LETTERS TO THE EDITOR

Kenny-Caffey syndrome without the CATCH 22 deletion

With regard to the recent report by Sabry et al, we would like to present an additional case of Kenny-Caffey syndrome who, unlike their case, did not have a chromosomal deletion at 22q11.2 (the CATCH 22 region). We also report detailed test results for calcium metabolism and response to combination therapy with vitamin D, magnesium, and growth hormone.

The female patient was born after 40 weeks of an uneventful pregnancy to non-consanguineous, healthy, Japanese parents. She weighed 2750 g and measured 46 cm at birth. At 1 month, she had an episode of generalised convulsions because of hypocalcemia. During this episode, her serum calcium, phosphorus, magnesium, and intact PTH were 5.0 mg/dl (reference range 8.6-9.7), 9.1 mg/dl (2.7-4.3), 1.2 mg/dl (1.8-2.2), 120 pg/ml (94-156), and <15 pg/ml (15-50), respectively. Oral 1a-vitamin D (0.3 μg/kg/day) was started on the basis of a diagnosis of hypoparathyroidism. The patient's serum calcium levels were normalised although her intact PTH remained at low to low-normal levels. She had another episode of hypocalcemic convulsions at 9 months of age. At the age of 5 years 1 month, she was referred to our hospital for further examination.

Physical examination showed her to be of proportionally short stature. Her height was 84.2 cm (mean ~5.3 SD) and her weight was 12.2 kg. She had normal intelligence, a prominent forehead, and slender extremities. Her anterior fontanelle still showed an opening of 1x1 cm. She had severe hyperopia with normal optic fundi. Radiological examination showed medullary stenosis of the long bones typical of Kenny-Caffey syndrome. CT scan of the brain showed fine calcification in the basal ganglia. Although her serum calcium remained normal with relatively low doses of vitamin D, the EDTA loading test (50 mg/kg) indicated a blunted response for i-PTH (basal 12.8 pg/ml, peak 17.5 pg/ml).

The PTH loading test showed a normal response to exogenous PTH with increased urinary excretion of phosphorus and cAMP. Growth hormone provocative tests showed normal response.

As in the case of Sabry et al, we also suspected the possibility of the patient having a deletion in the CATCH 22 region. However, FISH analysis on peripheral blood lymphocytes (probe D22S75, and in) showed a normal diploid state. The patient was then put on a combination therapy of vitamin D (1 μg/day) and magnesium sulphate (0.4 g/day). Since her short stature did not improve with this therapy, growth hormone therapy (0.5 IU/kg/week) was initiated at the age of 7 years 5 months. After two years of this therapy, the height standard deviation for her chronological age improved from ~5.4 SD to ~4.4 SD without appreciable acceleration of bone maturation.

The reason for the discrepancy between the Bedouin family reported by Sabry et al and our case remains unclear. One possibility is that the genetic heterogeneity of the syndrome. Of the 47 reported cases, more than half were familial and both autosomal dominant and recessive forms have been reported. The cases reported by Sabry et al had interesting and unusual features for the syndrome, such as marked IUGR, microcephaly, and severe mental retardation, while our case had more typical features of the syndrome. Most of the Bedouin cases of the syndrome show mental retardation, while this is rare in other populations. It is therefore possible that the syndrome in Bedouins is genetically different from that in other ethnic groups. Another possibility is that the gene is actually in the CATCH 22 region but the defect varies from large scale deletion to subtle mutations. It is also possible that the different phenotypes are caused by a contiguous gene effect. Without a large scale deletion, the phenotype would be more typical of the syndrome.

Finally, a combination therapy of vitamin D, magnesium, and growth hormone seems to be moderately effective in the treatment of Kenny-Caffey patients without increasing the risk of hypocalcaemic attacks. More efforts should therefore be made to improve the final height of these patients.

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