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CASE REPORT

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A patient with primary hyperoxaluria who developed excessive pericardial effusion despite intensive dialysis

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Abstract

Primary hyperoxaluria type 1 (PH type 1) is a hereditary disorder with excessive production of oxalate caused by deficient liver specific enzyme alanine-glyoxylate aminotransferase (AGT). Increased oxalate production leads to calcium oxalate deposition in different organs and tissues, such as kidney, heart, nervous system, skin, bone and bone marrow. Early diagnosis is essential to prevent complications. Family history, urine oxalate assesment, oxalaemia, determination of oxalate deposits in tissues and genetic analysis are beneficial for diagnosis. Treatment should be started at early stages of the disease in order to decrease urinary saturation of calcium oxalate. High fluid intake, urinary crystallisation inhibitors and pyridoxine may be used. In chronic kidney failure patients renal replacement therapies are necessary, early transplantation is mandatory. We present a 30 year old man with PH type 1 who admitted with severe pericardial effusion, despite the fact that he was maintained both peritoneal dialysis and frequent hemodialysis.

Keywords: Primary hyperoxaluria type 1, chronic kidney failure, severe pericardial effusion

Introduction

Primary hyperoxaluria (PH) type I is a genetic disorder of glyoxylate metabolism and the most common type of PH. Excessive oxalate production causes calcium oxalate salt deposition in different organs, including kidney. Although it may be thought as a causative factor for urolithiasis and chronic kidney failure (CKF) in children, clinicians may miss the diagnosis of PH because of the rarity of new onset in adulthood [1]. We present a case of PH type 1 who admitted with severe pericardial effusion, despite the fact that he was maintained both daily peritoneal dialysis (PD) and frequent hemodialysis (HD).

Case presentation

A 30 year- old man is on PD for 4 years because of CKF due to nephrolithiasis as underlying etiology. He was admitted to Nephrology Clinic, complaining of progressive fatigue, vomiting, anorexia and arthralgia. On admission, physical examination findings were pallor, hypotension (90/50 mmHg), cachexia and decreased respiratory sounds at bases of the lungs. His clinical and laboratory parameters were compatible with malnutrition-inflammation-atherosclerosis (MIA) syndrome with hypoalbuminemia (1,1 mg/dl), elevated inflammation markers such as Erythrocyte Sedimantation Rate, CRP and accelerated atherosclerosis (Table 1). In his medical history, there was diagnosis of bilateral nephrocalcinosis, left nephrolithiasis at the age of 21, and reccurrent surgical treatment. However, no pathological evaluation of the material was performed. Because of the clinical deterioration, he was hospitalized and HD was added to PD. As he had bilateral nephrocalcinosis and kidney failure PH was considered suspicious as an etiologic factor. Bone marrow biopsy was performed and revealed oxalic acid crystals (Figure). Additionally, genetic analysis proved the PH type 1. Echocardiography was normal in that time of period. Because of the poor health condition, he had long periods of hospital care. During a HD session palpitatition, chest pain, dyspnea and hypotension occured. Sinusal tachycardia was observed on electrocardiagram, echocardiography revealed diffuse pericardial effusion in the pattern of fibrinous web. He underwent urgent pericardiosynthesis and 500 ml effusion fluid and fibrin clots in pericardial space were removed. After the intervention his complaints regressed. On the

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cytopathological evaluation of pericardial effusion fluid, there was oxalic acid crystals in addition to blood cells. Both daily PD and frequent HD could not prevent the progression of pericardial effusion and systemic oxalosis. He died because of clinical deterioration, while waiting for liver and kidney transplantation.

Table 1. Pathological laboratory findings

	Result	Normal range
BUN (mg/dl)	64	8.9-20.6
Creatinin (mg/dl)	8.52	0.72-1.25
Total Protein (g/dl)	4.2	6.4-8.3
Albumin (g/dl)	1.1	3.5-5
Alkaline phosphatase (U/L)	361	40-150
Alanine aminotransferase (U/L)	46	5-34
Calcium (mg/dl)	9.4	8.4-10.2
Phosphorus (mg/dl)	3.6	2.3-4.7
Hemoglobin (g/dl)	7.8	13.6-17.2
Hematocrit (%)	24.6	39.5-50.3
Ferritin (IU)	2571	5-148
Erythrocyte Sedimantation Rate (mm/h)	56	0-20
CRP (IU)	1	0-0.35

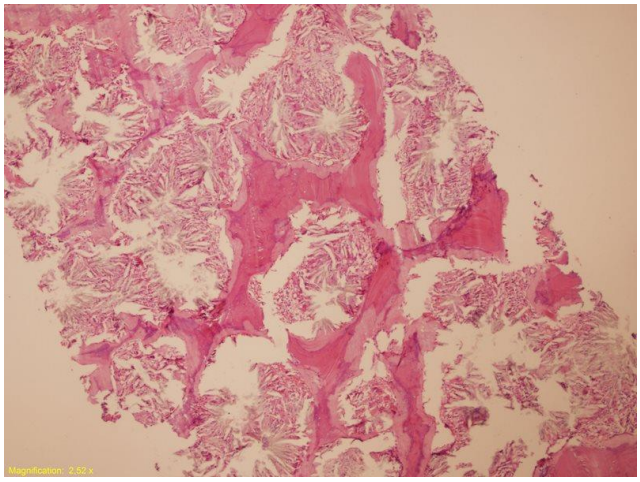

Fıgure. Bone marrow trephine biopsy showing radially arranged aggregates of grey crystals. H&E x100)

Discussion

Primary hyperoxaluria (PH) type 1 is a rare autosomal-recessive disease caused by deficient, mistarget or absent activity of the liver specific enzyme alanine-glyoxylate aminotransferase (AGT) and which is the most common type of PH (80%) [2]. Glyoxalate does not convert glycine, consequently this situation leads to an increase in the glyoxlate pool and later overproduction of oxalate. Oxalate is mainly excreated by the kidneys and increased urinary oxalate excretion results in urinary calcium oxalate supersaturation, which leads to crystal aggregation within the renal interstitium and renal tubule cells [3]. When the kidney functions are normal, blood oxalate levels are generally in normal range (<6 µmol/l), as the GFR<30-40 ml/min/1.73 m^2, plasma oxalate levels increases (>30 µmol/l).

The median age at initial symptoms is 5 to 6 years and CKF develops between 25-40 year-old in half of patients with PH type 1 and unfortunately, in developing countries the mortality rate may reach 100 % in the absence of adequate treatment [4,5]. Along with progressive decline of glomerular filtration rate (GFR< 30 ml/min/1.73 m^2) oxalate deposition occurs in many tissues and organs, such as heart (cardiomyopathy, conduction defects), nerveous system (dysesthesia, mononeuritis multiplex, optic atropy), muscles (myopathy) joints (arthropathy), skin (subcutaneous calcinotic nodules, masses, ulcerating), bone and bone marrow (pain, erythropoetin-resistant anemia and spontaneous fracture), blood vessels (vasospasm, livedo reticularis, vascular calcification), thyroid (hypothyroidism) and retina (crystaline macolopathy), leading to systemic involvement named oxalosis. Oxalosis is responsible for poor quality of life and severe complications [6-10]. Current information is limited to case reports and small case series, which are restricted to cardiomyopathy, valvular disease and conduction abnormalities [9,11]. Although it is known that cardiac function impairment may be observed due to oxalate accumulation, it is not reported presentation with severe pericardial effusion in a patient whom ECO was normal short time ago. He was maintained on both frequent HD and daily PD as his clinical situation assummed as MİA and even this could not prevent development of severe pericardial effusion and progression of oxalosis.

Early diagnosis is crucial in PH type 1 patients to prevent both CKF and other systemic complications. In addition to a detailed family history, oxaluria tests are essential in clinically suspected cases. Presence of monohydrate calcium oxalate crystals in urine sediment, glycolate in 24-hour urine, oxalaemia and determination of oxalate deposits in tissues by biopsies may also be beneficial for diagnosis. CT is useful to determine tissue oxalate depositions and calcifications. For comfirmation of the diagnosis and determination of the variant mutations, genetic analysis may be necessary. If no mutation has been found, the diagnosis can be made by a liver biopsy demonstrating absent or significantly reduced ATG activity [1,10,12].

Treatment should be started at early stages of the disease in order to decrease urinary saturation of calcium oxalate. For this aim, fluid intake should be increased (urinary output>3 L/day/1.73 m^2) and urinary crystallisation inhibitors such as potassium citrate, orthophosphate and magnesium may be used [10]. Pyridoxine therapy is useful and it reduces oxalate production effectively. All this general precautions are effective before established CKF, but in CKF patients renal replacement therapies should be considered. Oxalate is reasonably well-removed by dialysis, even so, the amount removed in a standard 3 day per week HD treatment can not keep up with production rates, in part because oxalate is only removed from the blood compartment, and equilibration of plasma oxalate with

extravascular compartments like bone is slower [13]. Thus, more frequent HD treatment are more efficient than longer but less frequent HD regimens [14]. Although dialysis modalities are generally inadequate for the clearence of oxalate load, in a study showed that combining HD and PD prior to transplantation facilitates the mobilization of oxalic depositions with decreased oxalate and favors better short- and long term kidney graft survival (15). Liver transplantation is the only curative intervation for PH type 1. Preemptive isolated liver transplant may be an option in selective patients with 30 <GFR < 59 ml/min/1.73m^2 has been proposed as curative treatment. Combined liver and kidney tranplantation is recommended in the most patients and isolated kidney transplantation is recommended if there is no other option [10].

In summary, PH type 1 is a rare autosomal recessive disease that may present in adulthood often have a history of only sporadic stone disease, over 50% of these patients present with CKF at the time of diagnosis. Oxalate accumulation in different tissues and organs, impairs quality of life. The physicians must consider PH in any patient with history of nephrocalcinosis and/ or urolithiasis. Early diagnosis and treatment is essential to prevent systemic complications.

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