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Lymphocytic hypophysitis and central diabetes insipidus during adolescence: what are the criteria for diagnosis?

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Sir: We read with interest the paper of Cemeroglu et al [1] describing a 14-year-old girl with acute central diabetes insipidus (DI), secondary amenorrhea and normal neurological and visual examinations. MRI of the brain revealed a 10 × 10 × 10 mm mass involving the pituitary stalk and hypothalamus which spontaneously reduced within 3 months and returned to 10 × 8 × 10 mm 3 months later. At 6 months the T1-weighted posterior pituitary hyperintensity was absent (no mention of the posterior pituitary status on initial MRI). Endocrine evaluation revealed hypogonadotrophic hypogonadism and low insulin-like-growth-factor-I (IGF-I) level. Histological examination showed signs of chronic inflammation with a predominant lymphocytic infiltrate compatible with lymphocytic hypophysitis.

We wish to make some comments and suggestions.

We have described an 8-year-old girl with acute onset central DI and acquired growth hormone (GH) insufficiency in whom the first MRI showed a thick pituitary stalk and undetectable posterior pituitary hyperintensity [2]. Serial MRI studies were unchanged for 5 years when a huge mass involving the pituitary stalk and hypothalamus was documented together with clinical and laboratory features of panhypopituitarism. Histopathology revealed perivascular inflammatory lymphocytic infiltrates with absence of granulomatosis and necrosis and negative staining for S-100 protein. The patient was treated with high dose prednisolone (30 mg/kg per day, total dose of 2.4 g in 20 min infusion for 3 days). MRI performed 1 month later showed an approximately 50% decrease in the mass, with partial anterior pituitary recovery (thyroid and adrenal) maintained for 2 years after treatment began.

In our case the features reported by Cemeroglu et al. [1] do not permit a convincing diagnosis of classical lymphocytic hypophysitis as traditionally conceived: the disease onset is unrelated to pregnancy, the posterior pituitary is involved, the mass on coronal MRI is confined to the pituitary stalk and hypothalamus while the anterior pituitary is spared, there is no evidence of lymphocytic infiltration and/or destruction of the anterior pituitary tissue and no other co-existing auto-immune disorders are associated [3]. We believe that the disease reported by Cemeroglu et al. [1] belong to a unique spectrum of inflammatory auto-immune vascular-mediated conditions variably affecting the hypothalamic-pituitary area.

The statement that “the loss of the normal posterior pituitary T1-weighted hyperintensity may have been a clue to the diagnosis of lymphocytic hypophysitis before biopsy in this case” is rather misleading because the lack of posterior pituitary hyperintensity in central DI is a non-specific hallmark of a hypothalamic-neuro-hypophyseal axis lesion [2, 4]. The conservative management of these tumour-like conditions appears reasonable but in the patient reported by Cemeroglu et al., the chronic growth pattern and the size of the mass as well as the documentation of an inflammatory process after pituitary stalk biopsy require in our opinion a tentative treatment approach. Only few controversial data with different treatment modalities and outcome have been reported but the favourable response to glucocorticoids in our patient underlines the possible role of steroids in the management of such inflammatory masses. We believe that the low IGF-I level and patient weight increase (6.8 kg) may have been due to acquired GH insufficiency which is frequently associated with such lesions. Thus, evaluation of GH secretion and clinical indication for GH treatment (metabolic and quality of life effects in adults) in case of GH deficiency merit consideration.

References


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Reply

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Sir: We are pleased to have the opportunity to update our report on each of the issues addressed in Dr. Maghnie's letter.

In the last few years, the broad spectrum of presentation of the condition known as lymphocytic hypophysitis (LYHY) has been established. Thus, LYHY can affect men and women and need not be related to pregnancy [1, 4, 5, 9, 10]. LYHY is not only confined to the anterior pituitary but can involve the posterior pituitary and the stalk [2, 14]. The term LYHY is used globally to describe a spectrum of pathology. Based on anatomical site and severity of the inflammatory process, LYHY can be subclassified as lymphocytic hypophysitis, lymphocytic infundibulo-neurohypophysitis and necrotizing infundibulo-hypophysitis. We elected to use the global term of LYHY in our report. We absolutely agree that the imaging studies performed in our patient point to pituitary stalk and hypothalamic involvement. As stated by Dr. Maghnie, this does not fit the classical diagnosis of lymphocytic hypophysitis strictly defined by anatomical features but, again, LYHY was used in the broader sense which encompasses the whole spectrum of this condition. Because of the age of our patient, we did not originally
consider LYHY in the differential diagnosis and were surprised at the biopsy results.

We agree that current diagnostic techniques limit our ability to diagnose and differentiate LYHY from other processes that may or may not be related to LYHY (LYHY vs lymphocytic infundibulo-neurohypophysis vs necrotizing infundibulo-hypophysis). Serum antipituitary antibodies, measured by an immunofluorescence technique using rodent pituitary cell lines GH3 and AtT-20 may become useful tools to confirm the diagnosis of LYHY in the future [4].

Treatment options are limited for LYHY. Glucocorticoid treatment is indicated in LYHY when increased intracranial pressure is documented or suspected. In the absence of signs of increased intracranial pressure, clear benefits from glucocorticoid therapy are observed in only 50% to 60% of cases [13]. Considering the benefit/risk ratio of a glucocorticoid trial, this treatment option was declined by the family.

Hormone supplementation is indicated for treatment of specific hormone deficiencies. As mentioned in our article, we suspected growth hormone (GH) deficiency in our patient. However, at 14 years of age, our patient had achieved most of her height potential. GH supplementation in adults is beneficial particularly for maintenance of lean body mass and muscle strength [6, 8]. However, the use of GH in adolescence is still controversial. Even in adults, the effect of GH treatment on mood, lipid profile and bone density is disputed [3]. Detrimental effects from GH include reduction of circulating cortisol levels [12], increased left ventricular wall thickness [7] and elevated lipoprotein-a which is an independent risk factor for cardiovascular disease [11]. Dose, duration of GH treatment, long-term side-effects, quality of life changes and economic implications of the treatment remain to be assessed. Only if they are firmly established can we justify a lifelong, expensive injection treatment.

References


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