CYSTINOSIS AS A CAUSE OF HYPOPHOSPHATEMIC RICKETS: A SINGLE-CENTER EXPERIENCE

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Introduction

Cystinosis is an inherited (autosomal recessive) lysosomal storage disorder characterized by accumulation of cystine crystals in kidney, liver, eyes and brain. Dysfunction of lysosomal membrane protein cystinosin caused by mutation of Cystinosin gene (CTNS) disrupts membrane transport of cystine. Patients can present to pediatric endocrinology clinics with growth retardation and vitamin D resistant rickets particularly in nephropathic infantile form (1-4). Here, we aimed to present genetic and clinical spectrum of 10 patients who have been followed with the diagnosis of cystinosis, a rare cause of hypophosphatemic rickets, in our clinic.

Material and method: The study included 10 patients who have been followed with diagnoses of Fanconi syndrome and/or cystinosis in Pediatric Endocrinology and Metabolism outpatient clinic of Van Yüzüncü Yıl University, Medicine School. Data regarding presenting complaint, history, physical examination findings, anthropometric measurements, age, and laboratory findings were extracted from electronic database. Blood samples were drawn into EDTA tubes from all patients and mutation analyses were performed.

Findings: It was found that age range was 2 and 12 years in patients and age at diagnosis was ranging from 6 to 24 (12,6±5,5) months. Overall 10 patients (4 girls and 6 boys) from 9 families were identified. There was first degree consanguinity between parents in 7 families and there was an affected sibling in 3 families. The epidemiological data, clinical findings and CTNS mutation analysis were shoed in table. Proteinuria of varying degrees and hypophosphatemic rickets were present in all patients at presentation. Renal failure of varying degrees developed in 4 patients during follow-up and peritoneal dialysis was initiated in one of these patients. Metabolic acidosis were detected in eight patients as expected, interestingly in three patients metabolic alkalosis were detected (P1,2,8). In patients with meyabolic alkalosis, c.18-21del4bp mutation were found in P1,2 and p.E227E (c.681 G>A) (Hm) mutation was detected in P8. In one patient, cystine crystals were detected in eyes at presentation. No cystine crystal was detected in patients underwent bone marrow aspiration. In CTNS gene, c18-21del14bp mutation was detected in 4 patients, whereas homozygote p.E227E (c.681 G>A) mutation was detected in 6 patients. These mutations were among those recently identified and should considered as explanatory for the disease. Additionally on follow up, two patients (P1 and P4) were given l-thyroxine due to hypothyroidism development.

Conclusion: In the present study, we aimed to emphasize that patients presented with hypophosphatemic rickets should be evaluated for proximal tubular dysfunction and cystinosis should be considered in such patients, as consanguinity between parents is relatively high in our province. Additionally, we also emphasized that some cystinosis patients can be presented with metabolic alkalosis, therefore physician must be know that metabolic alkalisis is not an exclusion criter of cystinosis

	P_1	P_2	P_3	P_4	P_5	P_6	P_7	P_8	P_9	P_{10}	P_{11}
Age at diagnosis (months)	18	18	24	6	12	11	12	9	9	6	14
Age at last control (year)	5	3	4.5	4.5	4.5	12	13	3.5	3.5	6	1.5
Gender	M	M	F	M	M	M	F	F	M	F	M
Consanguity marriage	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	No	No
Affected siblings	No	No	No	No	No	Yes	Yes	Yes	No	No	No
CTNS mutation	Mut 1	Mut 1	Mut 1	Mut 2	Mut 2	Mut 2	Mut 2	Mut 2	Mut 2	Mut 2	Mut 2
Proximal tubulopathy	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Renal Failure	No	No	No	CRF	No	CRF	CRF	No	No	CRF	No
Complaints at diagnosis	V	FtT	FtT, PU, PD	FtT	PU, PD	FtT	FtT	V	PU, PD	FtT	FtT
Eye involvement	No	Yes	No	No	No	No	No	No	No	No	No
Metabolic acidosis	No	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Metabolic alkalosis	Yes	Yes	No	No	No	No	No	Yes	No	No	No
Electrolyte disturbances	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
BM involvement	No	No	No	No	No	No	No	No	No	No	No
Hypophospatemic Rickets	Var	Var	Var	Var	Var	Var	Var	Var	Var	Var	Var
Hypothyroidism	Var	Yok	Yok	Var	Yok	Yok	Yok	Yok	Yok	Yok	Yok

M: Male; F: Female; Mut 1; c.18-21del4bp; Mut 2: p.E227E (c.681 G>A) (Hm); V: Vomiting; FtT: Failure to thrive; PU: Polyuria, PD: Polydipsia;

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