# Pituitary Tumor Apoplexy in Adolescents

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**Key words**
- Adenoma
- Adolescents
- Apoplexy
- Pituitary
- Prolactinoma

**Abbreviations and Acronyms**
ACTH: Adrenocorticotropic hormone
MRI: Magnetic resonance imaging
RCHSD: Rady Children's Hospital San Diego

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OBJECTIVE: **The aim of this study was to determine whether there are differences in pituitary apoplexy and subclinical apoplexy secondary to adenoma hemorrhage in the adolescent population with regard to symptomatology, neuroimaging features, pathology, and outcomes compared with adults.**

METHODS: **A retrospective series of 9 consecutive patients with a diagnosis of pituitary hemorrhage who were surgically treated at Rady's Children's Hospital San Diego, between 2008 and 2013 were evaluated for clinical, endocrine, neuroradiographic, and pathologic features in association with clinical outcomes.**

RESULTS: **Nine patients (6 girls, age 14—21 years) presented to our institution with headache (9/9), nausea (3/9), dizziness (4/9), and visual disturbances (6/9) in the setting of a sellar hemorrhagic tumor on magnetic resonance imaging (MRI). Three patients presented with apoplexy and 6 with subclinical apoplexy. Duration of symptoms ranged from 3 days to 1 year. MRI revealed hemorrhage (9/9), rim enhancement (6/9), sphenoid sinus mucosal thickening (2/9), mass effect on the optic chiasm (8/9), and sellar remodeling (9/9). The percentage of hemorrhage preoperatively observed on MRI ranged from 50% to greater than 95%. On presentation, hyperprolactinemia was recorded in 7 patients, 6 of whom had galactorrhea and/or amenorrhea. Open transsphenoidal decompression was performed in 8/9 patients; 7 of 9 were diagnosed with prolactinoma. Biopsy specimens revealed 10%—90% hemorrhage and no infarction in any of the cases. All patients treated showed improvement of symptoms after surgery (average follow-up, 28.2 months). Postoperative complications included transient diabetes insipidus (n = 5), persistent cerebrospinal fluid rhinorrhea (n = 3), and meningitis (n = 1). Five patients had long-term endocrine sequelae of hyperprolactinemia requiring ongoing medical treatment.**

CONCLUSIONS: **Pituitary hemorrhage resulting in apoplexy or subclinical apoplexy in adolescents may represent a distinct entity with a more indolent symptomatology and more favorable neurologic and endocrine outcome compared with adults that is worthy of further validation in a multi-institutional cohort.**

## INTRODUCTION

Pituitary apoplexy can occur as the result of infarction, hemorrhage, or a combination of hemorrhagic infarction in a pituitary tumor. It is a clinical syndrome identified by a rapid onset of signs and symptoms caused by either hemorrhage or infarction of a pituitary tumor (4, 16, 32). Contributing to pituitary apoplexy is relatively rapid enlargement of a pituitary tumor resulting in compression of surrounding structures, potentially causing pituitary insufficiency (2, 4-7, 9). Potential predisposing factors that have been documented in the literature include coagulation disorder, dopamine agonist therapy, coronary artery bypass surgery, anticoagulant therapy, radiotherapy, head trauma, diabetes mellitus, pregnancy, hypophyseal dynamic testing, carotid angiography, or upper respiratory tract infections (33). Some authors prefer to distinguish pituitary apoplexy from subclinical presentations, where magnetic resonance imaging (MRI) indicates isolated areas of hemorrhage or infarction that is later confirmed intraoperatively and on pathologic analysis (7, 13, 14, 22, 33). Therefore, the incidence of this clinical syndrome varies depending on definitions used by the reporting authors. In the adult population subclinical hemorrhage has been reported in 14%—22% of pituitary macroadenomas (31). However, symptomatic pituitary apoplexy is seldom seen, occurring in 0.6%—9% of the population (16, 31).

The overwhelming majority of data and information for this clinical presentation comes from the adult literature. Patients typically experience a rapid onset of symptoms that varies from headache with or without endocrine dysfunction, visual deficits, ophthalmoplegia, altered mental status, or coma (4, 20, 28, 31, 34). Literature regarding pituitary apoplexy in the pediatric or adolescent population is restricted to case reports or individual cases that are part of a larger series discussing pituitary adenomas in this

population (18, 19, 21, 23). There is no reported patient series dedicated to pituitary apoplexy or subclinical apoplexy in the pediatric or adolescent population after our review of the literature. Therefore, there remain gaps in our knowledge of the differences between adults and children in the presentation, severity of symptoms, and outcomes of this disease between the 2 groups. In this study, from a single pediatric neurosurgical center, we review the clinical presentation, radiologic features, histopathology, and outcomes of 9 adolescent patients treated for pituitary apoplexy and subclinical apoplexy secondary to hemorrhage during a 6-year period.

## CLINICAL MATERIALS AND METHODS

The retrospective series includes patients with pituitary mass hemorrhage who were treated at Rady Children's Hospital San Diego (RCHSD), California, by a single neurosurgeon between 2008 and 2013. Chart reviews were performed in accordance to University of California San Diego and RCHSD Human Research Protections Program guidelines. The diagnosis of pituitary apoplexy or subclinical apoplexy was determined from the clinical presentation and neuroimaging features. Patient with clinical (acute) pituitary apoplexy had rapid onset of neurologic symptoms that included headaches, nausea, vomiting, cranial nerve deficits, loss of visual acuity, or altered level of consciousness. Patients with subclinical apoplexy were defined as showing pituitary hemorrhage on MRI along with evidence of hemorrhage on histopathologic analysis without acute clinical symptoms. Patients who presented with symptoms of Rathke cleft cysts, craniopharyngiomas, or nonadenomatous lesions were excluded.

### Patient Population

Records were identified during a 6-year period of 9 consecutive patients who were treated for pituitary apoplexy and subclinical apoplexy. Six female and 3 male patients ranged in age from 14 to 23 years with a mean age of 17 and median age of 17. The overall incidence of combined pituitary apoplexy and subclinical apoplexy in patients treated surgically for pituitary adenomas between 2008 and 2013 at our institution was 22% (9 of 41 cases). Three patients presented with apoplexy and 6 with subclinical apoplexy. Length of follow-up in the study group ranged from 5 to 49 months, with a mean of 28.2 months. Seven patients had prolactinomas, 1 had an ACTH secreting tumor, and 1 had a nonfunctioning adenoma. One patient with a known pituitary mass was lost to follow-up and presented 5 years later after developing acute visual impairment. Predisposing factors of pituitary apoplexy were seen in 4 patients. Three patients were taking a dopamine agonist, and the other patient presented after a motor vehicle accident.

### Histopathology

All 9 patients included in the study had a histopathologic examination performed of the pituitary lesion removed during surgery and could therefore be included in the retrospective analysis. The histopathologic results were divided to show the percentage of hemorrhage and percentage of necrosis in each sample.

### Pre- and Postoperative Imaging/Vision/Endocrine Assessment

All 9 patients in the analysis underwent pre- and postoperative MRI. MRIs and reports were collected and reviewed by a pediatric neuroradiologist at RCHSD. The neuroradiographic features that were reviewed included the following: presence of blood products indicating hemorrhage; the appearance of infarction alone without hemorrhage; the appearance of a pituitary tumor alone without imaging evidence of apoplexy; pituitary mass rim enhancement; evidence of sphenoid sinus mucosal thickening; mass effect on surrounding structures; and remodeling of the sella turcica.

All patients in the series were evaluated by a pediatric endocrinologist both pre- and postoperatively. Every patient in the group who complained of visual symptoms underwent formal presurgical vision testing and postsurgical evaluation by a neuro-ophthalmologist at RCHSD.

## RESULTS

### Presenting Symptoms

All patients presented with a Glasgow Coma Scale of 15. Duration of symptoms ranged from 3 days to 1 year in our group. Time to presentation to RCHSD neurosurgery department ranged from 1 to 39 days. Headache was the most common symptom present in 9 patients (100%), followed by visual impairment seen in 6 patients (66%). Four patients (44%) had dizziness, and 3 had nausea (33%) (Table 1). No patients in the study presented with nonfunctional vision or blindness. From the 6 patients with complaints of visual impairment, 3 had confirmed visual field deficits on formal testing whereas 2 patients had photophobia with normal visual fields and 1 had blurry vision with no deficits on formal visual field exam. One patient experienced a cranial nerve 3 palsy that was improving when he arrived to clinic. Galactorrhea and/or amenorrhea were present in 6 of the 9 patients (66%). One patient experienced sleep disturbance and altered mood. No patient presented in a mentally altered or comatose state.

### Ophthalmologic Findings and Endocrine Status

Visual impairment was seen in 6 patients (66%). There were no patients with nonfunctional vision loss or blindness. One patient had ophthalmoplegia caused by a cranial nerve 3 palsy that was improving when he presented. Three patients had confirmed visual field deficits on formal testing. Two had peripheral field deficits greater on the left compared with the right side. One had developed bitemporal field cuts. The remaining 3 had no deficits on formal visual field examination, one had blurry vision, and the other 2 photophobia but no deficits of visual acuity. No patients in our group had specific changes in their visual acuity on presentation. Regarding endocrine evaluation, 1 patient had panhypopitiuitarism from previous transsphenoidal surgeries. Seven patients (77%) experienced Hyperprolactinemia; from these, 6 had symptoms of amenorrhea, galactorrhea, or both (Table 1). Serum prolactin values in the 7 patients ranged from 26 to 5620 ng/mL. Two patients were on cabergoline and 1 on bromocriptine before their operations. One patient experienced symptoms of weight gain initially suspected to be attributed to an adrenocorticotropic hormone (ACTH)-producing tumor but no preoperative laboratory values were collected to confirm this hypothesis.