J Anesth (2011) 25:108–111
DOI 10.1007/s00540-010-1070-7

CLINICAL REPORT

Pituitary apoplexy precipitating diabetes insipidus after living donor liver transplantation

Takashi Matsusaki · Hiroshi Morimatsu · Junya Matsumi · Hiroaki Matsuda · Tetsufumi Sato · Kenji Sato · Satoshi Mizobuchi · Takahito Yagi · Kiyoshi Morita

Received: 3 May 2010 / Accepted: 18 November 2010 / Published online: 6 January 2011

Abstract Pituitary apoplexy occurring after surgery is a rare but life-threatening acute clinical condition that follows extensive hemorrhagenous necrosis within a pituitary adenoma. Pituitary apoplexy has been reported to occur spontaneously in the majority of cases or in association with various inducing factors. Reported is a case of pituitary apoplexy complicated by diabetes insipidus following living donor liver transplantation (LDLT). To the best of our knowledge, this has not been previously reported. A 56-year-old woman with nonalcoholic steatohepatitis underwent LDLT from her daughter. The patient also required dopamine support and transfusions because of massive intraoperative bleeding. Postoperatively, her coagulopathy continued, and she underwent a second laparotomy because of unknown bleeding on postoperative day 7, when she needed transfusions and dopamine support to maintain her vital signs. She complained of severe headache, excessive thirst, frequent urination, and diplopia from postoperative day 10. She also had polyuria greater than 300 ml/h and was diagnosed with pituitary apoplexy precipitating diabetes insipidus on postoperative day 13. She was treated conservatively without surgery because of the hormonally inactive status and slight mass effect of her tumor. It is important for anesthesiologists and critical care personnel in LDLT settings to take into consideration this complication as a differential diagnosis.

Keywords Pituitary apoplexy · Diabetes insipidus · Living donor liver transplantation

Abbreviations

LDLT	Living donor liver transplantation
FFP	Fresh frozen plasma
BMI	Body mass index
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
PT-INR	Prothrombin time-International normalized ratio
APTT	Activated partial thromboplastin time
AT-III	Antithrombin III
CT	Computed tomography
DDAVP	Deamino-8-D-arginine-vasopressin

Introduction

Pituitary apoplexy is a rare but potentially life-threatening clinical syndrome resulting from acute hemorrhage or infarction of the pituitary gland [1]. It classically presents with sudden onset of headache, vomiting, visual disturbances, altered consciousness, and impaired pituitary function. Pituitary apoplexy usually occurs in the presence of a pituitary adenoma. The incidence of pituitary apoplexy presenting with classical symptoms was reported to be about 3% in a series of surgically treated pituitary adenomas [2]. However, histopathological evidence of pituitary hemorrhage (subclinical pituitary apoplexy) in asymptomatic patients is much more common and has been observed in up

T. Matsusaki (✉) · H. Morimatsu · J. Matsumi · T. Sato · K. Sato · S. Mizobuchi · K. Morita
Department of Anesthesiology and Resuscitology, Okayama University Medical School, 2-5-1 Shikata-cho, Okayama, Okayama 700-8558, Japan
e-mail: matusakik@ybb.ne.jp

H. Matsuda · T. Yagi
Department of Surgery, Okayama University Medical School, Okayama, Japan

to 25% of surgically removed pituitary adenomas [3]. The true incidence of pituitary apoplexy remains an estimate, particularly because this entity initially can present as an encephalopathy without localized clinical symptoms. Pituitary apoplexy has been reported to occur spontaneously in the majority of cases or in association with various inducing factors. Potential etiologies of the complication have been postulated, including (1) ischemia caused by hypotension, (2) intrapituitary hemorrhage resulting from hypocoagulability, and (3) transient hypertension [2–4]. Numerous hormonal deficiencies may occur after pituitary apoplexy, although diabetes insipidus is quite rare, occurring in only 3% of published reports [5]. Reported here is a clinical course of a patient with pituitary apoplexy and central diabetes insipidus after living donor liver transplantation (LDLT); to the best of our knowledge, this type of case has not been previously reported.

Case report

A 56-year-old woman was admitted for living donor liver transplantation (LDLT) for liver cirrhosis caused by nonalcoholic steatohepatitis. Her body mass index (BMI) was 25.9 kg/m^2 (height, 160 cm; weight, 66.2 kg). She had a previous history of hypercholesterolemia. General examination was unremarkable, except for grade 2 hepatic coma. Laboratory results other than liver function were normal. Laboratory evaluations showed hemoglobin 11.8 g/dl, white blood cell count 155,000/mm^3, platelet count 36,000/mm^3, aspartate aminotransferase (AST) 31 IU/l, alanine aminotransferase (ALT) 27 IU/l, total bilirubin (T-Bil) 4.68 mg/dl, prothrombin time (PT) international normalized ratio (INR) 1.32, activated partial thromboplastin time (APTT) 46.1 s, antithrombin III (AT-III) 35%, and fibrinogen 137 mg/dl. Her model for end-stage liver disease (MELD) score was 15. Preoperative endocrine function, including thyroid gland function, was normal. She underwent living donor liver transplantation (LDLT) and received a graft from her daughter, who was healthy and had no history of previous liver disorders. The transplant surgery was performed following a standard piggyback technique. Graft-to-recipient mass ratio was 0.87. Operative time was 570 min. Intraoperative bleeding was about 6,000 ml, and the patient received 12 units of packed red cells, 30 units of fresh-frozen plasma (FFP), and 30 units of concentrated platelets. Her blood pressure decreased at induction and reperfusion, for which she required a vasopressor to maintain systolic pressure >80 mmHg. The temporary hypotension (within 1 min) recovered with a shot of ephedrine or calcium chloride. Except for these times, the mean arterial pressure was >55 mmHg with dopamine. Her intraoperative hemodynamic status was relatively stable and uneventful. On postoperative day 1, the patient was extubated safely, but her postoperative coagulopathy remained (INR was 1.49, 1.37, 1.5 1.29, 1.3, and 1.41 on postoperative day 1, 2, 3, 4, 5, and 6, respectively), and she needed FFP administration for postoperative bleeding from abdominal drains. She underwent the second laparotomy because of bleeding on postoperative day 7; however, no clear sources of the bleeding were identified. Intraoperative hemodynamics were uneventful and stable with dopamine support. After re-laparotomy, her bleeding problem and coagulopathy were resolved. Her graft function was also stable. From postoperative day 10, she developed a headache that was controlled with analgesics and hypertension controlled with calcium blocker therapy. On postoperative day 13, she complained of a sudden and severe headache that did not respond to nonsteroidal antiinflammatory drug treatment. She also complained of thirst and frequent urination. Her physical examination revealed no abnormalities except for diplopia. Her urine output was 5,900 ml/days without diuretics on postoperative day 13. Her urine output continued at more than 300 ml/h, and her symptoms worsened. Urine specific gravity was 1.003 (normal range, 1.010–1.030). Her serum sodium was slightly elevated at 148 (normal, 137–145) mEq/l. Her serum and urine sugars were within normal limits. Her blood pressure was slightly elevated, and her heart rate was normal. Diabetes insipidus was suspected as the cause of polyuria, and her water intake was restricted. Her serum electrolytes remained normal. Her liver graft function was relatively stable consequent to tacrolimus and steroid (prednisolone, 20 mg/days) therapy. Her coagulation status was also normal, and she did not have any trouble with bleeding. A 5-μg trial of deamino-8-D-arginine-vasopressin (DDAVP) reduced her urine output by 50% and increased her urine specific gravity to 1.016. On this basis, the diagnosis of central diabetes insipidus was made. On postoperative day 14, laboratory values were essentially normal: serum osmolarity was 322 mOsm/kg, serum sodium was 141 (normal range, 137–145) mEq/l, follicle-stimulating hormone (FSH) was 66.9 mIU/ml, prolactin was 21.8 (normal range, 1.8–23) ng/mL, random cortisol was 2.4 (normal range, 5–15) μg/dl, adrenocorticotropic hormone (ACTH) was 9 (normal range, 7.4–55.7) pg/ml, antidiuretic hormone (ADH) was 0.9 (normal range, 0.3–3.5) pg/ml, growth hormone (GH) was 0.51 (normal range, 0.11–3.9) ng/ml, thyroid-stimulating hormone (TSH) was 2.45 (0.33–4.05) μU/ml, and free T_4 was 1.18 (normal range, 0.97–1.69) ng/dl. At postoperative day 14, her headache and hypertension continued. Brain computed tomography (CT) showed a high-density area in the pituitary gland that was not seen preoperatively. Magnetic resonance imaging (MRI) of her pituitary gland also revealed a 0.5-cm suspicious area between the anterior and posterior of the pituitary gland not compressing the optic chiasm (Fig. 1). The area was

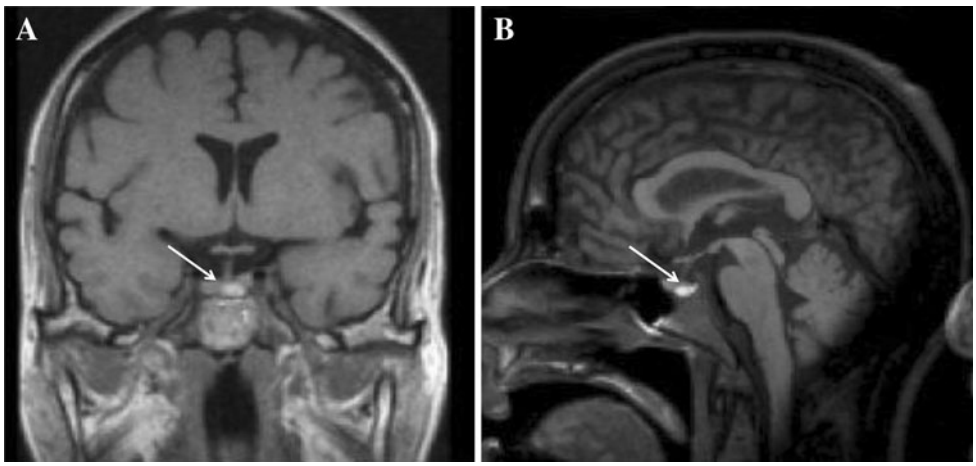

Fig. 1 Magnetic resonance imaging of the pituitary gland. **a** Coronal T_1: nonenhanced image of the pituitary gland shows a 0.5-cm hyperintense area between the anterior and posterior pituitary and a bulky sellar mass that did not compress the optic chiasm. The hyperintense area suggested necrotic-hemorrhagic phenomena (*arrow*). **b** Sagittal T_1: nonenhanced image of the pituitary gland shows a 0.5-cm hyperintense area between the anterior and posterior pituitary (*arrow*)

heterogeneous with a hypointense area on T_2 and a hyperintense area on T_1, which suggested necrotic-hemorrhagic phenomena. Thus, pituitary apoplexy caused by an unknown chronic tumor was diagnosed. A neurosurgeon was consulted regarding decompression, but conservative treatment was chosen because of the slight mass effect and hormonally inactive nature of the tumor. Additional blood chemistry values at postoperative day 15 included serum uric acid of 4.5 (normal range, 2.5–7.5) mg/dl, serum osmolality of 279 (normal range, 275–295) mOsm/kg, blood urea nitrogen of 17 (normal range, 7–17) mg/dl, creatinine of 0.7 (normal range, 0.7–1.2) mg/dl, and urine osmolality of 218 (normal range, 200–850) mOsm/kg. Subsequently, her urine output was controlled without DDAVP. On postoperative day 15, her headache also disappeared. Her diabetes insipidus was temporary. Brain MRIs were conducted regularly and revealed no change compared with the first image. At discharge, she had no ophthalmic complications clinically. At her most recent follow-up appointment (1 year after LDLT), she reported feeling well and denied experiencing excessive thirst or urination.

Discussion

Presented is a case of pituitary apoplexy precipitating diabetes insipidus after LDLT. This patient had a headache, hypertension, diplopia, and diabetes insipidus, which were transient and reversible. The central diabetes insipidus suggested pituitary disease, and this pituitary apoplexy was diagnosed by brain CT and MRI on postoperative day 14, which may have been the first presentation of a previously undiagnosed pituitary adenoma. Conservative management enabled a favorable outcome without surgery.

Pituitary apoplexy is an uncommon clinical syndrome that results from hemorrhage or infarction of the pituitary gland. Most cases of pituitary apoplexy are the first symptom of a previously unknown pituitary adenoma, although pituitary apoplexy can occur in a normal pituitary gland [6]. The true prevalence of pituitary apoplexy is difficult to determine. In the literature, the incidence varies from 0.4% to 8.2% [7]. The development of CT and MRI has resulted in the discovery of an increasing number of unsuspected silent pituitary masses. We checked the brain CT but could not find any abnormalities, so perhaps should have obtained a brain MRI preoperatively. The present patient presented with classic symptoms in addition to diabetes insipidus, which strongly suggested pituitary pathology. Endocrinopathies, both transient and permanent, may occur with pituitary apoplexy, but in the present case, the absence of any clinical features of endocrine dysfunction suggested that the present patient probably had a nonfunctioning adenoma. In our institution, full-dose steroid (10 mg/kg methylpredonisolone) was used preemptively from postoperative day 5 to postoperative day 7 to prevent acute cellular rejection. This early full-dose steroid therapy might have had an effect on this nonfunctioning adenoma [8]. Cozzi et al. [8] reported that hypothalamic–pituitary–adrenal function might be preserved by perioperative full-dose steroid for patients with clinically nonfunctioning pituitary macroadenoma.

Pituitary apoplexy is associated with many predisposing factors, and the exact pathogenesis remains unclear. In the literature, predisposing conditions include not only transient hypertension or hypotension, but also diabetes mellitus, angiographic studies, cardiac surgery, hemodialysis, and certain medications (anticoagulants, isosorbide, and-estrogen) [2–4, 9]. In the present case, some predisposing factors could have been implicated in the process inducing pituitary apoplexy. The first is ischemia from hypotension

during LDLT and re-laparotomy. However, because intraoperative hypotension (systolic pressure <80 mmHg) was temporary and recovered immediately by intervention, this hypotension might not have been associated with this complication. The second is that coagulopathy occurred during surgery and the postoperative course. Some reports have implicated anticoagulants, such as heparin, as a possible predisposing factor [4, 6]. The patient underwent laparotomy again because of bleeding on postoperative day 7, when her platelet counts had been below 30,000/μl and her PT-INR was above 1.5. She was given platelets and FFP to improve her coagulopathy. Since her re-laparotomy, her coagulation status had been normal until her symptom started to appear. Symptoms and signs typically develop during 24–48 h after surgery, but the hypocoagulability during this pre- or intraoperative re-laparotomy might have been associated with this pituitary apoplexy condition. The third factor is transient hypertension. Her hypertension (systolic pressure >160 mmHg, requiring antihypertensive drugs) appeared beginning with re-laparotomy. The cause of hypertension was thought to be a side effect of tacrolimus, abdominal pain, and headache. The fourth factor is dopamine agonist therapy [10]. The patient needed dopamine support to maintain her vital signs during LDLT and re-laparotomy. Knoepfelmacher et al. reported that a causal relationship between dopamine agonist (bromocriptine) and apoplexy has been suggested because adenomas have sometimes shown necrosis at surgery after bromocriptine treatment [11, 12]. This patient received the dopamine agonist only because of the surgery, so this factor might be associated with this complication. Recently, intraoperative beach chair positioning because of cerebral hypoperfusion has been reported as a precipitating factor [13]. The patient in the present report was also in the sitting position for a few hours for rehabilitation. On postoperative day 13, she was in the sitting position for the whole day. This factor also might be associated with this complication. The role of these factors remains purely hypothetical, and further studies are necessary to elucidate the exact role of these factors in the pathophysiological pathway of pituitary apoplexy.

Management of patients with pituitary apoplexy involves both medical and surgical interventions. The outcome of pituitary apoplexy can be fatal if it remains unrecognized. However, if the patient receives immediate medical treatment and surgical decompression, the long-term prognosis is good. The role and timing of pituitary surgery in this condition remains controversial, and some cases have reported that conservative treatment was used with success if no visual field deficit and ophthalmoplegia was present [3]. In the present case, conservative treatment was chosen because of the absence of hormonal activity and mass effects. The availability of MRI scanning may be partly responsible for our confidence in the conservative management of a significant proportion of cases of pituitary apoplexy. Early full steroid replacement might contribute to the success of our conservative management because our patient did not have hormone abnormalities such as irregular thyroid function [8].

A case of pituitary apoplexy occurring after LDLT was reported. Pituitary apoplexy must be suspected in any patients presenting with a headache, polyuria, and hypertension. For anesthesiologists and critical care personnel, it is important to consider this complication as a differential diagnosis in the LDLT setting, especially when the patients postoperatively experience headache, polyuria, and hypertension.

References

1. Cardoso ER, Peterson EW. Pituitary apoplexy: a review. Neurosurgery. 1984;14:363–73.
2. Randeva HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA. Classical pituitary apoplexy: clinical features, management and outcome. Clin Endocrinol. 1999;51:181–8.
3. Sibal L, Ball SG, Connolly V, James RA, Kane P, Kelly WF, Kendall-Taylor P, Mathias D, Perros P, Quinton R, Vaidya B. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. Pituitary. 2004;7:157–63.
4. Liberale G, Bruninx G, Vanderkelen B, Dubois E, Vandueren E, Verhelst G. Pituitary apoplexy after aortic abdominal aneurysm surgery: a case report. Acta Chir Belg. 2006;106:77–80.
5. Sweeney AT, Blake MA, Adelman LS, Habeebulla S, Nachtigall LB, Duff JM, Tully GL 3rd. Pituitary apoplexy precipitating diabetes insipidus. Endocr Pract. 2004;10:135–8.
6. Wiesmann M, Gliemroth J, Kehler U, Missler U. Pituitary apoplexy after cardiac surgery presenting as deep coma with dilated pupils. Acta Anaesthesiol Scand. 1999;43:236–8.
7. Sanno N, Oyama K, Tahara S, Teramoto A, Kato Y. A survey of pituitary incidentaloma in Japan. Eur J Endocrinol. 2003;149:123–7.
8. Cozzi R, Lasio G, Cardia A, Felisati G, Montini M, Attanasio R. Perioperative cortisol can predict hypothalamus-pituitary-adrenal status in clinically non-functioning pituitary adenomas. J Endocrinol Invest. 2009;32:460–4.
9. Punnose J, Agarwal MM, Premchandran JS. Transient diabetes insipidus and hypopituitarism after pituitary apoplexy: a rare association with pericardial effusion and painless thyroiditis. Am J Med Sci. 2000;319:261–4.
10. Murad-Kejbou S, Eggenberger E. Pituitary apoplexy: evaluation, management, and prognosis. Curr Opin Ophthalmol. 2009;20:456–61.
11. Knoepfelmacher M, Gomes MC, Melo ME, Mendonca BB. Pituitary apoplexy during therapy with cabergoline in an adolescent male with prolactin-secreting macroadenoma. Pituitary. 2004;7:83–7.
12. Nawar RN, AbdelMannan D, Selman WR, Arafah BM. Pituitary tumor apoplexy: a review. J Intensive Care Med. 2008;23:75–90.
13. Koga T, Miyao M, Sato M, Hirota K, Kakuyama M, Tanabe H, Fukuda K. Pituitary apoplexy during general anesthesia in beach chair position for shoulder joint arthroplasty. J Anesth. 2010;24:476–8.