



# Pituitary adenoma apoplexy associated with vardenafil intake

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## Abstract

Vardenafil is a potent phosphodiesterase-5 (PDE-5) inhibitor used in the treatment of erectile dysfunction. Several cases of stroke related to the use of PDE-5 inhibitors have been reported. Here, we describe the case of a 51-year-old man with headache and right ophthalmoplegia subsequent to vardenafil consumption. Computed tomography and magnetic resonance imaging showed a suprasellar mass with hemorrhage suggesting pituitary apoplexy. He underwent transsphenoidal resection of the pituitary mass. Histopathology confirmed the diagnosis of a necrotic pituitary adenoma with hemorrhage. This report suggests a possible association between pituitary apoplexy and vardenafil use. In patients with preexisting pituitary adenoma, vardenafil may enhance the risk of pituitary apoplexy. Although headache is the most commonly reported side effect of vardenafil, pituitary apoplexy should be considered in the differential diagnosis of a patient with headache and ophthalmoplegia subsequent to vardenafil intake.

**Keywords** Phosphodiesterase-5 inhibitor · Pituitary adenoma · Pituitary apoplexy · Stroke · Vardenafil

## Abbreviations

CT	Computed tomography
ED	Erectile dysfunction
MRI	Magnetic resonance imaging
PDE-5	Phosphodiesterase-5

## Introduction

Pituitary apoplexy, defined as acute hemorrhage or infarction of a pituitary mass, is a rare event [1]. Several risk factors for pituitary apoplexy have been reported, such as hypertension, hypotension, trauma, surgery, pregnancy, and hormone loading tests [1]. Vardenafil is a potent phosphodiesterase-5 (PDE5) inhibitor prescribed for the

treatment of erectile dysfunction (ED) [2]. Headache is the most commonly reported adverse effect of PDE5 inhibitors [2]. Although several cases of stroke related to PDE5 inhibitor use have been reported [3–9], there is no reported case of pituitary apoplexy associated with PDE5 inhibitor consumption. Here, we describe the case of a patient who developed pituitary apoplexy after vardenafil intake.

## Case description

A 51-year-old man with headache and right ophthalmoplegia presented to our hospital. Five hours prior to symptom onset, he had taken 10 mg vardenafil for the first time in 3 months for ED and had sexual intercourse. The following morning, he woke up with the most severe headache he had ever experienced. His neurological examination showed right oculomotor nerve paralysis. Computed tomography (CT) and magnetic resonance imaging (MRI) showed an acute hemorrhage in the pituitary mass (Fig. 1). Laboratory tests showed hypoglycemia (plasma glucose 60 mg/dl) and hyponatremia (134 mEq/l). Hormone testing demonstrated low levels of cortisol (4.2 µg/dl). Results from additional endocrinology testing were as follows: adrenocorticotrophic hormone: 12.6 pg/ml, normal 7.2–63.3 pg/ml; free T3: 2.0 pg/ml, normal

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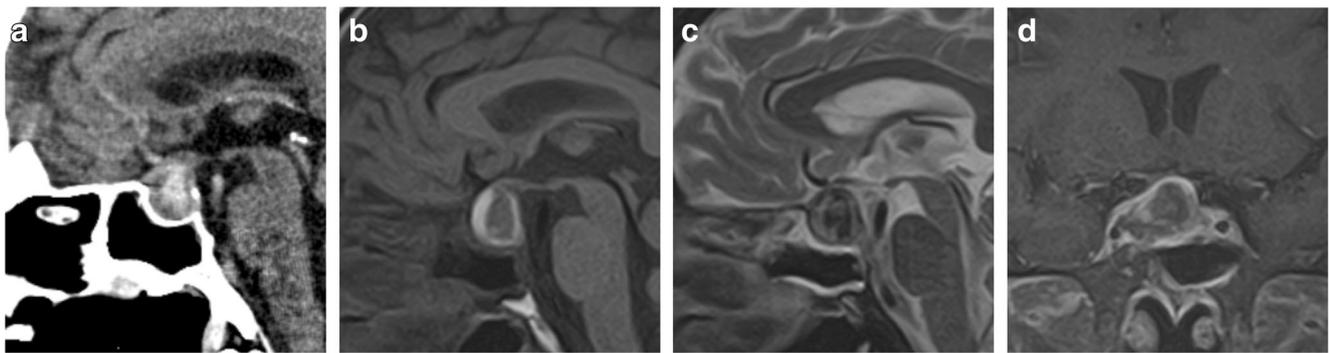
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**Fig. 1** **a** Sagittal brain computed tomography shows a suprasellar mass and acute hemorrhage. **b** Sagittal pituitary magnetic resonance imaging shows a lesion in the pituitary mass that is iso-intense on unenhanced T1-weighted imaging and **c** hypointense on T2-weighted imaging due to the

presence of deoxyhemoglobin. **d** Coronal pituitary magnetic resonance imaging shows right cavernous sinus invasion on contrast-enhanced T1-weighted imaging

1.7–3.7 pg/ml; free T4: 0.8 ng/dl, normal 0.8–1.5 ng/dl; thyroid-stimulating hormone: 1.1  $\mu$ IU/ml, normal 0.4–5.0  $\mu$ IU/ml; prolactin: 5.4 ng/ml, normal 4.3–13.7 ng/ml; follicle-stimulating hormone: 3.7 mIU/ml, normal 2.0–8.3 mIU/ml; luteinizing hormone: 2.8 mIU/ml, normal 0.8–5.7 mIU/ml; and growth hormone: 1.6 ng/ml. Hormone loading tests were not performed. He was treated with hydrocortisone and underwent transsphenoidal resection of the pituitary mass. Histopathology confirmed the diagnosis of a necrotic pituitary adenoma (Fig. 2). Post-operatively, the right oculomotor nerve paralysis improved and he was discharged with a prescription for continued hydrocortisone use.

## Discussion/conclusion

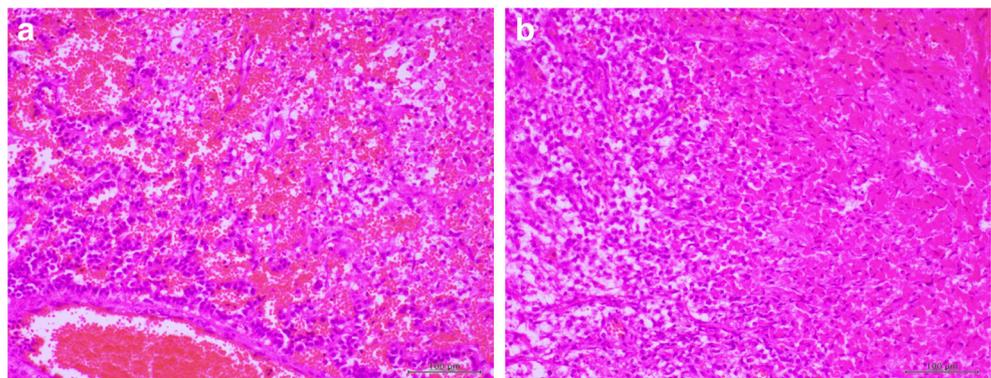
This is the first reported case of pituitary apoplexy associated with vardenafil intake. To date, several cases of intracerebral hemorrhage, subarachnoid hemorrhage, ischemic stroke, and vertebral artery dissection associated with the use of PDE5 inhibitors have been reported [3–9]. However, there is no

reported case of pituitary apoplexy associated with PDE5 inhibitor consumption.

The mechanisms underlying the development of PDE5-inhibitor-related stroke remain unclear. Some authors have hypothesized that transient hypotension and embolization provoked by brief atrial fibrillation, both of which are induced by PDE5 inhibitors, were responsible for the ischemic strokes [2]. Others have proposed that PDE5-inhibitor-induced vasodilation and antiplatelet effects increase the risk of intracerebral hemorrhage [3]. Embolization and unstable blood pressure have also been implicated in pituitary apoplexy [10, 11]. Therefore, hypotension, embolization, vasodilation, and antiplatelet effects which are provoked by PDE5 inhibitor might result in pituitary apoplexy.

This report suggested a possible association between pituitary apoplexy and vardenafil use. In patients with preexisting pituitary adenoma, vardenafil may enhance the risk of pituitary apoplexy. Although headache is the most commonly reported side effect of vardenafil, pituitary apoplexy should be considered in the differential diagnosis of a patient with headache and ophthalmoplegia subsequent to vardenafil intake.

**Fig. 2** **a** Hematoxylin and eosin staining of the resected specimen reveals viable tumor cells with hemorrhage ( $\times 200$ ). **b** Hematoxylin and eosin staining of the resected specimen reveals necrosis and infiltrating leukocytes ( $\times 200$ )



## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

**Informed consent** Informed consent was obtained from all individual participants included in the study.

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