CASE REPORT

Steroid Psychosis Caused by Perioperative Steroid Replacement for Pituitary Adenoma: A Case Report

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(Received for publication on June 15, 2014)
(Revised for publication on July 26, 2014)
(Accepted for publication on September 19, 2014)

Steroid psychosis is a frequent complication of steroid treatment. Although perioperative steroid replacement therapy is generally administered in patients undergoing pituitary surgery, there are no previous reports concerning the development of steroid psychosis after perioperative steroid replacement therapy following pituitary surgery. We herein report a case of steroid psychosis induced by perioperative steroid replacement therapy for pituitary surgery. A 35-year-old man presented with a visual disturbance that had persisted for 1 year. A magnetic resonance imaging scan showed a large pituitary tumor, and a laboratory study revealed slight dysfunction of the hypothalamo-pituitary-adrenal axis. The patient was diagnosed with a non-functioning pituitary tumor and underwent tumor resection via the endoscopic endonasal approach. The initial dose of perioperative steroid replacement therapy was 200 mg of hydrocortisone administered immediately before the operation. The replacement dose was gradually tapered and discontinued over a 7-day period. On postoperative day 4, the patient exhibited an elated mood, grandiose delusions, anxiety, and agitation. We diagnosed these psychiatric symptoms as steroid psychosis induced by steroid replacement and we prescribed risperidone as a treatment. The symptoms gradually improved and did not recur. This case highlights the risk of steroid psychosis following treatment with perioperative steroid replacement therapy for pituitary adenoma and raises questions regarding the appropriateness of perioperative steroid replacement for pituitary adenoma.

Keywords: pituitary adenoma, steroid psychosis, replacement therapy, complication

Introduction

In general, perioperative steroid replacement therapy is traditionally administered for pituitary adenoma. Although the use of perioperative steroid replacement for pituitary adenoma was advocated by Inder et al.,1 there are no clear guidelines regarding its application; therefore, the dose and period of steroid replacement depends on the institution.

Steroid psychosis is a frequent adverse event of steroid therapy. The incidence of steroid psychosis has been estimated to be 5.7%, increasing to 18.6% in patients who receive >80 mg/day of prednisone (PSL).2 Despite the high incidence of steroid psychosis, there are no reports concerning its development after perioperative replacement therapy for pituitary surgery. We herein report the case of a 35-year-old man who received steroids in the perioperative period for pituitary surgery and subsequently presented with psychiatric symptoms. The present case report highlights the risk of steroid psychosis following treatment with perioperative steroid replacement for pituitary adenoma and raises questions regarding the appropriateness of perioperative steroid replacement for pituitary adenoma.
Case Presentation

A 35-year-old man complained of visual disturbance that had persisted for 1 year and visited a nearby hospital. He had no history of medical or psychiatric conditions. Magnetic resonance imaging (MRI) (Fig. 1) showed that a large pituitary tumor with a cyst had compressed the optic chiasm and slightly invaded the cavernous sinus (Knosp Grade 1). Preoperative endocrine studies revealed slight dysfunction of the hypothalmo-pituitary-adrenal axis (HPA axis): free thyroxine 0.5 µg/dl, prolactin 30.1 ng/ml, cortisol 5.8 µg/dl, and dehydroepiandrosterone, 67 µg/dl (normal ranges: 0.7–1.8, 5–20, 6.2–19.4, and 98–516, respectively) (Table 1). We diagnosed the patient with a non-functioning pituitary adenoma and performed surgery under general anesthesia via the endoscopic endonasal approach. He received 200 mg of hydrocortisone immediately before the operation, followed by 100 mg of the drug at night after the procedure. The dose of steroid replacement was tapered over 1 week (200 mg on postoperative day (POD) 1, 100 mg on PODs 2 and 3, 30 mg on PODs 4 and 5, and 10 mg on POD 6). Postoperative MRI (Fig. 2) showed no brain parenchymal injury resulting from the operation and no residual tumor tissue. His visual disturbance improved soon after the operation. A postoperative endocrine study revealed an improvement in the function of the HPA axis (Table 1). The pathological diagnosis was pituitary adenoma.

Postoperatively, the patient made steady progress before complaining of respiratory discomfort, causeless anxiety, and insomnia at night on POD 4. His vital signs were normal, and we prescribed brotizolam for his complaints. On POD 5, he exhibited an elated mood, irritation, grandiose delusions (he insisted he was a rich person), persecution mania (he insisted someone had embedded microchip in his brain), anxiety, aggressive behavior, and agitation. We therefore referred him to the Department of Neuropsychiatry, where he was diagnosed with steroid psychosis and given risperidone (0.5 mg/day). His symptoms of mania worsened over the following several days, and the dose of risperidone was increased to 2 mg. Meanwhile, the dose of steroid replacement was tapered as planned. His morning cortisol level on POD 7 was 11.8 µg/dl, and the steroid replacement treatment was discontinued. His psychiatric symptoms were gradually relieved, disappearing on POD 14. He experienced no recurrent psychiatric symptoms for 10 months after this episode.

Fig. 1 Preoperative coronal enhanced T1 MR image of the patient’s brain. The 35-mm tumor on the sella turcica slightly invaded the cavernous sinus, grew upward, and compressed the optic chiasm.
Psychosis is a common adverse effect of steroid therapy. The incidence of steroid psychosis is directly related to the dose of steroid treatment. Previous reports have found an overall incidence of steroid psychosis of 5.7%, which decreases to 1.3% among patients who receive a dose of PSL of <40 mg. Among patients who receive a dose of PSL of 41–80 mg or more than 80 mg, the incidence increases to 4.6% and 18%, respectively. The risk of steroid-induced psychosis sharply increases in patients taking 40 mg/day or more of PSL. Despite such a high incidence of steroid psychosis, we could find no reports concerning steroid psychosis after perioperative steroid replacement following pituitary surgery. Although we have performed 143 pituitary surgeries via the endoscopic endonasal approach since 2007, this was the first time we had experienced perioperative steroid psychosis. This incidence is lower than those found in previous reports. It is possible that we have overlooked some mild symptoms of steroid psychosis.

The time of onset, severity, type, and/or duration of steroid psychosis cannot be predicted. Even low doses of steroids can cause steroid-induced psychiatric symptoms. In the present case, prior to the onset of psychiatric symptoms, the patient was given 300 mg of hydrocortisone, which is equivalent to approximately 75 mg of PSL, followed by 200 mg (equivalent to 50 mg of PSL) and 100 mg (25 mg of PSL) for 2 days. He subsequently manifested psychiatric symptoms 4 days after the start of steroid replacement therapy.

There was little possibility that operative invasion itself directly caused his psychosis, i.e., perioperative delirium was unlikely because the patient did not have any additional symptoms after the operation before POD 4, and he only manifested psychiatric symptoms 4 days after the operation. This clinical course is consistent with the findings of a previous report which showed that the symptoms of steroid psychosis generally appear 3–4 days after the start of treatment and persist from a few days to up to 3 weeks.

The present patient had no history of psychiatric disease or steroid-induced psychosis and there was nothing worthy of mention in his premorbid character. There are several reports that a positive psychiatric history and/or history of previous steroid-psychosis are associated with future episodes of the disorder, however, other authors have reported that there is no apparent relationship be-
The most effective treatment for steroid psychosis is to reduce or discontinue the dose of steroids, if possible.4 Atypical antipsychotics, such as olanzapine and risperidone, are associated with fewer extrapyramidal symptoms than typical antipsychotics and are therefore recommended as first-line treatment.4,13 In the present case, the patient received risperidone for his psychiatric symptoms, although they did not rapidly improve. Rather, his symptoms were palliated following the withdrawal of steroid replacement. As mentioned in previous reports, the discontinuation of steroid therapy is the most effective treatment for steroid psychosis.

To prevent perioperative complications associated with hypoadrenalism, the administration of perioperative stress doses of hydrocortisone in patients undergoing pituitary surgery has become common;14 however, there are no clear guidelines for the appropriate dose or duration of glucocorticoid replacement. Kehlet et al. estimated the level of glucocorticoid secretion in response to major surgery to be 75–150 mg/day of hydrocortisone and the secretion in response to minor surgery to be 50 mg/day;15 other studies have demonstrated similar conclusions.16–18 Based on these data, the level of cortisol secretion within the first 24 h after surgery rarely exceeds 200 mg.13 Inder et al. suggested guidelines for the perioperative assessment and management of pituitary surgery in 2002,1 in which it was recommended that no perioperative glucocorticoid cover should be given in patients with a normal HPA axis function and/or those in whom selective adeno-mectomy can be performed. In cases involving extensive pituitary surgery, the guidelines recommend the following regimen of hydrocortisone: 50 mg every 8 h on day 0, 25 mg every 8 h on day 1, and 25 mg at 0800 on day 2, measuring the plasma cortisol level at 0800 on days 1–3 postoperatively to determine the need for subsequent glucocorticoid replacement. In patients with abnormal HPA axis function, it is recommended that a standard maintenance dose of glucocorticoids be administered preoperatively followed by the above regimen perioperatively. The dose of steroids used in the present case was higher than that suggested by Inder et al. and may have been excessive.

Recently, Regan et al. demonstrated that perioperative management without the use of any stress doses of steroid coverage results in no adverse events and is safe and beneficial in patients with a normal preoperative serum morning cortisol level who do not suffer from apoplexy.19 The need for perioperative replacement therapy may be lower than was once thought. An excess of glucocorticoids leads to adverse clinical consequences, such as a reduced rate of tissue repair, decreased glucose tolerance, increased susceptibility to infection due to immune compromise, hypertension, gastric ulceration, weight gain, and aseptic necrosis of the femoral head.13,20 Although the outcome in the present case was fortunately favorable, surgeons should provide the appropriate minimum dose of steroids required for perioperative steroid replacement therapy in patients undergoing pituitary surgery only in those who need it, so as to avoid complications such as steroid psychosis.

**Conclusions**

This case highlights the risk of steroid psychosis following the use of perioperative steroid replacement therapy for pituitary adenoma. Only the minimum appropriate dose of steroids should be given as replacement therapy, and close attention to the possibility of steroid-induced complications, such as steroid psychosis, is required.
References