# Third, Fourth, and Sixth Cranial Nerve Palsies in Pituitary Apoplexy

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■ BACKGROUND: **Pituitary apoplexy (PA) often presents with acute headache and neuro-ophthalmic manifestations, including ocular motility dysfunction (OMD) from cranial nerve palsies (CNPs). Our goal was to describe the epidemiology and outcomes of OMD in a large, single-center series of patients with PA.**

■ METHODS: **We conducted a retrospective chart review of all patients with PA seen in our pituitary center between January 1995 and December 2012. Presenting neuro-ophthalmic, endocrine, and radiologic data, as well as neuro-ophthalmology follow-up data, were collected.**

■ RESULTS: **We identified 235 patients with PA, 59 of whom (25%) had OMD. Twenty-seven of those 59 patients underwent neuro-ophthalmic evaluation. Preoperatively, 23 of these 27 patients had unilateral OMD, 18 (78%) with a single CNP and 5 (22%) with multiple CNPs. Bilateral OMD was present in 4 of the 27 patients. Postoperatively, 24 of the 27 patients with OMD had follow-up (median duration, 7 months; interquartile range [IQR], 3–17 months). At the last postoperative follow-up, 7 of these 24 patients (29%) had OMD (5 unilateral, 2 bilateral). OMD resolved in 3 of the 24 patients (12%) within 1 month, in 13 of 21 patients (62%) within 6 months (3 lost to follow-up), and in 17 of 19 patients (89%) within 1 year (2 lost to follow-up). Surgery was performed at ≤14 days after presentation in 16 of 18 (89%) resolved cases and in 4 of 6 (67%) unresolved cases. Patients with OMD were more likely than those without OMD to have larger tumors (2.6 vs. 2.0 cm; $P < 0.001$), panhypopituitarism (31% vs. 14%; $P = 0.005$), and necrosis (58% vs. 37%; $P = 0.03$).**

■ CONCLUSIONS: **OMD from CNPs is common in PA, occurring in one-quarter of patients, and is frequently associated with certain radiologic, endocrinologic, and pathological features. The prognosis is excellent, with 90% of cases of OMD resolving by 1 year after early pituitary surgery.**

Pituitary apoplexy (PA) is a potentially life-threatening clinical syndrome occurring after rapid expansion of the contents of the sella turcica, generally caused by hemorrhage within or infarction of a preexisting pituitary adenoma.[1-3] Clinical presentations range from isolated headache to a conglomerate of additional symptoms, including vomiting, altered consciousness, visual loss, and diplopia.[4,5] In PA, diplopia arises from ocular motility dysfunction (OMD) due to cranial nerve palsies (CNPs), which have been reported in 40%–100% of patients with PA.[5] Data on the neuro-ophthalmic presentation of OMDs in patients with PA are limited, however, especially when altered mental status is present or immediate surgery is performed.[5] In those cases, neuro-ophthalmic examination is often postponed and sometimes never performed. The aims of the present study were to describe the characteristics of OMDs in patients with PA, and to analyze the relationships between patient clinical outcomes and neuro-ophthalmologic, pathological, endocrine, and radiologic findings.

**Key Words**
- Cranial nerve palsy
- Diplopia
- Pituitary adenoma
- Pituitary apoplexy

**Abbreviations and Acronyms**
CN: Cranial nerve
CNP: Cranial nerve palsy
GVF: Goldmann visual field
HVF: Humphrey visual field
IQR: Interquartile range
MD: Mean deviation
OMD: Ocular motility dysfunction
OR: Odds ratio
PA: Pituitary apoplexy
VA: Visual acuity

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## METHODS

The study was approved by our university's Institutional Review Board.

### Inclusion Criteria and Patient Characteristics

All consecutive charts of patients with PA seen at our institution's Pituitary Center between January 1995 and December 2012 were reviewed. PA was defined as a radiologically, surgically, or pathologically confirmed hemorrhagic or necrotic pituitary tumor in a patient with acute headache and/or visual changes.[6] The following data were collected for each patient: age, sex, date of presentation, clinical symptoms (e.g., headache, visual loss, diplopia, altered mental status), size of the tumor, endocrine status (e.g., secreting/nonsecreting, panhypopituitarism), surgical or medical management, date of surgery, and dates of neuro-ophthalmic evaluations, if any. Patients with PA (with or without OMD) seen at least once in our neuro-ophthalmology service were included in the subsequent analyses.

### Neuro-Ophthalmic Evaluation

All patients seen in our neuro-ophthalmology service were evaluated in a standardized fashion. The following assessments were performed at presentation and at every follow-up visit: best corrected Snellen visual acuity (VA) or VA with pinhole (converted into logarithm of the minimal angle of resolution for statistical analysis), formal visual fields, ocular motility, pupil examination, and fundus examination. For formal visual fields assessment, Humphrey visual field (HVF) and Goldmann visual field (GVF) data were obtained and graded according to pattern (bitemporal hemianopia, homonymous hemianopia, or unilateral visual field defect) and size (small, less than a quadrant; partial, at least an entire quadrant; complete, involving the entire hemifield), and when HVF was performed, the mean deviation (MD) was recorded.

In patients with OMD, the time to recovery after surgery was assessed when follow-up examinations were available. For patients without a neuro-ophthalmic examination before surgery, a bedside history and physical examination (performed by the neurosurgeon) were obtained, including patient-reported symptoms of visual loss and diplopia, ocular motility examination, and confrontation visual field examination.

### Statistical Analysis

Descriptive statistics were calculated for all variables of interest, both overall and for the patients seen in the neuro-ophthalmology unit. Data were collected and analyzed using Stata 1998 (StataCorp, College Station, Texas, USA) and R 3.2.2 (R Institute for Statistical Computing, Vienna, Austria). The t test was used to compare continuous variables, and the $\chi^2$ test with Yates correction was used to compare qualitative variables. Fisher's exact test was used when cell sizes were small ($n \leq 5$). To deal with intereye and intrapatient correlations, VA and MD for the right and left eyes were averaged for each patient. Logistic regression was used to assess OMD as an independent risk factor for visual loss, panhypopituitarism, and altered mental status, controlling for tumor maximum diameter, and patient age and sex. A $P$ value $<0.05$ was considered statistically significant.

## RESULTS

Of the 235 patients with PA, 147 underwent surgery (median time to surgery postpresentation, 21 days), and 88 were treated only medically. Fifty-nine of these patients (25%) had at least 1 documented OMD, and only 3 of them did not undergo surgery (Table 1). Patients with OMD were more likely to be men (59% vs. 36%; $P = 0.002$). Altered mental status (14% vs. 5%; $P = 0.03$) and visual loss (64% vs. 35%; $P < 0.001$) were more frequently

**Table 1.** Features of Patients with PA With OMD and Without OMD

| Characteristic | With OMD (n = 59) | Without OMD (n = 176) | *P* Value |
|---|---|---|---|
| Age at presentation, years, mean ± SD | 48 ± 12 | 46 ± 17 | 0.47 |
| M/F sex ratio (n) | 1.10 (31/28) | 0.63 (68/107) | **0.002** |
| Clinical presentation, n (%) | | | |
| Headaches | 50 (85) | 142 (80) | 0.48 |
| Altered mental status | 8 (14) | 9 (5) | **0.03** |
| Vomiting | 14 (24) | 30 (17) | 0.25 |
| Complaint of decreased vision | 38 (64) | 62 (35) | **<0.001** |
| Endocrine evaluation, n (%) | | | |
| Secreting adenoma | 13 (22) | 58 (33) | 0.11 |
| Panhypopituitarism | 18 (31) | 25 (14) | **0.005** |
| Endocrine deficiency (axes), n (%) | | | |
| Adrenal | 17 (29) | 36 (20) | 0.18 |
| Somatotropic | 9 (15) | 26 (15) | 0.92 |
| Thyroid | 14 (24) | 48 (27) | 0.59 |
| Gonadal | 37 (62) | 84 (47) | **0.04** |
| Prolactin | 5 (8) | 19 (11) | 0.07 |
| Radiologic evaluation, median (IQR) | | | |
| Maximum diameter, cm | 2.6 (1.85–3.2) | 2.01 (1.2–2.5) | **<0.001** |
| AP, cm | 2.04 (1.5–2.6) | 1.7 (1–2.1) | **0.045** |
| CC, cm | 2.48 (1.7–3.2) | 1.87 (1.1–2.5) | **<0.001** |
| T, cm | 2.36 (1.9–3) | 1.77 (1.1–2.3) | **<0.001** |
| Pathology, n (%) | | | **0.03*** |
| Necrosis alone | 28 (58) | 23 (37) | |
| Necrosis and hemorrhage | 9 (19) | 14 (8) | |
| Hemorrhage alone | 11 (23) | 25 (22) | |
| Surgical management, n (%) | 56 (95) | 91 (52) | **<0.001** |

Significant *P* values are in bold type.
PA, pituitary apoplexy; OMD, ocular motility dysfunction; SD, standard deviation; M, male; F, female; IQR, interquartile range; AP, anteroposterior; CC, craniocaudal; T, transverse.
*Necrosis alone vs. any hemorrhage.