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

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Abstract

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 PA patients.

Methods—A retrospective chart review of all patients with PA seen in our Pituitary Center (1/1995–12/2012) was conducted. Presenting neuro-ophthalmic, endocrine, and radiologic data as well as neuro-ophthalmology follow-up were collected.

Results—We identified 235 PA patients, among whom 59 (25%) had OMD; 27/59 had neuro-ophthalmic evaluation. Pre-operatively, 23/27 patients had unilateral OMD, 18/23 (78%) had single and 5/23 (22%) multiple CNPs. Bilateral OMD was present in 4/27 patients. Postoperatively, 24/27 OMD patients had follow-up (median duration: 7 months [IQR: 3–17]). At last post-operative follow-up, 7/24 (29%) patients had OMD (5 unilateral, 2 bilateral). OMD resolved in 3/24 (12%) patients within 1 month, 13/21(62%) patients within 6 months (3 lost to follow-up), and 17/19 (89%) within one year (2 lost to follow-up). Surgery occurred ≤14 days post-presentation in 16/18 (89%) of resolved vs. 4/6 (67%) of 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%, $p=0.03$).

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Conclusion—Ocular motility dysfunction from cranial nerve palsies is common in PA, occurring in one-quarter of patients, and are more frequently associated with certain radiologic, endocrinologic, and pathologic features. The prognosis is excellent, with 90% of OMD resolved at one year after early pituitary surgery.

Keywords

Pituitary apoplexy; diplopia; cranial nerve palsy; pituitary adenoma

Introduction

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 pre-existing 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) from cranial nerve palsies (CNPs, which have been reported in 40–100% of patients with PA.[5] However, limited data regarding the neuro-ophthalmic presentation of OMDs in PA patients are available, 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 aim of our study was to describe the characteristics of OMDs in PA patients, and to analyze the relationship between patient clinical outcomes and neuro-ophthalmologic, pathologic, endocrine, and radiologic findings.

Materials and 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, gender, date of presentation, clinical symptoms (headaches, visual loss, diplopia, and altered mental status), size of the tumor, endocrine status (secreting/non-secreting, panhypopituitarism), surgical or medical management, date of surgery and, if any, dates of neuro-ophthalmic evaluations. PA patients (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 data were collected at presentation and at every follow-up visit: 1) best corrected Snellen visual acuity (VA) or VA with pinhole (converted into logMAR for statistical analysis); 2) formal visual fields (Humphrey visual field (HVF) and Goldmann visual field (GVF)) were obtained, and were graded according to their 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 hemi-field) and when HVF was performed, the mean deviation (MD) was recorded; 3) ocular motility; 4) pupil examination; and 5) fundus examination.

In patients with OMD, the time to recovery after surgery was assessed when follow-up examinations were available. When patients did not have a neuro-ophthalmic examination prior to surgery, the bedside history and physical examination performed by the neurosurgeon was obtained and included 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 patients seen in the neuro-ophthalmology unit. Data were collected and analyzed using Stata 1998 and R 3.2.2. A t-test was used to compare continuous variables. A χ^2 test with Yates' correction was used to compare qualitative variables. Fisher's exact test was employed when cell sizes were small ($N \leq 5$). To deal with inter-eye, intra-patient correlations, VA and MD for the right and left eyes were averaged for each patient. Logistic regression was used to assess whether OMD was in independent risk factor for visual loss, panhypopituitarism, and altered mental status controlling for tumor maximum diameter, age, and sex. A p-value <0.05 was considered as statistically significant.

Results

Of the 235 patients with PA, 147 had surgery (median time to surgery post-presentation: 21 days) and 88 were treated only medically. Fifty-nine (25%) had at least one 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 reported in patients with OMD than those without OMD. Of the 147 patients who had surgery, 57 were seen by neuro-ophthalmology and 27 of them had OMD.

1. Initial presentation

Twenty of these 27 PA patients with OMD were seen by neuro-ophthalmology prior to surgery. The 7 remaining patients were seen in neuro-ophthalmology after surgery (4 within one month and the other within 5 months of surgery), and data regarding their initial presentation were collected from the neurosurgeon's examination.

a. Cranial nerve palsies (Table 2; Figure)—CNP VI was the most frequent (n=21 eyes), followed by CNP III (n=17) and CNP IV (n=7). CNP VI was bilateral in 3 patients. Two of these patients had a large sellar mass invading both cavernous sinuses, and they both had other CNPs (one had associated bilateral CNP III and CNP IV, and one had CNP III, CNP IV and CNP VI in only one eye); in the third patient, the suprasellar mass was abutting both cavernous sinuses. In the 17 eyes with CNP III, the pupil was involved in 6 eyes and ptosis was present in 11 eyes. CNP IV was always associated with another CNP in the same eye.

b. Visual acuity—Median VA in OMD patients was worse, but not significantly different, than the median VA of patients without OMD (0.35 [IQR: 0.05–0.87] vs. 0.1 logMAR [IQR: 0.1–0.35]; p=0.17). Among the 27 patients seen in neuro-ophthalmology, 6 (22%) patients with OMD had at least one eye worse than 20/200 vs. 7 (23%) patients in the non-OMD group.

c. Visual field (Table 3)—Forty-four eyes had a visual field examination, and 26 (59%) of these had a pituitary-tumor-related visual field defect. Twelve patients had a bitemporal hemianopia (including one junctional syndrome) and 2 patients had a unilateral optic neuropathy. Median MD in OMD patients was lower, but not significantly different, from median MD of patients without OMD (−6.58 [IQR: −2.25, −9.31] vs. −4.62 [IQR: −1.88, −11.54]; p=0.98).

2. Endocrine findings

Of the 235 overall patients with PA, secreting adenomas were less frequent in patients with OMD (22% vs. 33%, p=0.11), and instead patients with OMDs were significantly more likely to have panhypopituitarism (e.g., 31% vs. 14%, p=0.005). Only 14% of secreting pituitary adenomas with apoplexy exhibited OMD whereas 44% of PA patients with panhypopituitarism had OMD (p<0.001). There were no significant differences in the axis deficiencies (Table 1), except for the gonadal axis deficiency, which was more common in patients with OMD (37% vs. 84%, p=0.04).

3. Radiologic findings

The tumor's radiological size was significantly larger in patients with OMD (mean maximum diameter: 2.6 vs. 2.0 cm; p<0.001) as were the measurements in every plane (Table 1). All patients exhibited hemorrhage and/or signs of necrosis of the pituitary gland. Various mechanisms of nerve compression were observed including unilateral or bilateral cavernous sinus invasion (16 patients, including 7 with a single CNP VI, 1 with a single CNP III and the remaining had multiple CNPs), abutment without invasion of the cavernous sinuses (9 patients, including 8 with a single CNP III and 1 with a single CNP VI), and nerve compression outside of the cavernous sinus (2 patients with CNP VI). When compression of the nerves occurred outside of the cavernous sinus, there was invasion of the clivus along the route of CN VI.

4. Post-operative examination (Table 4)

Overall, patients with OMD were more likely to undergo surgery (95% vs. 52%, p<0.001; Table 1). Twenty-four patients had at least one neuro-ophthalmic evaluation after surgery. Surgery occurred ≤30 days post-presentation in 23 (96%; median 12 days). Median VA improved from 0.28 (IQR: 0.07–1.07) preoperatively to 0.1 (IQR: 0.0–0.2) postoperatively (p=0.001). Forty-eight eyes had a visual field examination and 16 of 48 (33%) had at least a small hemianopic defect. Seven patients had a bitemporal hemianopia and 2 patients had a unilateral optic neuropathy. All patients with secreting adenomas who did not undergo surgery had prolactinomas. OMD resolved in 3 of 24 (12%) patients within one month, in 13 of 21 (62%) patients within 6 months (3 lost to follow-up), and 17 of 19 (89%) within one year (2 additional lost to follow-up). No patient experienced aberrant regeneration of CN III

after surgery. Surgery occurred ≤14 days post-presentation in 16/18 (89%) of resolved vs. 4/6 (67%) of cases who did not resolve or had incomplete follow-up at one year (p=0.25).

5. Pathology findings

In the overall series of PA patients, 110 underwent surgery of which 51 (46%) had only necrosis of the pituitary gland. In patients with OMD, necrosis of the gland was more frequently reported, with 58% of the patients having only necrosis of the pituitary gland, 9% both necrosis and hemorrhage, and 23% only hemorrhage. In the group without OMD, 37% of the patients had a necrotic only PA, 8% had both necrosis and hemorrhage, and 22% had hemorrhage only in the pituitary gland. There were significantly more patients with necrosis alone in the group with OMD vs. without OMD (p = 0.03).

6. Multivariable analysis

Multivariable logistic regression models controlling for maximum tumor diameter, age, and sex supported OMD as an independent risk factor for visual loss (odds ratio [OR] = 2.6; 95%CI: 1.2–5.3; p=0.007) and panhypopituitarism (OR = 2.9; 95%CI: 1.2–6.2; p=0.008), but not altered mental status (OR = 2.6; 95%CI: 0.83–8.5; p=0.10).

Discussion

Pituitary apoplexy commonly presents with neuro-ophthalmic symptoms and signs. In our large, single-center series of PA patients, 25% had uni- or bilateral OMDs at presentation. In the neurosurgical literature, several retrospective case series of PA patients report on OMD, but very few provide detailed neuro-ophthalmic data. In these series, OMD was reported to occur in 16–100% of PA patients.[2,3,7–30]

In our series, the most common OMD was CN VI followed by CN III, consistent with several previous reports,[7,10–12] although other series have reported more frequent CN III than CN VI involvement.[3,13–16,9,17–20,31] Our higher frequency of CN compression within the cavernous sinuses (14 patients) vs. abutment without invasion of the cavernous sinuses (10 patients) may partially explain the higher prevalence of CN VI vs. CN III in our series. This is because abutment without invasion most commonly results in CNP III since CN III is located in the same horizontal plane as the pituitary gland,[32] and this pattern was also seen in our series. However, direct CN III compression outside the cavernous sinus is also possible. For example, Kobayashi et al. reported 2 cases of isolated CNP III in PA without cavernous sinus invasion in which the tumor had some mass effect on CN III at the level of the oculomotor trigone after erosion of the posterior clinoid process.[33]

CN VI may also be involved outside the cavernous sinus at the level of Dorello's canal.[34] In fact, 2 of our patients with isolated CNP VI had involvement of the clivus, neither with invasion of the cavernous sinus. One of these patients had a bilateral CNP VI that resolved after the clivus was opened during the procedure even though a coexisting abutment of the cavernous sinus persisted post-operatively, strongly suggesting that the bilateral CNP VI occurred at the level of the clivus rather than from the cavernous sinus abutment.

In our series, all CNP IV occurred in association with other CNPs, suggesting that an isolated CNP IV is very unlikely to be secondary to PA. To our knowledge, there is no such report in PA, and we are aware of only one published case of isolated CNP IV in the setting of pituitary macroadenoma.[21]

While we found the VA of our patients with OMD to be worse at presentation compared to those without OMD, the difference was not significant. Very few studies provide specific data on the VA of PA patients, especially specific to those with OMD. However, two studies have suggested a possible association between OMD and very poor VA,[7,8] and another reported normal visual acuity in only 2 out of 7 eyes with OMD.[9] Among our patients with PA and OMD, nearly two thirds overall reported vision loss.

Given the high co-occurrence of OMD and vision loss in our patients, and that there is essentially no disagreement about the need for early surgery when vision loss is present in PA, it is unsurprising that all but three of our patients with OMD had surgery. Our nearly universal use of early surgical management makes it difficult for us to comment on the benefit or harm of later surgery in PA despite considerable controversy about the management of PA patients with OMD and no vision loss. Indeed, several studies report improvement after delayed surgery and even with conservative management,[19,25,35,36] and Rajasakeran et al.'s 2010 proposed guidelines suggest that immediate surgery is not indicated for OMD without visual field defects or reduced VA.[22] Based primarily on descriptive case series, they further conclude that conservative management alone leads to OMD resolution typically within days or weeks. On the other hand, Verrees et al. advocate for early surgery, [23] which they and others have found to be a successful treatment for PA patients with OMD [3,15,9,17,8,23]. Jho et al. also advocated for early surgery in patients with OMD and no visual loss in 2014 when they proposed a grading of PA syndromes from 1 (asymptomatic) to 5 (all patients with vision loss) with higher grades indicating a need for more urgent/timely surgical management.[24] Grade 4 included all patients with OMD but no visual loss (n=26), and all but 2 underwent surgery. Randeva et al. demonstrated that complete resolution of OMD was more frequently seen in patients operated within 8 days (73%) vs. later (42%).[18] In our study, all but one patient with OMD had surgery within one month of presentation, and his OMD did not resolve.

In our study, pituitary necrosis was more frequent than isolated hemorrhage on pathologic examination of the PA patients with OMD who had surgery. A previous report has suggested a less severe presentation of patients from pituitary infarction compared to hemorrhage, although 'ophthalmoplegia' was more frequent in patients presenting with both hemorrhage and infarction of the pituitary gland.[37] Our PA patients with OMD were also more likely to develop panhypopituitarism and endocrine deficiencies than those without OMD, likely due to the higher frequency of necrosis in the OMD vs. non-OMD group since necrosis is a known risk factor for endocrine deficiencies.[38]

Finally, we note that the detailed assessment of subjects by neuro-ophthalmology may have been limited to subjects who were generally less urgent although patients are frequently assessed at bedside in the hospital or emergency department by our unit. Our results should be cautiously interpreted considering this potential source of selection bias.

Conclusion

Pituitary apoplexy frequently causes OMD, and OMD appears to be more frequently associated with visual loss at presentation, a higher risk of panhypopituitarism, and with necrosis rather than hemorrhage of the pituitary. In our series, nearly all OMD either improved or resolved within one year after surgery, suggesting that these patients may need to be observed for at least one year before recommending strabismus surgery. While early pituitary surgery appears to result in good outcomes, our nearly universal application of early surgery makes it difficult for us to comment on the relative merits or risks of later surgery.

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Abbreviations list

CN	cranial nerve
CNP	cranial nerve palsies
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

References

1. Rovit RL, Fein JM. Pituitary apoplexy: a review and reappraisal. J Neurosurg. 1972; 37(3):280–288. [PubMed: 5069376]
2. Mohr G, Hardy J. Hemorrhage, necrosis, and apoplexy in pituitary adenomas. Surg Neurol. 1982; 18(3):181–189. [PubMed: 7179072]
3. Ebersold MJ, Laws ER, Scheithauer BW, Randall RV. Pituitary apoplexy treated by transsphenoidal surgery. A clinicopathological and immunocytochemical study. J Neurosurg. 1983; 58(3):315–320. [PubMed: 6827315]
4. Hernandez A, Angeles Del Real M, Aguirre M, Vaamonde J, Gudin M, Ibanez R. Pituitary apoplexy: a transient benign presentation mimicking mild subarachnoid hemorrhage with negative angiography. Eur J Neurol. 1998; 5(5):499–501. [PubMed: 10210880]

5. Nawar RN, AbdelMannan D, Selman WR, Arafah BM. Pituitary tumor apoplexy: a review. J Intensive Care Med. 2008; 23(2):75–90. [PubMed: 18372348]
6. Cardoso ER, Peterson EW. Pituitary apoplexy: a review. Neurosurgery. 1984; 14(3):363–373. [PubMed: 6369168]
7. Agrawal D, Mahapatra AK. Visual outcome of blind eyes in pituitary apoplexy after transsphenoidal surgery: a series of 14 eyes. Surg Neurol. 2005; 63(1):42–46. [PubMed: 15639521]
8. Kaplan B, Day AL, Quisling R, Ballinger W. Hemorrhage into pituitary adenomas. Surg Neurol. 1983; 20(4):280–287. [PubMed: 6623335]
9. Onesti ST, Wisniewski T, Post KD. Clinical versus subclinical pituitary apoplexy: presentation, surgical management, and outcome in 21 patients. Neurosurgery. 1990; 26(6):980–986. [PubMed: 2362675]
10. Tsitsopoulos P, Andrew J, Harrison MJ. Pituitary apoplexy and haemorrhage into adenomas. Postgrad Med J. 1986; 62(729):623–626. [PubMed: 3748928]
11. Pelkonen R, Kuusisto A, Salmi J, et al. Pituitary function after pituitary apoplexy. Am J Med. 1978; 65(5):773–778. [PubMed: 707535]
12. Suri A, Narang KS, Sharma BS, Mahapatra AK. Visual outcome after surgery in patients with suprasellar tumors and preoperative blindness. J Neurosurg. 2008; 108(1):19–25. [PubMed: 18173306]
13. Zhang X, Fei Z, Zhang W, et al. Emergency transsphenoidal surgery for hemorrhagic pituitary adenomas. Surg Oncol. 2007; 16(2):115–120. [PubMed: 17643985]
14. Woo HJ, Hwang JH, Hwang SK, Park YM. Clinical outcome of cranial neuropathy in patients with pituitary apoplexy. J Korean Neurosurg Soc. 2010; 48(3):213–218. [PubMed: 21082047]
15. Bills DC, Meyer FB, Laws ER, et al. A retrospective analysis of pituitary apoplexy. Neurosurgery. 1993; 33(4):602–608. [PubMed: 8232799]
16. Semple PL, Webb MK, de Villiers JC, Laws ER. Pituitary apoplexy. Neurosurgery. 2005; 56(1): 65–72. [PubMed: 15617587]
17. Kim SH, Lee KC, Kim SH. Cranial nerve palsies accompanying pituitary tumour. J Clin Neurosci Off J Neurosurg Soc Australas. 2007; 14(12):1158–1162.
18. Randeva HS, Schoebel J, Byrne J, Esiri M, Adams CB, Wass JA. Classical pituitary apoplexy: clinical features, management and outcome. Clin Endocrinol. 1999; 51(2):181–188.
19. Sibal L, Ball SG, Connolly V, et al. Pituitary apoplexy: a review of clinical presentation, management and outcome in 45 cases. Pituitary. 2004; 7(3):157–163. [PubMed: 16010459]
20. Dubuisson AS, Beckers A, Stevenaert A. Classical pituitary tumour apoplexy: clinical features, management and outcomes in a series of 24 patients. Clin Neurol Neurosurg. 2007; 109(1):63–70. [PubMed: 16488532]
21. Petermann SH, Newman NJ. Pituitary macroadenoma manifesting as an isolated fourth nerve palsy. Am J Ophthalmol. 1999; 127(2):235–236. [PubMed: 10030582]
22. Rajasekaran S, Vanderpump M, Baldeweg S, et al. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol. 2011; 74(1):9–20.
23. Verrees M, Arafah BM, Selman WR. Pituitary tumor apoplexy: characteristics, treatment, and outcomes. Neurosurg Focus. 2004; 16(4):E6.
24. Jho DH, Biller BMK, Agarwalla PK, Swearingen B. Pituitary Apoplexy: Large Surgical Series with Grading System. World Neurosurg. 2014; 82(5):781–790. [PubMed: 24915069]
25. Lubina A, Olchovsky D, Berezin M, Ram Z, Hadani M, Shimon I. Management of pituitary apoplexy: clinical experience with 40 patients. Acta Neurochir. 2005; 147(2):151–157. [PubMed: 15570437]
26. Wakai S, Fukushima T, Teramoto A, Sano K. Pituitary apoplexy: its incidence and clinical significance. J Neurosurg. 1981; 55(2):187–193. [PubMed: 7252541]
27. Symon L, Mohanty S. Haemorrhage in pituitary tumours. Acta Neurochir. 1982; 65(1–2):41–49. [PubMed: 7136877]
28. McFadzean RM, Doyle D, Rampling R, Teasdale E, Teasdale G. Pituitary apoplexy and its effect on vision. Neurosurgery. 1991; 29(5):669–675. [PubMed: 1961395]

29. Keane JR. Cavernous sinus syndrome. Analysis of 151 cases. Arch Neurol. 1996; 53(10):967–971. [PubMed: 8859057]
30. Seuk JW, Kim CH, Yang M-S, Cheong JH, Kim JM. Visual outcome after transsphenoidal surgery in patients with pituitary apoplexy. J Korean Neurosurg Soc. 2011; 49(6):339–344. [PubMed: 21887391]
31. Bujawansa S, Thondam SK, Steele C, et al. Presentation, management and outcomes in acute pituitary apoplexy: a large single-centre experience from the United Kingdom. Clin Endocrinol. 2014; 80(3):419–424.
32. Saul RF, Hilliker JK. Third nerve palsy: the presenting sign of a pituitary adenoma in five patients and the only neurological sign in four patients. J Clin Neuroophthalmol. 1985; 5(3):185–193. [PubMed: 2934421]
33. Kobayashi H, Kawabori M, Terasaka S, Murata J, Houkin K. A possible mechanism of isolated oculomotor nerve palsy by apoplexy of pituitary adenoma without cavernous sinus invasion: a report of two cases. Acta Neurochir. 2011; 153(12):2453–2456. [PubMed: 21947463]
34. Robert CM, Feigenbaum JA, Stern WE. Ocular palsy occurring with pituitary tumors. J Neurosurg. 1973; 38(1):17–19. [PubMed: 4682348]
35. Ayuk J, McGregor EJ, Mitchell RD, Gittoes NJL. Acute management of pituitary apoplexy--surgery or conservative management? Clin Endocrinol. 2004; 61(6):747–752.
36. Gruber A, Clayton J, Kumar S, Robertson I, Howlett TA, Mansell P. Pituitary apoplexy: retrospective review of 30 patients--is surgical intervention always necessary? Br J Neurosurg. 2006; 20(6):379–385. [PubMed: 17439089]
37. Semple PL, De Villiers JC, Bowen RM, Lopes MBS, Laws ER. Pituitary apoplexy: do histological features influence the clinical presentation and outcome? J Neurosurg. 2006; 104(6):931–937. [PubMed: 16776337]
38. Schneider HJ, Aimaretti G, Kreitschmann-Andermahr I, Stalla GK, Ghigo E. Hypopituitarism. The Lancet. 2007; 369(9571):1461–1470.

Highlights

- Ocular motility dysfunction is common in pituitary apoplexy, occurring in a quarter of patients
- Nearly all palsies resolved within 1 year of surgery, but our nearly universal use of surgery in pituitary apoplexy does not allow us to comment on the relative merits or risks of later surgery
- Ocular motility dysfunction is more frequently associated with vision loss, panhypopituitarism, and necrosis in pituitary apoplexy

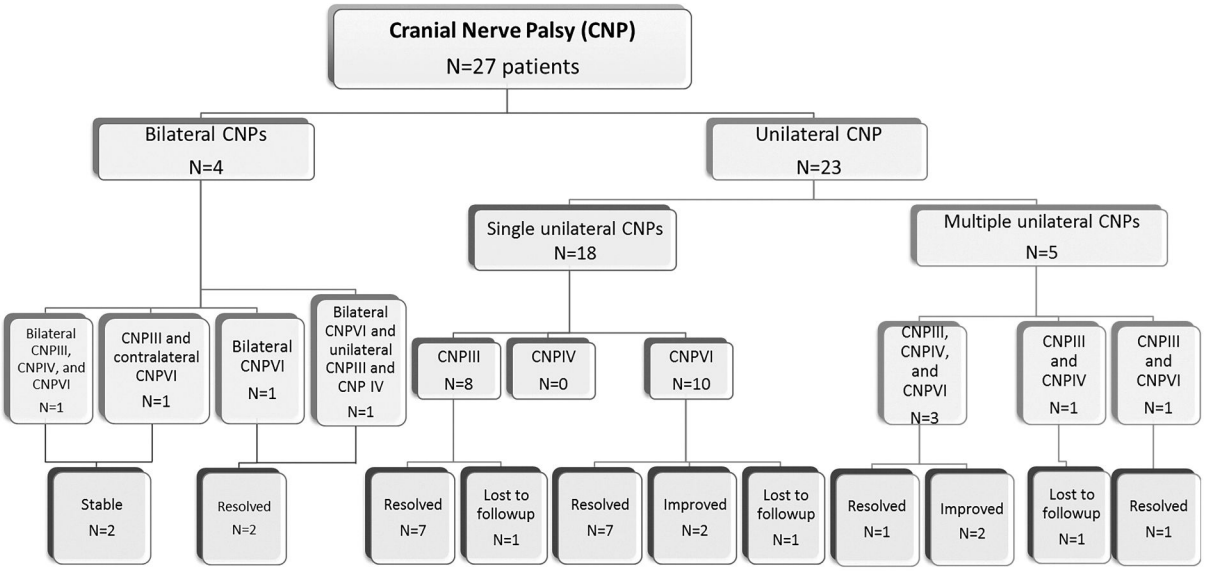

Figure.
Flow chart of patient characteristics.

Table 1

Features of pituitary apoplexy patients with and without ocular motility dysfunction

	PA patients with OMD (N= 59)	PA patients with no OMD (N= 176)	p
Age at presentation (y) ±SD	48 ±12	46 ±17	0.47
Sex ratio (M/F)	1.10 (31/28)	0.63 (68/107)	**0.002**
Clinical presentation			
- 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			
- Secreting adenoma	13 (22%)	58 (33%)	**0.11**
- Panhypopituitarism	18 (31%)	25 (14%)	**0.005**
- Endocrine deficiency (axes)			
○ 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
Radiological evaluation			
- Maximum diameter (median [IQR]) (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			
- Necrosis alone	28 (58%)	23 (37%)	**0.03** *
- Necrosis and hemorrhage	9 (19%)	14 (8%)	
- Hemorrhage alone	11 (23%)	25 (22%)	
Surgical management	56 (95%)	91 (52%)	**<0.001**

PA = pituitary apoplexy; OMCNP = ocular motility dysfunction; SD = standard deviation; M = male; F = female; IQR = interquartile range; AP = antero-posterior; CC = cranio-caudal; T: transverse.

* Necrosis alone vs. any hemorrhage

Table 2

Characteristics of cranial nerve palsies preoperatively

	III	IV	VI
Number of eyes	17 (63%)	7 (26%)	21 (78%)
Partial (vs. Complete)	10 (59%)	4 (57%)	14 (66%)
Associated cranial nerve palsies in the same eye	8 (47%)	7 (100%)	7 (33%)
Multiple cranial nerve palsies (number of eyes)			
- III+IV	7		
- III+VI	7		
- VI+IV	0		
- III+IV+VI	6		

Table 3

Visual fields in pituitary apoplexy patients with cranial nerve palsies at presentation (visual fields could not be performed in 10 eyes of 5 patients due to altered mental status)

Visual field test (eyes)	Humphrey	Goldmann	Confrontation*	Total
Number	23	5	16	44
Pattern				
• Normal	12	0	6	18
• Hemianopia	11	5	10	26
Size of abnormal patterns				
• Small	2	0	0	2
• Partial	8	1	4	13
• Complete	1	4	6	11
Mean Deviation (dB)		-	-	-
• (Median [Interquartile range])	−6.58 [−2.25, −9.31]			

*Includes all eyes of subjects seen at bedside or who were unable to perform reliable Humphrey or Goldmann visual fields

Table 4

Cranial nerve palsies and visual function outcomes in the 24 patients seen by neuro-ophthalmology before and after surgery.

	Before surgery	**After surgery**	**p**
Cranial nerve palsies			
III (partial; complete)	15 (10; 5)	5 (3; 2)	**0.04**
IV (partial; complete)	6 (3; 3)	4 (2; 2)	0.72
VI (partial; complete)	20 (13; 8)	6 (3; 3)	**<0.0001**
VA, logMAR (median [IQR])	0.28 [0.07–1.07]	0.1 [0–0.2]	**0.001**
VA lower than 20/200			
In one eye	3	2	0.5
In both eyes	3	0	0.11
Visual fields (eyes)	Performed in 18 patients	Performed in 24 patients	
Hemianopia	22/36 (61%)	16/48 (33%)	**0.01**
Small	2	3	0.38
Partial	12	10	0.62
Complete	8	3	0.23
Visual fields (patients)			
Bitemporal hemianopia	12	7	0.16
Homonymous hemianopia	0	0	-
Unilateral field defect	2	2	0.76
Visual field Mean deviation (dB) (Median [IQR])	−5.98 [−10.42, −1.72]	−3.13 [−5.65, −1.44]	**0.002**

VA = visual acuity; IQR = interquartile range