Growth hormone deficiency (GHD) in a patient with persistence of the craniopharyngeal canal with cephalocele

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There are no conflicts of interest

A 4-year-old patient was referred to our Centre for short stature. Weight and length at birth were within normal limits. In the neonatal period he showed jaundice and hypoglycemia. A reduced growth velocity was reported from the age of six months. At 15 months his length was 70 cm (-3,75 SDS), his weight 8,1 kg (-2,26 SDS). Parental target height was 167,6 cm (-1,38 SDS). He had normal psychomotor development. The examination showed macrocrania and nasal voice. The growth chart is shown in figure 1.
Blood count, liver and renal function, screening for coeliac disease, thyroid function tests, ACTH, cortisol were within normal limits. IGF1 was undetectable.
Growth hormone stimulation test with arginine (0,5 g/kg ev.) showed a growth hormone (GH) peak of 1,2 ng/ml (table 1).

Figure 1: growth chart

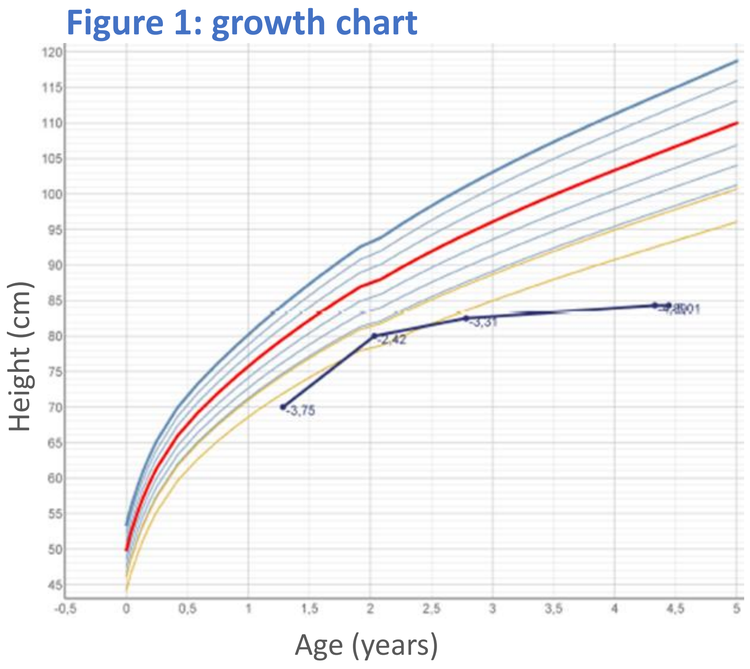

Table 1: blood test results

	Value	Reference range
TSH (µIU/mL)	2,63	0,25 – 5
FT4 (ng/dl)	0,99	0,93 – 1,7
ACTH (pg/ml)	22,1	7,2 – 52
Cortisol (ng/ml)	155	48 – 195
Prolactin (ng/ml)	68,7	2,1 – 17,7
Arginine Test (ng/ml)	0,3..0,2..1,2..0,5	
IGF1 (µg/l)	< 15	55 - 190

The brain MRI displayed the persistence of the craniopharyngeal canal with cephalocele and dysmorphic hypophyseal peduncle which reaches the nasopharynx mucosa with stenosis of the air column behind the choanae. Moreover, it showed a malformation of the hypothalamus-chiasmatic region, with apparent absence of the crossing of the fibers of the optic nerves (figure2). The patient was diagnosed with GHD associated to cerebral malformation. The patient underwent surgical reconstruction of the sellar floor and correction of the trans-sphenoidal cephalocele (figure 3). The histological examination of the rhinopharyngeal tissue showed "nasopharyngeal mucosa, and dense fibrous tissue due to meninges, infiltrated by adenohypophysal tissue".

Figure 2: brain MRI before surgery

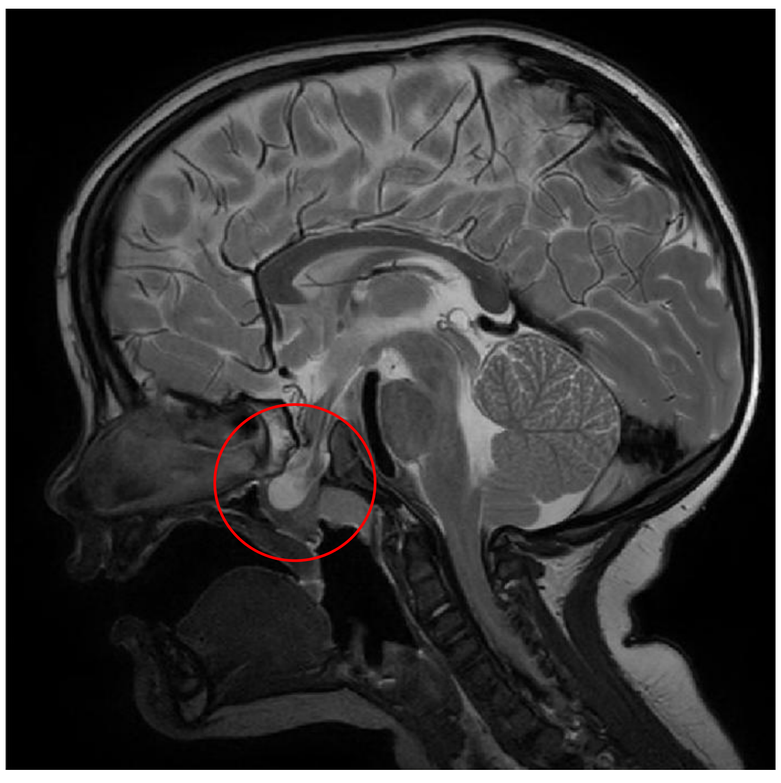

Figure 3: brain MRI after surgery

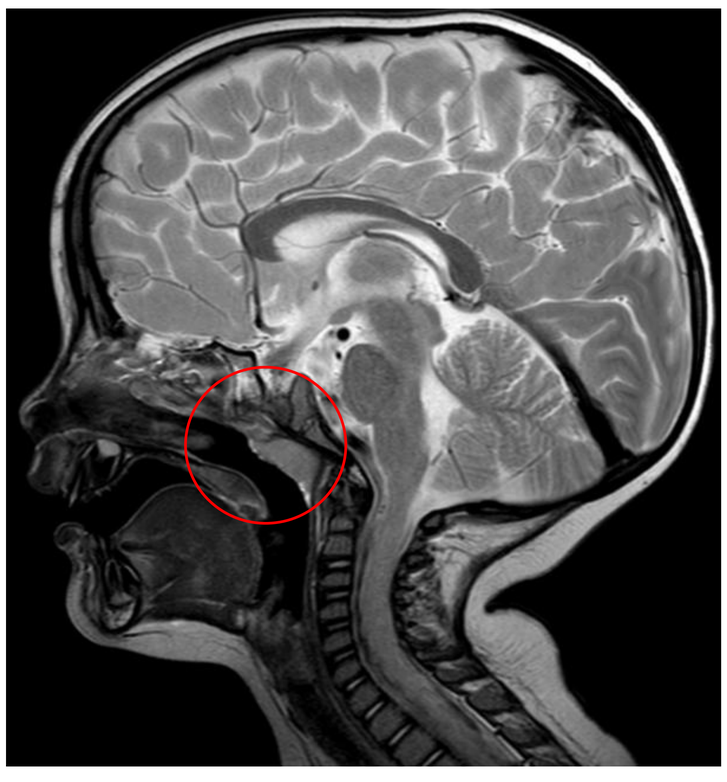

Table 2: blood test results after surgery

	Value	Reference range
TSH (µIU/mL)	0,26	0,25 – 5
FT4 (ng/dl)	0,73	0,93 – 1,7
FT3 (pg/ml)	1,43	2,42 – 5,5
ACTH (pg/ml)	2,2	7,2 – 52
Cortisol (ng/ml)	20	48 – 195
IGF1 (µg/l)	<15	55 - 190

After surgery, the blood test were diagnostic of panhypopituitarism (table 2). The patient was replaced with hydrocortisone, GH, and levothyroxine. He also developed diabetes insipidus and required desmopressin. Currently, the patient is on neuroradiological, ophthalmological, neurosurgical, and endocrinological follow up.
The persistence of the craniopharyngeal canal has been described in association to SOX3 deletion [1]. Genetic analysis with next generation sequence (NGS) technique for genes associated with short stature was performed and resulted negative.
The craniopharyngeal canal is a rare defect. According to the classification of T.A. Abele et al [2], our patient had a type 3A canal, which consists in a canal containing cephalocele.

[1] K. S. Alatzoglou et al. J Clin Endocrinol Metab 99: E2702–E2708, 2014
[2] T. A. Abele et al. AJNR Am Neuroradiol 35:772-77, 2014

Conclusions:
This case underlines the importance of performing brain MRI in children diagnosed with GHD to identify structural abnormalities of the hypothalamic-pituitary region. Accurate diagnosis and surgical treatment of craniopharyngeal canals are important in order to prevent infective complications such as meningitis, and to provide a multidisciplinary follow-up.