HYPERCALCEMIA DUE TO SIX NEWLY IDENTIFIED INACTIVATING MUTATIONS IN THE CASR GENE

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Introduction: Heterozygous inactivating mutations that occur in the calcium sensing receptor (CaSR) gene often lead to benign mild to moderate and parathormone (PTH) dependent familial hypocalciuric hypercalcemia (FHH). Neonatal severe hyperparathyroidism is a clinical condition that develops due to homozygous inactivating mutations in the CASR gene and results in severe, life-threatening hypercalcemia. In this study, we aimed to discuss the differences in clinical, genetic, laboratory findings and treatment needs of six cases in which we detected inactivation mutations in the CASR gene in the etiology of hypercalcemia.

Patients and Methods: There were no reports of drug use in six cases referred to the endocrinology polyclinic because of hypercalcemia. In these cases, hypocalciuria was detected and familial hypocalciuric hypercalcemia was considered. Novel mutations were detected in six patients. Parathyroidectomy was performed on the patient with severe hyperparathyroidism in the newborn due to continued hypercalcemia despite intravenous hydration, bisphosphonate and cinacalcet administration Pamidronate disodium was given to two patients for a short time and mild hypercalcemia was observed in their follow-up In the other three cases, there was mild hypercalcemia and no bisphosphonate treatment. The general and clinical characteristics, laboratory and genetic results of the cases are shown in table 1.

Cases	Age at diagnosis	Gender	Ca (mg/dl)	P (mg/dl)	ALP (U/L)	PTH (pg/mL)	25(OH)D3 (ng/mL)	Urine Ca/Cr	Mutation	Treatment
1	7 day	M	24,2	3,6	282	1043	33	0,01	p.N207Kfsx42 (Homozygous)	Bifosfonat, cinacalcet, parathyroidectomy
2	4 month	F	14,6	3,8	187	41	13,6	0,02	p.N867S (Heterozygous	Bifosfonat
3	11 month	F	11	3,9	211	90	33,7	0,15	p.Glu612del (Heterozygous)	Diet
4	22 month	F	11,3	4,4	227	24	23	0,076	p.Leu655pro (Heterozygous)	Diet
5	33 month	F	13,9	3,4	199	60	35,4	0,008	p.Glu612del/ p.Asn90Thr (compaund heterozygous)	Bifosfonat
6	13 year	M	11,7	3,6	308	108	26	0,02	p.602delE (Heterozygous)	Diet

Conclusion: Neonatal severe hyperparathyroidism can lead to life-threatening clinical and laboratory findings. Inactivated homozygous mutations in the CASR gene is resulted, severe hyperparathyroidism in the newborn, and the response to medical treatment may vary according to the mutation type. In our case, the newly identified mutation was clinically severe and parathyroidectomy was performed. Surgery should be performed at experienced centers without delay when medical treatment is ineffective. All of the mutations detected in six cases with familial hypocalciuric hypercalcemia were identified newly. Clinical findings and medical treatment needs of the cases were observed to vary according to the type of mutation.