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Effect of steroid therapy in a 16-year-old girl observed for lymphocytic hypophysitis

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Autoimmune hypophysitis (AH) is rare in children, with only < 100 cases described in the medical literature, of which only a few are biopsy-proven [1]. Usually, it results in hypophysis and pituitary enlargement. Arginine vasopressin deficiency (AVD) and growth retardation are the most significant presenting symptoms in children with hypophysitis, different from teenagers (13–19 years old) in whom adrenal insufficiency, hypogonadism, headache, or diplopia might be the leading manifestations. The majority of AH cases represent lymphocytic hypophysitis (LYH). The following types of LYH may be distinguished: lymphocytic adenohypophysis, lymphocytic infundibuloneurohypophysitis, and lymphocytic panhypophysitis. The coexistence of other autoimmune diseases has been described in 20–50% of adults, especially autoimmune thyroid disease [2]. Treatment consists of steroids or immunosuppressive therapy, seldom radiotherapy. Surgery is an extremely rare method of AH treatment. Sometimes, the pituitary lesion has a tendency to spontaneous regression, and observation is sufficient.

A 16-year-old previously healthy girl was admitted to the Department of Pediatrics due to suspected meningitis. Symptoms such as headaches, vomiting, fever, lethargy, weakness, diplopia, and binocular strabismus were presented. She had a medical history of headaches, polydipsia, and polyuria for 2 months before hospitalization. In basic laboratory tests, inflammatory markers were negative (leukocytosis 7.61 × $10^3/\mu$L, C-reactive protein 1.7 mg/dL), and hyponatremia (128 mmol/L) was found with normal potassium levels. The cerebrospinal fluid showed a cytosis of 266 k/uL with a predominance of lymphocytes, glucose, protein were normal, and the neurological panel and tests for tuberculosis, Lyme disease, and tick-borne encephalitis were negative. The ophthalmological assessment showed biocular strabismus and normal visual acuity and fields. Neurological examination confirmed nerve VI palsy (impaired eye abduction and horizontal diplopia worse when fixating at a distance); otherwise, no abnormalities.

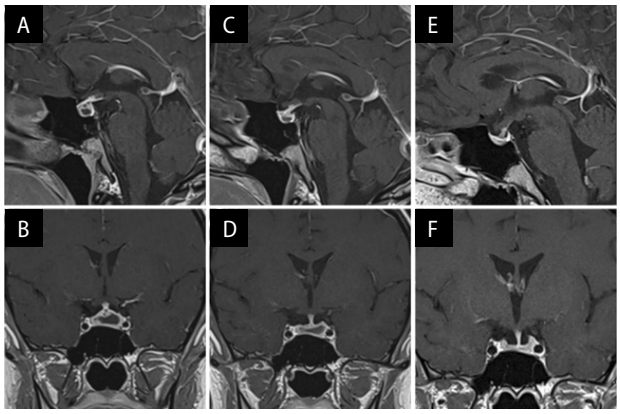

Figure 1. *Resonance magnetic imaging (MRI) of the pituitary gland, T1-weighted images after contrast agent administration in sagittal (A, C, E) and frontal sections (B, D, F).* **AB.** *First examination. A heterogeneous lesion measuring 9 mm (anterior-posterior [ap]) × 9 mm (height) × 21 mm (transverse) with thick rim contrast enhancement at its periphery; thickening of the pituitary stalk to 4.5 mm and altered hypothalamic signal.* **BC.** *After 3 weeks of steroid treatment. The heterogeneous lesion within the sella turcica has decreased to 6 mm (ap) × 5.5 mm (height) × 19 mm (transverse); thickening of the pituitary stalk to 4 mm; thick rim contrast enhancement around the periphery of the lesion.* **EF.** *After 2 months of steroid treatment. Further marked regression of the lesion within the pituitary, now slit-like, is difficult to measure; the pituitary stalk is not thickened, with slightly uneven outlines*

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The brain resonance magnetic imaging (MRI) identified a T1-hyperintense sellar/suprasellar lesion 10 mm x 9 mm x 21 mm with a thick rim of enhancement and minimal sella expansion, with pituitary stalk thickening (PST) to 4,5mm (Fig. 1AB). Ceftriaxone, dexamethasone and mannitol were ordered. She was referred to the Department of Endocrinology. Endocrine investigations showed central hypothyreosis [thyroid-stimulating hormone (TSH) 0.6100 mIU/L (normal range (N): 0.48–4.17), free thyroxine (fT4) 0.67 ng/dL (N: 0.83–1.43)]. Adrenocorticotropic hormone (ACTH) and dehydroepiandrosterone sulfate (DHEA-S) were below the normal range: 5 pg/mL (N: 10–60 pg/mL) and 30.8 μg/dl (N: 98.3–413.4 μg/dL), respectively, but both studies were performed during dexamethasone therapy. Estradiol concentration was 16.49 pg/mL (N: 21.9–297.2 pg/mL). Normal follicle-stimulating hormone (FSH) levels, luteinizing hormone (LH), and insulin-like growth factor 1 (IGF-1) were noticed. A diagnosis of AVD was established based on clinical presentation, serum and urine osmolality, and lack of MRI neurohypophyseal bright signal. Markers in serum, such as alpha-fetoprotein (AFP) and the beta-subunit of human chorionic gonadotropin (beta-HCG), were negative. In CSF, the level of AFP was normal, but slightly elevated beta-HCG was indicated. The concentration of immunoglobulins was within the normal range. Antinuclear antibodies, anti-neutrophil antibodies and anti-thyroperoxidase antibodies, anti-thyroglobulin antibodies were not presented. Angiotensin-converting enzyme was in the normal range. The QuantiFERON test was negative. Chest X-ray and abdomen computed tomography showed no abnormalities.

Treatment with desmopressin and levothyroxine was started. The antibiotic was administered for 21 days. During steroid therapy, headaches, strabismus, and lethargy were completely resolved.

After 3 weeks of steroid treatment, the heterogeneous lesion within the sella turcica has decreased, measuring 6 mm x 5.5 mm x 19 mm, PST to 4 mm persists (Fig. 1CD). ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography examination, performed during steroid therapy, showed no changes. After 2 months of steroid treatment, a brain MRI did not reveal the previously described pituitary focal lesion but only a heterogeneous image of the pituitary gland and stalk, indicating an inflammatory process in the past (Fig. 1EF).

Currently, 2 months after diagnosis, the patient feels well and remains on treatment with prednisone at a reduced dose, levothyroxine, and desmopressin.

LYH is a rare cause of hypopituitarism in children, mimicking sellar region tumors. Kalra et al. showed that the most common presenting symptoms in children are caused by AVD (85%), growth hormone deficiency was found in 76% of pediatric cases, while FSH/LH, TSH, and ACTH deficiencies were less common, 32%, 29% and 20% respectively [3]. Hyperprolactinemia can be found in 8% of children with hypophysitis [3]. Headache and visual disturbances can be found in 17% and 8% of cases [3]. MRI findings are nonspecific, including homogenous pituitary enlargement with symmetrical suprasellar expansion, chiasm displacement, pituitary stalk thickening, and often loss of bright spots of the neurohypophysis. After gadolinium, homogeneous enhancement of pituitary mass with thickening contrast enhancement around the lesion's periphery is visible [4]. Differential diagnosis includes neoplasms (germ cell tumors, craniopharyngioma, lymphoma, pituitary neuroendocrine tumors and other inflammatory and infectious diseases (neurosarcoidosis, histiocytosis, tuberculosis, abscess, lymphocytic hypophysitis) [5]. Hence, the combination of clinical manifestation, laboratory tests, and brain MRI assessment can suggest LYH, though histologic evaluation remains crucial. Because this procedure might cause morbidity, this decision should be reserved for the most severe cases, displaying visual acuity impairment due to gland compression, who are unresponsive to medical therapies.

Steroids are recommended as first-line treatment in LYH, and such treatment was applied to our patient. It proved to be effective after only 2 months. Follow-up MRI imaging showed decreased lesion volume, which may confirm our diagnosis of LYH.

Careful follow-up is necessary to manage endocrine deficiencies, and there is the possibility of recurrence of pituitary inflammatory changes.

Conflict of interest

The authors have no conflicts of interest to disclose.

Statements of ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Data were collected retrospectively.

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