Endoscopic Endonasal Surgery for Pituitary Apoplexy: Evidence On a 75-Case Series From a Tertiary Care Center

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■ BACKGROUND: **The optimal management of pituitary apoplexy (PA) remains debated. The aim of this study was to assess the outcome of the transsphenoidal approach for PA in a large surgical experience.**

■ MATERIALS: **Each consecutive case of PA consecutively operated by endoscopic endonasal approach from our tertiary care center, from 1998 to 2015, was included in this series.**

■ RESULTS: **Seventy-five patients (47 male; mean age 52.4 ± 16.2 years) were included. Mean follow-up was 69.3 ± 46.7 months. On admission, all patients presented with abrupt severe headache (100%), associated with anterior hypopituitarism in 51 patients (68%), visual disturbances in 55 (73.4%), ophthalmoplegia in 38 (50.7%), and a remarkable reduction of consciousness in 2 (2.6%). Apoplexy proved to be ischemic in 35 patients (46.7%) and hemorrhagic in 40 (53.3%). Patients with hemorrhagic necrosis presented more often with major suprasellar expansion ($P = 0.012$) Radical removal was achieved in 60 cases (80%). Surgical morbidity consisted in one case of postoperative cerebrospinal fluid leak (1.3%). Anterior hypopituitarism worsened in 15 cases (20%), and diabetes insipidus occurred in 4 cases (5.3%). Ophthalmoplegia improved/normalized in 71% and visual symptoms in 85.5% of the patients, with better results achieved in ischemic forms ($P = 0.043$). The 2 comatose patients regained normal consciousness.**

■ CONCLUSIONS: **The endoscopic endonasal approach represents a valid, effective, and safe technique in the management of PA. Favorable outcomes can be achieved by referring patients to dedicated pituitary centers with a multidisciplinary team. Further studies are still needed to define criteria for surgical indication and to identify outcome predictors.**

INTRODUCTION

In the last few years, pituitary apoplexy (PA) has been at the center of renewed interest in the medical literature.[1-11] Indeed, the release of the U.K. guidelines in 2010, and of the emergency guidance by the Society for Endocrinology in 2016, have raised a worldwide debate about the management of this serious, potentially dramatic condition, as demonstrated by the significant increase of publications in the field during the last 5 years.[12,13]

Many authors have contributed to the discussion on the appropriateness and indications of surgical or conservative management of symptomatic PA by reporting personal clinical and

Key words
- Cranial nerve palsy
- Endonasal approach
- Endoscopic pituitary apoplexy
- Headache
- Hemorrhagic necrosis
- Ischemic necrosis
- Pituitary apoplexy score
- Visual disturbances

Abbreviations and Acronyms
ACTH: Adrenocorticotropic hormone
CN: Cranial nerve
CSF: Cerebrospinale fluid
DI: Diabetes insipidus
EEA: Endoscopic endonasal approach
GH: Growth hormone
MRI: Magnetic resonance imaging
PA: Pituitary apoplexy
TA: Transsphenoidal approach

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Citation: World Neurosurg. (2017) 106:331-338. http://dx.doi.org/10.1016/j.wneu.2017.06.117

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

surgical experience.[1-6,8,10] However, the vast majority of these series are heterogeneous, with a low number of cases included, or a short follow-up.[6] This study aimed at evaluating the outcome and predictors of transsphenoidal approach (TA) in a large and homogenous cohort of patients with PA treated by a dedicated multidisciplinary team.

MATERIALS AND METHODS

Each consecutive patient with a clinical diagnosis of PA, confirmed by neuroimaging and histological tests operated on through an endoscopic endonasal approach (EEA), from May 1998 to December 2015, at the Center of Pituitary and Endoscopic Skull Base Surgery, IRCCS Institute of Neurological Sciences di Bologna (Italy), were included in this study.

Preoperative symptoms with particular attention to visual deficits and cranial nerve (CN) palsies were considered based on the medical records. Before surgery, all patients underwent a blood collection for the assessment of basal pituitary function (i.e., plasma adrenocorticotropic hormone [ACTH]; serum cortisol, prolactin, growth hormone [GH], follicle-stimulating hormone, luteinizing hormone, fT4, and thyroid-stimulating hormone), serum electrolytes, and plasmatic osmolarity. Hydrocortisone was administered intravenously just after blood collection. In patients complaining of visual defects, an urgent ophthalmologic consultation and evaluation of the visual field also were performed. All cases underwent a preoperative complete neurologic physical examination. PA score was applied retrospectively based on these findings (Table 1).[9] Each case underwent magnetic resonance imaging (MRI) with gadolinium to evaluate the size, the local invasiveness of the tumor, and the cavernous sinus infiltration, according to Knosp classification.[14]

Surgery was performed in the first 1–5 days after hospital admittance and as soon as possible on an emergency/urgency base in case of visual disturbances, progressive reduction of consciousness, or worsening of ptosis and/or ophthalmoplegia due to CN palsy. All surgical procedures were performed through an EEA. Our surgical technique has been reported previously.[15-17] To summarize in brief, the patient is placed in the semi-sitting position, with the thorax slightly elevated. In the great majority of cases, a midline TA, requiring a posterior septostomy and anterior wide sphenoidotomy, was performed to access to the sella.[16,17] Normally, we avoid to resect the middle turbinate.[16,17] For very selected cases with invasion of the lateral and/or anteroinferior compartment of cavernous sinus, a ethmoido-pterygo-sphenoidal approach was preferred to access to these paramedian extending apoplectic adenomas.[15]

Table 1. Pituitary Apoplexy Score

Grade	
1	Asymptomatic
2	Only endocrinologic deficit
3	Headache (acute onset or acute-to-chronic)
4	Ophthlmoplegia due to oculomotor CN palsies
5	Visual disturbances or decreased conscious level

Adapted from Jho et al.[9]
CN, cranial nerve.

The extent of the tumor removal was calculated on the basis of the surgical reports and postoperative MRI. Tumor removal was considered radical in case of absence of tumor remnants; subtotal for remnants <20% of the initial tumor mass; partial in all the other cases. Morbidity was considered on basis of clinical records.

The surgical specimens were immediately fixed for histologic and immunohistochemical examinations with 10% buffered formalin embedded in paraffin. Serial, 3-μm-thick paraffin sections were processed with standardized automated procedures with the use of prediluted antisera for the pituitary hormone antibodies (Ventana-Benchmark, Tucson, Arizona, USA). Hematoxylin and eosin, reticulin stain, and periodic Acid-Schiff staining were performed in all cases. The scant reticulin network of the adenoma is highlighted in cases of PA.

Cases were classified retrospectively into PA with ischemic and hemorrhagic necrosis by 2 board-certified pathologists (A.R. and S.A.) in double blind, according to the following criteria:

- hemorrhagic necrosis: hemorrhagic infarction of pituitary adenomas associated with intratumoral hemorrhage; and
- ischemic necrosis: extremely extensive coagulation necrosis with or without spotty hemorrhage and frequent involvement of the normal pituitary gland. The basic architecture of the infarcted adenoma and its stroma is best demonstrated on reticulin stain.

Postoperative MRI, ophthalmologic, neurologic, and endocrinologic evaluations were performed 3 months after surgery to assess early surgical outcome, then repeated annually. Mean follow-up was 69.3 ± 46.7 months.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation (SD), whereas categorical variables as absolute frequency and relative frequency (%). The Fisher exact test was used to evaluate the univariate association between postoperative outcomes (ophthalmologic, neurologic, and endocrinologic) and other variables (sex, age, Hardy-Wilson grade, Knosp grade, local invasiveness, cavernous sinus infiltration, necrosis). The Fisher exact test was used to evaluate the different characteristic between hemorrhagic and ischemic necrosis. All P values were based on 2-sided tests, and $P < 0.05$ were considered significant. Statistical analysis was performed with the statistical package Stata SE, 14.2 (StataCorp LP, College Station, Texas, USA).

RESULTS

Seventy-five patients (47 male, 28 female, ratio: 1.7) were included in the study. Mean age was 52.4 ± 16.2 years. All patients reported acute headache with abrupt onset associated with anterior pituitary deficiency in 51 patients (68%), whereas none suffered from diabetes insipidus (DI) (Table 1).