Effect of hydrocortisone on hypocorticolism caused by pituitary adenoma

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Case Report

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Abstract

Objectives: Pituitary adenoma is a tumor that can cause hormonal secretion problems, including hypocortisolism. Hypocortisolism may result in negative impacts such as an increase in proinflammatory cytokine and immune system activation. Hypocortisolism therapy is performed by giving high-dose hydrocortisone. This case report presented a hypocortisolism therapy using hydrocortisone in a patient with pituitary adenoma.

Case presentation: A 17-year-old boy was admitted to a hospital due to right-eye vision loss, headache, and swallowing difficulty. During the treatment at the hospital, the patient had light depression. The brain Magnetic Resonance Imaging (MRI) scanning with contrast showed there was a supratentorial axial lesion enlarged from the intrasellar to the suprasellar. The anamnesis and physical examination, as well as laboratory and supporting examinations, showed that the patient was diagnosed to suffer from pituitary macroadenoma. The laboratory examination showed that the size of hypocortisolism was at <0.5 µg/dL (reference value ranges from 4.30–22.40 µg/dL). The patient was treated with hydrocortisone IV therapy at 100 mg/dose administered in the morning and evening for 4 days. Then, the dose tapering off of 100 mg/dose was administered in the morning for 4 days. After that, the patient received hydrocortisone of 20 mg/dose peroral administration in the morning and evening until the patient was discharged from the hospital. Tapering off was performed to prevent the side effects of high-dose hydrocortisone. Besides, the patient was alsounder the Endoscopic Endonasal Transsphenoidal Hypophysectomy (EETH). The cortisol level in the pretreatment was at <0.5 and 5.3 µg/dL during the treatment. There were no side effects of the treatment when the patients were hospitalized.

Conclusions: The hydrocortisone IV therapy with 100 mg/do was administered in the morning and evening for 4 days, and then the dose tapering off of 100 mg/dose was done in the morning for 4 days. Then, the hydrocortisone therapy of 20 mg/dose peroral administration to the patient with pituitary macroadenoma in the morning and evening to improve the cortisol level. The cortisol level in the pretreatment was at 0.5 and 5.3 µg/dL in the post-treatment.

Keywords: hydrocortisone; hypocorticolism; pituitary adenoma.

Introduction

A pituitary adenoma is a hypophysis gland tumor found in the hypophysis anterior [1]. Pituitary adenoma emerges in one of the five hypophysis anterior cells, such as lactotrophs, gonadotrophs, somatotrophs, corticotropes, and thyrotropes. Pituitary adenoma rarely emerges in the combination of this anterior cells [2]. Based on its size, the pituitary adenoma is classified into three: microadenoma (<10 mm), macroadenoma (>10 mm), and giant adenoma (>40 mm) [3]. Based on the absence or presence of clinical syndrome due to hormonal hypersecretion, the pituitary adenoma is also classified into two: functioning pituitary adenoma and nonfunctioning pituitary adenoma [4].

The prevalence of pituitary adenoma was estimated to be at 0.2%, and the incidence reached two cases per 100,000 population [5]. The rate of microadenoma or macroadenoma rarely occurs in child and adolescent populations at the prevalence of 1:1,000,000 [6]. Pituitary adenoma in child and adolescent populations mostly suffer from functioning pituitary adenoma (80–97%) [7].

Clinical symptoms because of hypophysis adenoma consist of three manifestations: hypersecretion or hormonal deficiency, neurological manifestation because of the mass effect that develops to the gland, or incidental

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discoveries in the imaging performed. A hormonal manifestation that commonly occurs involves hyperprolactinemia, acromegaly, and Cushing syndrome. Other hormonal manifestations include partial or full hypopituitarism [2]. The most common hypopituitarism types include growth hormone deficiency and hypogonadism, while hypercortisolism rarely occurs [8].

Pituitary adenoma therapy aims to normalize prolactin serum, perform a tumor surgery, or lessen tumor size [8]. A therapy on hypercortisolism was done through glucocorticoid replacement. Decisions about the number of doses are also based on patient preference, differences in daily activities, and patient experience. There is no reliable biochemical marker to assess the appropriateness of dose in glucocorticoid replacement treatment, and so dose modification is guided by clinical judgment and subjective perception of symptoms and signs of glucocorticoid underreplacement and over-replacement [9].

Case presentation

A 17-year-old boy visited a hospital and complained that he experienced headache, swallowing difficulty, vomiting in the morning, and vision problems in the right-eye. Specifically, the patient experienced blurry eyes and double vision in the last 5 months before being hospitalized. The patient lost right-eye vision ability a week before being hospitalized. He was diagnosed to suffer from hypophysis macroadenoma in August 2019.

In the next anamnesis, he experienced slight depression and had a blood pressure of 110/80 mmHg, a pulse of 80 times per minutes, breathing frequency of 20 times per minutes, body temperature at 36.8 °C, and 98% of saturated oxygen through the administration of oxygen mask at 6 L per minutes. The neurological treatment in the Glasgow scale of E4V5M6 showed the patient has a negative meningeal sign, and negative facial palsy. The results of funduscopic and confrontation visual tests showed optic atrophy and blindness in the right-eye. The patient's sense was in the normal range, and the motoric condition was generally weak.

The brain Magnetic Resonance Imaging (MRI) scanning with contrast showed an extra supratentorial axial lesion enlarged from the intrasellar to suprasellar tumors. The irregular clean edge margin was 1.3 × 2.1 × 2.31 cm in size which stresses dextral optic nerves and optic chiasm and causes dextral optic nervous edema, which made the image of hypophysis macroadenoma cleaner (Figure 1).

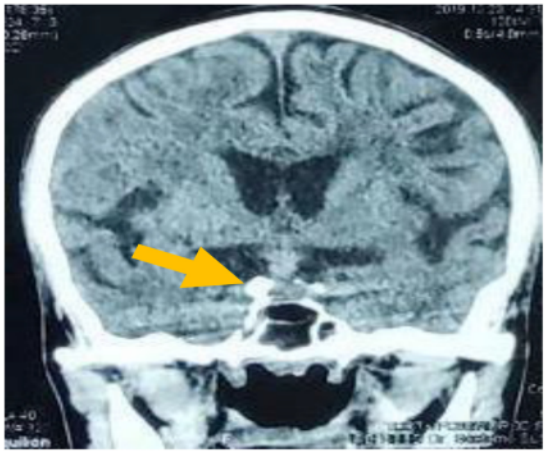

Figure 1: MRI results before the EETA procedure.
The brain MRI scanning with contrast showed an extra supratentorial axial lesion enlarged from the intrasellar to suprasellar tumors.

The laboratory examination in the presurgery on 20th December 2019 presented that the hypocortisolism level was at <0.5 µg/dL (reference value ranges from 4.30–22.40 µg/dL). On 23rd December 2019, a surgery using Endoscopic Endonasal Transsphenoidal Approach (EETA) was performed. The anatomical pathology test observed layers of tumor tissues. A tumor contains cells with rounded nuclear, relatively monotonous shape, smooth chromatin, eosinophilic cytoplasm, absence of mitotic, and absence of cancerous signs. The anatomical pathology test is presented in Figure 2. The patient received the hydrocortisone therapy IV with oral administration of 100 mg/dose in the morning and evening for 4 days, and then the dose tapering off of 100 mg/dose was administered in the morning for 4 days. Then, hydrocortisone was administered orally at 20 mg in the morning and evening until the patient was discharged from the hospital.

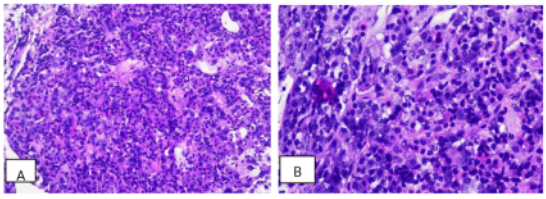

Figure 2: Tumor histopathological examination results (A) original objective 20×. (B) original objective 40×.
The anatomical pathology showed a tumor contains cells with rounded nuclear, relatively monotonous shape, smooth chromatin, eosinophilic cytoplasm, absence of mitotic, and absence of cancerous signs.

Discussion

A pituitary adenoma may cause hormonal problems as a clinical manifestation. Hormonal problems could be in the forms of hormonal excess or deficit [5]. Hypopituitarism is one hormonal deficit or more produced in the anterior pituitary or posterior pituitary. The most common hypopituitarism is hormonal growth deficiency and hypogonadism, while hypocortisolism rarely occurs [8]. Hypopituitarism is one of the causes of high mortality rate, and its main risk factor is cortisol deficiency due to hormonal adrenocorticotropic deficiency (ACTH) [10].

Symptoms and signs experienced by the patient with hypo cortisol involve nausea, vomiting, constipation/diarrhea, stomach pain, asthenia, anorexia, weakness, headache, fasting hypoglycemia, weight loss, and hypotension. However, almost all the symptoms are not specific [11, 12]. The present patient experienced headache, swallowing difficulty, morning vomiting, and vision problems in the right-eye. The next anamnesis showed that the patient had slight depression. Besides, the laboratory test showed the patient's cortisol level was at <0.5 µg/dL (reference value ranges from 4.30–22.40 µg/dL). To identify a hypopituitarism diagnosis, it was recommended to measure cortisol level serum at 8–9 AM, and the cortisol level under 3 g/dL was an indication of hypo cortisol [13]. In acute illness possibly attributable to hypocortisolism, a different diagnostic strategy should be applied as an immediate therapeutic intervention is required even before the diagnosis is formally confirmed [14].

The daily physiological production of cortisol is about 5–6 mg/m^2 body surface area. The recommended hormone replacement therapy for hypocortisolism is administering hydrocortisone of 15–25 mg usually in 2–3 doses per day and 50–66% given in the morning right after the patient is awake. If given two times a day, the second dose is usually administered 6–8 h after the morning administration. If given three times per day, the second dose is given 4–6 h after the early morning administration, and the third dose is given 4–6 h after this. Some clinicians recommend weight-adjusted dosing to reduce intervals of excess in cortisol concentrations during the day and decrease variability of cortisol profiles [9].

Hydrocortisone is short-action glucocorticoid, with an elimination half-life of 1–2 h. Hydrocortisone is primarily bound to corticosteroid-binding globulin (transcortin). When transcortin binding sites are saturated, hydrocortisone binds to albumin. Only 5–10% is unbound and biologically active. Hydrocortisone is metabolized in the tissues and the liver to biologically inactive compounds, including glucuronides and sulfates. Hydrocortisone is excreted in the renal, and less than 1% of hydrocortisone is excreted as the unchanged drug in the urine [15].

Side effects correlated with glucocorticoid may be in the forms of endocrine, neuropsychiatric, gastrointestinal, musculoskeletal, cardiovascular, dermatology, ocular, or natural immunology. Different side effects may occur due to the use of glucocorticoids in a long-term of more than 60 days. These side effects may result from various doses and administration patterns. A patient administered with a low dose (≤7.5 mg/day) might experience these side effects as well [16]. The side effects due to the use of corticosteroids are also associated with therapy duration and the use of glucocorticoids in a long-term period. glucocorticoid therapy duration is classified into short-term duration (<10 days), middle-term duration (10–30 days), and long-term duration (>30 days). The use of corticosteroids for long period can stress the HPA axis, and thus the glucocorticoid therapy should be stopped in the right manner. Inappropriate stopping will stimulate the adrenal crisis due to the persistent HPA axis stress. Therefore, dose tapering off is required [17].

Apart from experiencing hypocortisolism, the patient also experienced hyperprolactinemia and would receive dopamine agonist therapy, namely bromocriptine and also EETA. Hypocortisolism therapy modalities in patients undergoing pituitary surgery are recommended using stress doses of the steroids before surgery and tapered doses after surgery before the testing repetition. Patients in the same condition will receive hydrocortisone therapy before surgery [13]. The present patient received hydrocortisone of 100 mg IV in the morning and evening for 4 days from 21st–24th December 2019, and then the dose tapering off of 100 mg/day was performed on 25th–28th December 2019. The patient received hydrocortisone of 20 mg per oral administration in the morning and evening until he was discharged from the hospital on 4th January 2020 and received hydrocortisone of 20 mg in the morning and evening afterward. Tapering off was done to avoid the side effects of giving high-doses of hydrocortisone. The EETA was carried out on 23 December 2019. There was an increase in pretreatment cortisol <0.5 and 5.3 µg/dL after the patient received hydrocortisone therapy. There was no side effect while the patient was hospitalized.

Decisions about the number of doses are also based on patient preference, differences in daily activities, and patient experience. There is no reliable biochemical marker

to assess the appropriateness of dose in glucocorticoid replacement treatment, and so dose modification is guided by clinical judgment and subjective perception of symptoms and signs of glucocorticoid under-replacement and over-replacement. The goal is to achieve the best clinical results with the lowest possible daily dose of steroids. Cortisol day curves are of little value in routine monitoring [9].

Conclusions

The hydrocortisone IV therapy was performed through the administration of 100 mg/dose in the morning and evening for 4 days, and then dose tapering off of 100 mg/dose was administered in the morning only for 4 days. After that, hydrocortisone was administered orally each at 20 mg/dose in the morning and evening to the patient with hypophysis macroadenoma and hypercortisolism to increase the cortisol level. The cortisol level in the pretreatment was at <0.5 and 5.3 µg/dL in the post-treatment.

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