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ISOLATED CENTRAL DIABETES INSIPIDUS (CDI) AND PERIVENTRICULAR NODULAR HETEROTOPIA (PNH) IN A 9-YEAR-OLD GIRL

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Introduction

Central diabetes insipidus (CDI) can be caused by genes, tumors, malformations, inflammatory reactions. vascular injuries, infarctions, and radiation (3). Periventricular nodular heterotopia (PNH) defines grey matter malformations and occur due to abnormal neuronal migration in the embryo (1). An association between PNH, ectopic posterior pituitary and deficiencies of the anterior pituitary has been reported in the literature (2, 4).

Case Presentation

We present the case of a 9-year-old girl of non-consanguineous parents without preexisting conditions. Polyuria and polydipsia occurred after a Varicella infection at the age of 6 years with increasing amounts of water ingestion up to 5L per day. Constant nycturia lead to initial medical consultation. Linear growth and psychomotor development were regular.
Water deprivation testing suggested the diagnosis of a partial to complete central diabetes insipidus with failure to increase urine osmolality and low copeptin levels despite hypernatremia (Tab. 1, Fig. 1). cMRI revealed PNH and isolated absence of the posterior pituitary (Fig. 2, 3). The patient was treated with 30µg desmopressin and the urine output decreased from 5 liter to 2-3 liters per day. Other pituitary deficiencies were ruled out and no signs for external malformation were found. Genetics with regard to PNH was initiated but no genetic cause for the phenotype could be detected.

Tab 1: Water depriviation test

Parameter	Results
Duration	9h
Serum Sodium	151mmol/L
uOsm	305 mOsm/kg
pOsm	221 mOsm/kg
Copeptin	1.24pmol/L

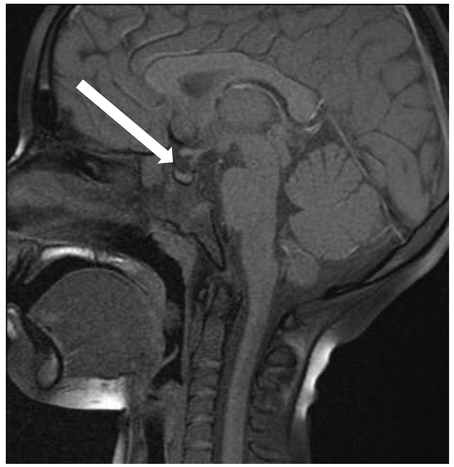

Fig. 2: Missing bright spot in T1

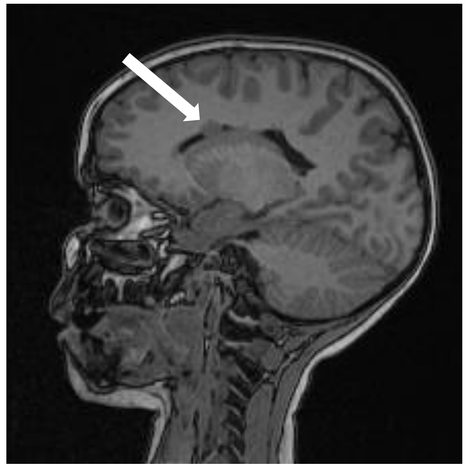

Fig. 2: Sagital MRI of the brain with peri-ventricular nodular heterotopia (arrow)

Discussion

Classic filaminopathy caused by a mutation on the *filamin A (FLNA)* is associated with PNH and other brain malformations. While PNH in filaminopathy are contiguous and symmetric, our patient exhibited asymmetric lesions. Furthermore , typical coexisting symptoms such as cardiac valvular disease, skeletal anomalies, other brain malformation and seizures are missing (1). Besides the classic bilateral PNH associated with *FLNA* mutations, Bilateral posterior PNH (BP-PNH) as described by Mandelstam et al. 2013 (1), represents a distinct subtype of PNH, featuring noncontiguous and asymmetric lesions similar to our patient. While all patients with posterior PNH share the absence of mutations in FLNA genes, a genetic cause is suspected (1).
Compared to classic PNH, bilateral posterior PNH are more likely to have more frequent abnormalities of other brain structures: severe dysplasia/hypoplasia of the cerebellar hemispheres, dysplastic cerebella with vermian abnormalities, posterior fossa cysts, abnormalities of the corpus callosum, hippocampal pathologies, cortical/sulcation abnormalities, decreased posterior white matter volume, ventricular abnormalities (colpocephaly) and abnormalities of the pituitary gland. While an ectopic posterior pituitary has been reported repeatedly in patients with bilateral posterior PNH, only one patient has been described featuring an absent bright spot of the posterior pituitary (1).
Regarding further pituitary symptoms, Mitchell et al. described 4 patients with PNH featuring growth hormone deficiency and ectopic posterior pituitary lobe. All 4 cases exhibited small anterior pituitary lobes and pituitary stalks and presented during early childhood with short stature and growth disorders. One patient showed a heterozygous HESX1 mutation but did not fulfill the features for septo-optic dysplasia (SOD) (4).

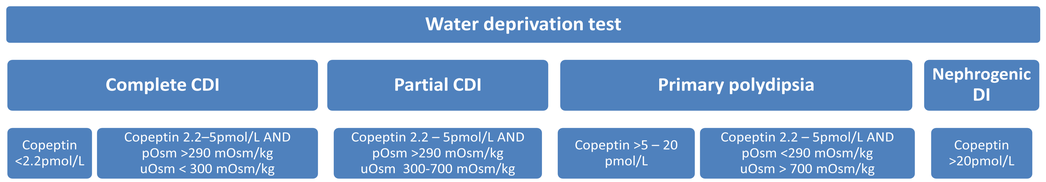

Fig 1: Diagnostic flow chart for the differential diagnosis in children affected by polyuria-polydipsia based on Tuli et al (5).

Conclusion

Central-diabetes insipidus due to an absent posterior pituitary is rarely described in literature. BP-PNH as distinct entity to classical PNH seems to be associated with development alterations of midline structures including the pituitary.
Previous reports of cases with both BP-PNH and ectopic or absent posterior pituitary suggest the inclusion of diagnostics for pituitary deficiency, in particular for CDI and GH-deficiency.
A common genetic origin in the distinct sub-entity of BP-PNH remains to be determined (1, 2, 4).

References

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