OUR CASES OF FAMILIAL HYPOCALCIURIC HYPERCALCEMIA

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Abstract: Familial hypocalciuric hypercalcemia is an inherited disease caused by inactivating heterozygous mutations in the gene encoding calcium-sensitive receptors, that affects calcium metabolism and generally follows a benign course. It must be also considered in the differential diagnosis of hyperparathyroidism. Six patients presenting to our internal diseases clinic between January, 2010, and June, 2015, were evaluated in terms of clinical and biochemical parameters. The youngest of our patients was 21 and the oldest was 86. Four were women and two were men. The children of five of our cases and the mother of one were assessed in a polyclinic environment. At evaluation, the presence of familial hypocalciuric hypercalcemia was considered on the basis of moderate hypercalcemia, threshold elevated parathormone levels and a significant decrease in daily calcium expulsion in urine. Diagnosis was confirmed in five patients through determination of similar laboratory findings for calcium metabolism in the children, and also in the mother of our young patient, and on the basis of exclusion of other causes of hypercalcemia. Assessment of calcium metabolism following correction of other factors that may be affected will help clinicians avoid misdiagnosis. Consideration of familial hypocalciuric hypercalcemia in the diagnostic approach to hypercalcemia and at differential diagnosis of primary hyperparathyroidism will prevent unnecessary surgery.

Introduction: Asymptomatic hypercalcemia is a clinical condition frequently detected incidentally and that generally produces no symptoms in the absence of a poor clinical picture. When clinical symptoms are observed, the condition may affect the neuromuscular, gastrointestinal, renal, skeletal and cardiovascular systems. The most commonly encountered causes are hyperparathyroidism and malignities . The first element needing to be investigated in the diagnostic algorithm approach to hypercalcemic patients is serum parathormone levels. Suppressed or elevated parathormone levels frequently indicate primary hyperparathyroidism .

However, since lithium use can cause similar laboratory findings, this must also be investigated. Another clinical condition proceeding with normal or elevated parathormone levels is familial hypocalciuric hypercalcemia (FHH). Although FHH is rare, it can be differentiated from primary hyperparathyroidism by exhibiting a marked familial transmission and significantly low daily levels of calcium excretion in urine. FHH must be considered and assessed at differential diagnosis in patients with· asymptomatic hypercalcemia in order to avoid unnecessary advanced tests and procedures such as parathyroid surgery

Discussion: FHH is a rare, generally benign and genetically transmitted disease affecting calcium metabolism. One study reported a prevalence of FHH of 1/78,000. The disease is characterized by mild-moderately elevated serum calcium levels, inappropriately elevated serum parathormone and a decrease in the daily amount of calcium eliminated in urine . FHH exhibits high transmission autosomal dominant inheritance and involves inactivating mutations in the gene coding calcium-sensitive receptor (CaSR) . It is mainly found in parathyroid chief cells and renal tubular cells. The intracellular signal pathway is activated by calcium binding to the receptor, and parathormone secretion from the chief cells decreases. CaSR also regulates calcium secretion and reabsorption in the distal nephron and collector channels in the kidney. This enables serum calcium levels to be maintained within a narrow range. The CaSR gene is located on the 3q13.3–21 chromosome and codes a gene sequence consisting of 1078 amino acids . In conclusion, considering benign FHH in a case with hypercalcemia following investigation of other factors that may affect calcium metabolism, as in our patients, will make it possible to differentiate these cases from other diseases affecting calcium metabolism. Such evaluation will help avoid false diagnoses. Considering FHH in the diagnostic approach to hypercalcemia and in differential diagnosis of primary hyperparathyroidism will prevent unnecessary surgery.