Combined Pituitary Hormone Deficiency and PROP-1 Mutation in Two Siblings: A Distinct MR Imaging Pattern of Pituitary Enlargement

SUMMARY: Mutations of the PROP-1 gene are the most frequent genetic defect in patients with combined pituitary hormone insufficiency. We present the cases of 2 siblings with PROP-1 mutations whom we observed longitudinally. Their initial pituitary MR imaging examinations showed identical findings: an enlarged adenohypophysis, with striking hypointensity on T2-weighted images and slight hyperintensity on T1-weighted images. In one of the children, the follow-up MR imaging obtained 3 years after hormonal replacement revealed a decrease in the size of the anterior pituitary lobe.

Discussion

In contrast to patients with CPHD of other genetic origins who show symptoms soon after birth, neonates with PROP-1 defects lack perinatal signs of hypopituitarism and generally have normal birth lengths. Most patients present initially with profound growth retardation at a mean age of 4 years. Previous data regarding the pituitary size in humans with PROP-1 mutation was not consistent. Most MR imaging reports of PROP-1 mutations show a hypoplastic anterior pituitary lobe. Fofanova et al reported hypoplasia in 7 patients.

Voutetakis et al described some patients with gland enlargement on MR imaging. Mendonça et al and Riepe et al reported enlarged adenohypophysis with high signal intensity on T1-weighted images and a marked reduction in height in the follow-up of patients with PROP-1 mutation. Nevertheless, none of these studies have reported the MR imaging pituitary findings on T2-weighted images.

We assume that the gland enlargement observed in our patients is related to an increased size of the adenohypophysis, with an important hypointensity on T2-weighted images. There was no mass but an abnormality involving the entire anterior pituitary lobe. The adenohypophysis may vary in size and shrink after hormonal replacement, but it remains with the same pattern of signal intensity on MR imaging. Consequently, T2-weighted images are very useful in such cases.

Unfortunately, we are not able to characterize the substance responsible for these abnormal and striking features on T2-weighted images because none of our patients were submitted to any kind of surgical procedure, and clinical management is the rule in such cases. A high protein content might be considered.

Regarding the pituitary stalk and posterior lobe, MR images showed a clearly normal aspect, just as the other cases.
described in the literature, once the PROP-1 gene is expressed only in the anterior pituitary lobe.\textsuperscript{1,3,7}

In summary, we advocate that in the clinical setting of a child with CPHD associated with an enlarged adenohypophysis (or small-sized after hormonal replacement) who presents with slight hyperintensity on T1-weighted images and a striking hypointensity on T2-weighted images, the PROP-1 gene mutation should be suspected and genetic analyses be performed.

As far as we know, such a distinct MR imaging pattern of adenohypophysis enlargement with striking hypointensity on T2-weighted images attributable to PROP-1 mutation has never been described in the radiologic literature.

References
1. Riepe FG, Partsch CJ, Blankenstein O, et al. Longitudinal imaging reveals pituitary enlargement preceding hypoplasia in two brothers with combined pituitary hormone deficiency attributable to PROPI mutation. J Clin Endocrinol Metab 2001;86:4353–57
2. Marui S, Souza SLC, Carvalho SLC, et al. The genetic bases of growth abnormalities. Arq Bras Endocrinol Metab 2002;46:444–56
3. Voutetakis A, Argyropoulou M, Sertedaki A, et al. Pituitary magnetic resonance imaging in 15 patients with PROPI gene mutations: pituitary enlargement may originate from the intermediate lobe. J Clin Endocrinol Metab 2004;89:2200–06
4. Rosenbloom AL, Almonte AS, Brown MR, et al. Clinical and biochemical phenotype of familial anterior hypopituitarism from mutation of the PROPI gene. J Clin Endocrinol Metab 1999;84:50–57
5. Cogan JE, Wu W, Phelps JA III, et al. The PROPI 2-base pair deletion is a common cause of combined pituitary hormone deficiency. J Clin Endocrinol Metab 1998;83:3346–49
6. Böttner A, Keller E, Kratzsch J, et al. PROPI mutations cause progressive deterioration of anterior pituitary function including adrenal insufficiency: a longitudinal analysis. J Clin Endocrinol Metab 2004;89:5256–65
7. Fosanovra O, Takamura N, Kinoshita E, et al. MR imaging of the pituitary gland in children and young adults with congenital combined pituitary hormone deficiency associated with PROPI mutations. AJR Am J Roentgenol 2000;174:555–59
8. Pernasetti F, Toledo SP, Vasilyev VV, et al. Impaired adrenocorticotropin-adrenal axis in combined pituitary hormone deficiency caused by a two-base pair deletion (301–302delAG) in the profit of Pit-1 gene. J Clin Endocrinol Metab 2000;85:590–97
9. Mendonça BB, Osório MG, Latronico AC, et al. Longitudinal hormonal and pituitary imaging changes in two females with combined pituitary hormone deficiency due to deletion of A301, G302 in the PROPI gene. J Clin Endocrinol Metab 1999;84:942–45