Recurrent 2,8-DHA Crystalline Nephropathy after Kidney Transplantation due to APRT deficiency

서울성모병원 내과[1], 인천성모병원 신장내과[2], 서울성모병원 신장내과[3]

이승환[1], 음상훈[2], 이한비[3], 윤혜은[2], 양철우[3], *정병하[3]

Adenine phosphoribosyltransferase (APRT) deficiency is a rare autosomal recessive disorder characterized by the absence of APRT activity, resulting in the metabolization of adenine to 2,8-dihydroxyadenine (DHA). DHA may precipitate in tubular lumina and interstitium of the kidneys, which can lead to the progression of ESKD (End Stage Kidney Disease) and has the potential to recur even after kidney transplantation. However, since DHA and oxalate crystals share same microscopic features, diagnosis of DHA nephropathy is often challenging. A 52-year-old woman with a history of well-controlled hypertension presented with elevated serum creatinine levels. The patient mentioned taking herbal medication and multiple NSAIDs. Additionally, her older sister had a history of ESKD at the age of 54. A CT scan of her kidneys showed no evidence of nephrocalcinosis or stones. A kidney biopsy revealed a moderate degree of interstitial inflammation and fibrosis. Based on above findings, she was diagnosed with chronic interstitial nephritis. Despite treatment with steroid, her condition worsened to ESKD. The patient received a kidney transplant from her daughter, but after 11 months, her serum creatinine level rose from 1.18 mg/dl to 2.57 mg/dl. An allograft biopsy was performed, which revealed the presence of interstitial crystal deposition with diffuse intratubular crystal formations. There was no evidence of rejection or calcineurin inhibitor toxicity. Upon conducting a thorough review of the patient's initial kidney biopsy, crystalline nephropathy was identified, which had been previously overlooked. Considering the family history of ESKD, we decided to perform next-generation sequencing. The sequencing results revealed a pathogenic homozygous variant in exon 3 of APRT gene(c.294G>A, p.Trp98Ter), which is responsible for causing APRT deficiency. Consequently, the patient was treated with febuxostat and her kidney function showed significant improvement. DHA nephropathy is an under-recognized disease that can lead to irreversible renal failure. It should be included in the differential diagnosis of crystalline nephropathy to optimize the treatment.

Figure 1. Adenine metabolism pathways and the role of APRT

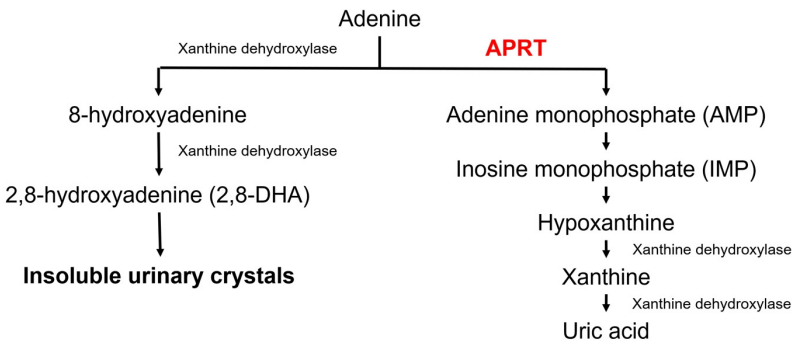

Figure 2. Comparison of crystals between Native and Allograft kidney