate deposits in bone and retina [12]. Thus far, to our knowledge, restrictive cardiomyopathy in PH II has not been reported, but myocardial affection has been reported in some cases of PH I [4–6, 11, 13, 16, 17]. The present case report is the first report on an impressive case of restrictive cardiomyopathy in a patient with primary hyperoxaluria type II.

Case report

A 41 year-old caucasean male was sent for further cardiac evaluation because of a decreased left ventricular ejection fraction in an out-patient echocardiography. In his cardiac history he reported the first appearance of dyspnea on exertion, pleural effusion and ankle edema in 1998. In 2002 he experienced for the first time exertional angina pectoris. On admission he had dyspnea NYHA grade III and angina pectoris CCS class II. His further medical history revealed nephrolithiasis since he was 12 years old. In 1998, he had nephrectomy of his right kidney due to nephrocalcinosis. On admission he was in end-stage renal failure and had been depending on dialysis for six years. Furthermore he reported neurological symptoms with muscle atrophy as well as an absence of deep tendon reflexes of the legs and peripheral paraesthesia of both lower legs. Echocardiography performed prior to catheterization showed a cardiomyopathy with a decreased ejection fraction of 25–30%. The myocardium was markedly echo-dense and therefore cardiac amyloidosis was suspected. However, two rectal biopsies had been negative for amyloid.

On physical examination, a patient in a reduced general condition was seen. The heart rate was 100 beats per minute, on cardiac auscultation there was a fixed split second heart sound and a II/VI holosystolic murmur heard loudest over the tricuspid valve area. Blood pressure was 130/90 mmHg. The auscultation of the lung was without any abnormalities. The liver was enlarged and palpable 3 finger breadths below the costal margin and he had mild ankle edemas. Laboratory analysis showed normal values for sodium, potassium, urea, leucocytes, thrombocytes and clotting times. Creatinine was elevated with 355 µmol/l. The patient was anemic with a hemoglobin of 7.8 mmol/l.

The ECG showed sinus rhythm with a rate of 100 beats per minute. There was a right axis deviation, the PQ time was 180 ms, QRS width was 100 ms and a terminal negative T-wave in V6 was seen.

Transthoracic echocardiography revealed a severely hypertrophied (intraventricular septum 17 mm, left