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Review Article

The impact of surgical timing on visual outcome in pituitary apoplexy: Literature review and case illustration

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Abstract

Background: Neuro-ophthalmologic signs are common clinical manifestations of pituitary apoplexy. Managing sudden visual loss is critical for achieving a good outcome. The timing of pituitary surgery remains controversial. In fact, various points of view have been reported in the literature.

Methods: We reviewed the impact of surgical intervention timing on visual outcome. The surgical intervention time was classified as urgent, early, intermediate, and late interventions based on the literature review. We report a case of a 40-year-old male patient who presented with headache and sudden visual loss for 3 days. He was diagnosed with pituitary apoplexy and had transnasal-transsphenoidal resection. Three days later, he achieved a complete recovery of his vision.

Results: This paper is an addition to several studies that favor early surgical decompression of pituitary fossa for apoplexy cases with severe neuro-ophthalmologic involvement. There is an increasing trend for early surgical intervention for pituitary apoplexy in the literature, especially for severe visual deterioration.

Conclusion: The visual outcome appears to be better in early intervention as compared to late. Nevertheless, good visual recovery is also seen in late surgical intervention.

Key Words: Pituitary apoplexy, transsphenoidal surgery, visual outcome

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INTRODUCTION

Pituitary apoplexy is a clinical syndrome characterized by sudden onset of headache, visual disturbances, altered mental status, vomiting, and hormonal dysfunction. It results from rapid expansion of a preexisting pituitary adenoma due to hemorrhage or infarction.[1,2] Neuro-ophthalmologic signs are common clinical presentations of pituitary apoplexy, with sudden visual loss and/or ocular motor palsy. In fact, visual impairments are found in 75% of the cases.[3] The rapid

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deterioration of vision is a serious condition because the tolerance of optic nerve to ischemia is unpredictable.[2] Management of pituitary apoplexy cases that presented with visual loss remains controversial. There is no consensus in the literature regarding the best timing to surgically intervene. Some authors advocate for early surgical decompression of pituitary fossa, whereas others have concluded that timing of surgery did not influence the outcome and that improvement may still occur even when decompression is delayed. In contrast, other authors have suggested a more conservative medical approach particularly for cases with mild neuro-ophthalmologic involvement. Here, we review the literature and illustrate a case report of a patient who presented with sudden visual loss, was diagnosed with pituitary apoplexy, and operated 3 days after his symptoms manifested. The timing of pituitary surgery for apoplexy cases with the decrease in visual acuity is discussed and classified based on a review of the available literature.

MATERIALS AND METHODS

A literature review was conducted through PubMed. The published articles were classified based on the timing of surgical intervention. Urgent surgical intervention was classified for all interventions within the first 24 hours of acute visual deterioration, and early intervention was done within 72 hours (after 24 hours), intermediate intervention during the first week after the first 72 hours, and late intervention after 1 week of visual deterioration. The degree and duration of visual recovery were considered as the main factors to measure the impact of intervention timing.

CASE ILLUSTRATION

A 40-year-old male patient presented to the emergency room of our hospital with a history of left frontal headache, which was severe in intensity and pressure-like in quality and associated with significant acute decrease in visual acuity and vomiting for 3 days. He was seen at a local hospital before being referred to us as they lacked the facilities and expertise to perform neurosurgical intervention. At the local hospital, proper radiological surveillance was performed for him that showed a sellar-suprasellar lesion with optic chiasm compression and hemorrhagic foci. On physical examination, the patient was conscious, alert, and oriented to time, person, and place with a Glasgow coma score (GCS) of 15. He had bilateral light perception but denied any noticeable visual loss prior to the event as he was able to see and drive his own car. The visual field was difficult to be assessed, and there was no evidence of papilledema. Right third nerve palsy was also noted. These findings were confirmed by our ophthalmology team. He was also seen by our endocrinology team where he was given stress dose of hydrocortisone. Urgent magnetic resonance imaging (MRI) brain was done that showed 3 × 2.8 × 2 cm irregular lesion involving the sellar-suprasellar area, extending to the right cavernous sinus and showing irregular high signal intensity on T1 and correspondingly low signal intensity on T2, keeping with acute hemorrhage. The optic chiasm was dislocated and stretched by the lesion, and there was remolding of the roof of the sphenoid sinus [Figure 1].

The patient was taken to the operating room 3 days after his symptoms started and on the same day of his admission to our institution. Endoscopic transnasal-transsphenoidal resection of the pituitary lesion was performed. The lesion was heterogeneous in consistency, ranging from firm and rubbery to friable and hemorrhagic. A blood clot was exposed and removed accordingly, confirming the diagnosis of pituitary apoplexy.

The procedure went smoothly without any complications and with minimal blood loss. Postoperative MRI showed good resection of the tumor with residual [Figure 2].

The patient recovered well and reported progressive improvement of his vision in both the eyes few hours after the surgery. He was revaluated by the ophthalmology team 3 days after the operation. He had complete recovery of his vision and his third nerve palsy.

DISCUSSION

Pituitary apoplexy occurs in 2–7% of patients with pituitary adenoma.[3] With the advancement of medical imaging, subclinical apoplexy is being increasingly detected, occurring in up to 25% of adenomas.[4,5] However, the term apoplexy (derived from the Greek word apoplēxia meaning "to cripple by a stroke") should be reserved to the acute clinical syndrome.[6] The first case was reported by Pearce Baily in 1898.[7] However, the

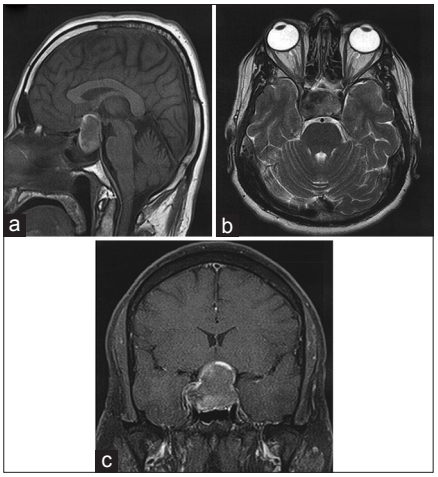

Figure 1: Preoperative sagittal T1 (a), axial T2 (b) and contrasted coronal T1 (c) MR images demonstrating large pituitary adenoma apoplexy with extension to the suprasellar region and compressing the medial wall of the right cavernous sinus

term apoplexy was first used by Brougham *et al*. in 1950 after describing five cases of this clinical entity.[8]

The pathophysiology of pituitary apoplexy is not fully understood. It is proposed that the adenoma outgrows its blood supply or compresses against its portal vessels resulting in necrosis of the tumor followed by hemorrhage.[2,9] Considering the fact that pituitary adenomas are more prone to bleed than other intracranial tumors, Cardoso and Peterson postulated the possibility of some type of intrinsic vasculopathy of pituitary tumors.[6] Moreover, Kim *et al*. showed that vascular endothelial growth factor (VEGF) has a significant relationship with the intratumoral hemorrhage of the pituitary adenomas, and suggested that VEGF expression may be responsible for the hemorrhage.[10]

Conservative medical approach might have a role in pituitary apoplexy cases with mild neuro-ophthalmologic involvement. Ayuk *et al*. and Gruber *et al*. validated the safety of medical approach for these cases because medical management did not adversely affect the outcome.[11,12] However, comparison with the surgical group is insignificant keeping in mind the baseline difference between both the groups. A prospective study rather than a retrospective one is needed.

The timing of pituitary surgery remains controversial. Several studies with multiple results have been published in the literature. Certain authors advocated for urgent within 24 hours surgical decompression of the pituitary fossa [Table 1]. Others were in favor of early decompression within 3 days from visual loss [Table 2], and some defined early as decompressing within a week [Table 3]. Lastly, various authors showed that improvement of vision happens regardless of the timing [Table 4]. The following tables include selected summarized studies demonstrating the different arguments.

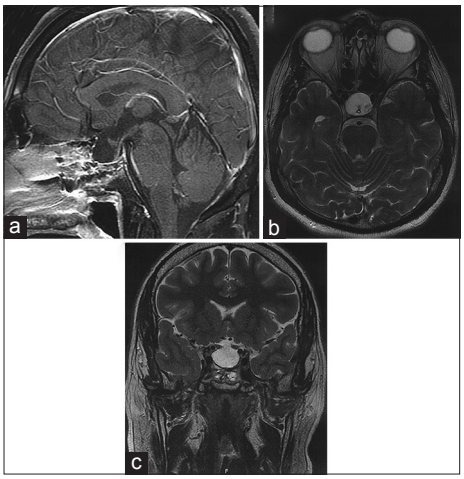

Figure 2: Postoperative contrasted sagittal T1 (a), axial (b) and coronal (c) T2 MR images demonstrating gross total resection of the pituitary adenoma

Both Choudhry *et al*. and Zhang *et al*. concluded that urgent surgical decompression within 24 hours is crucial to result in better visual outcomes.[1,13] It is noteworthy that five patients had bilateral blindness in the Zhang series where two remained blind following urgent surgical decompression [Table 1].[13]

Chen *et al*., Woo *et al*., and Chuang *et al*. advocated for early surgery, where the earlier the surgery, the better the outcome. The resolution of impaired visual function was higher in patients who were operated within almost 3 days compared to those operated later. There were two blind eyes in Woo's series and three blind eyes in Chuang's series that had early surgery, which resulted in partial recovery and complete recovery, respectively [Table 2].[2,14,15]

Liu *et al*. and Imboden *et al*. operated on their patients within 7 days of visual deficit and recovery was achieved in 64% and 100%, respectively. Out of the 4 blind patients in Liu's study, 3 remained blind. It could be postulated that the noted difference in the results is due to the small number of patients in Imdboden's study, and total resection rate was achieved in only 57% of Liu's cases.[16,17] Agrawal *et al*., Randeva *et al*., and Bills *et al*. concluded that operating within a week had better visual outcome than operating later. Similarly, the recovery of operated blind patients followed similar results. It is noteworthy to mention that improvement was also noticed in patients who were operated after a week [Table 3].[9,18]

Singh *et al*., Gruber *et al*., and Sibal *et al*. concluded that timing of surgery did not appear to influence the outcome, and the difference between the treatment groups was not significant.[12,19,20] Furthermore, Takeda *et al*. operated on their patients with different timing and all showed improvement. However, they concluded that early surgery is necessary for cases of acute deterioration of visual acuity. This was evidenced by the significant recovery of a bilateral blind patient who was operated 3 days after presentation [Table 4].[21]

Table 1: Urgent Surgical Decompression

Author, Year	Number of patients	Symptoms	Duration until surgery	Follow-up period	Recovery
Choudhry, 2012	4	Decrease VA	Within 24 hours	Mean 40 months	100% all patients
Zhang, 2011	38	Decrease VA	Within 24 hours	Median 41.6 months	CR 68.4% #26pts PR 23.7% #9 pts Unchanged 7.9% #3 pts

VA: visual acuity. CR: complete recovery. PR: partial recovery. Pts: patients

Table 2: Early Surgical Decompression (within 3 days)

Author, Year	Number of patients	Symptoms	Duration until surgery	Follow-up period	Recovery	Details
Chen, 2011	32	Decrease VA	6 hours to 7 days	Mean 5.5 years	90% improvement	6hr to 3 days (n=18) CR 66.7% #12 PR 33.3% #6 4 to 7 days (n=14) CR 35.7% #5 PR 42.9% #6
Woo, 2010	12	Decrease VA	6pts within 72 hours 6 pts after 1-15 days mean 7	Average 12 months	91.60% 3 pts CR 8 pts PR	100% improvement within 3 days 83.3% (5/6) improvement beyond 3 days
Chuang, 2006	13 1st group=6 2nd group=7	Decrease VA	1st group=3.5 days 2nd group=8.7 days	Up to 3 months	73% 19 out of 23 eyes	1st group=100% 2nd group=50%

VA: visual acuity. CR: complete recovery. PR: partial recovery. Pts: patients

Table 3: Intermediate Surgical Decompression (within a week)

Author, year	Number of patients	symptoms	Duration until surgery	Follow-up period	Recovery	Details
Liu, 2010	22	Visual deficit (4 blind)	Range 1-7 days	Mean 44 months	64%	CR in 6 pts (27%) PR in 8 pts (36%) No recovery in 8 (36%)
Agrawal, 2005	8	Complete blindness	Range 4-30 days	Up to 6 months	50% 4 pts	CR in 2 pts and PR in 2 pts within 7 days
Imboden, 2005	4	Decrease VA	3-6 days	Not specified	CR in all pts	
Randeva, 1999	23	Decrease VA	Range 1-34 days	Mean 6.3 years	86% 20 pts	CR in all pts within 8 days CR in 46% and PR in 31% beyond 8 days
Bills, 1993	16	Decrease VA 3 pts with unilateral blindness	Average 16.8 days 1st after 1 D 2nd after 4 D 3rd after 14 D	2.8 years	88% 14 pts CR in 1st & 2nd pts PR in 3rd pt	CR in all pts operated within 7 days

VA: visual acuity. CR: complete recovery. PR: partial recovery. Pts: patients. D: day

Table 4: Late Surgical Decompression

Author, year	Number of patients	Symptoms	Duration until surgery	Follow-up period	Recovery
Singh, 2015	28 early 5 late	Decrease VA	Early median time 5 days (3-10) Late median time 126 days (64-776)	Median 26 months	93.8% for early 100% for late
Takeda, 2010	8	Decrease VA 1 pt with Bilateral blindness	8 pts <than 8 days 2 pts 8-14 days 2 pts >than 2 weeks	Average of 35 months	100% CR in 75% (6 out of 8pts)
Gruber, 2006	7	Decrease VA 2 pts blind (uni & bilateral blindness)	Median 7.5 days Range (1-24) days	Median 4.4 years	88% (6 out of 7pts) CR in 4 pts PR in 2 pts (unilateral blind pt)
Sibal, 2004	14	Decrease VA	Median 6 days Range (1-121 days)	Median 49 months	93% (13 out of 14pts) CR in 8 pts (57%) PR in 5 pts (36%)

VA: visual acuity. CR: complete recovery. PR: partial recovery. Pts: patients

It is crucial to understand the pathophysiology of these visual disorders. They are induced by pituitary apoplexy's compression on optic chiasm or nerve which is suspected by the displacement noted on imaging. The mechanisms of injury are categorized as reversible and irreversible. The initial axoplasmic flow disorder, conduction blockage, and

demyelinization are reversible functional mechanisms. Longer and/or more intense compression leading to axonal fiber degeneration, which is seen in the fundus as optic atrophy is irreversible.[22] It is, however, noteworthy that optic atrophy is often found at diagnosis.[18] The reason is that gradual decrease in vision might not be consciously noticed by the patient until the onset of apoplexy. McFadzean *et al*. concluded that the presence of a normal optic disc was only associated with an improved visual outcome, which was not the case for either the length of the visual history or the severity of the visual defect.[23]

We speculate the mechanism behind the fast complete recovery 3 days after the surgery to the release of the conduction block caused by the compression. In fact, this is the first phase of recovery identified by Kerrison at al. Recovery continuous in some patients until a couple of years postoperatively because of possible neural plasticity.[24] In addition, our patient had bilateral light perception not complete blindness, implying that most probably the compression was not intense enough to cause axonal degeneration. However, complete blindness caused by pituitary apoplexy often improves, and especially if operated early. Muthukumar *et al*. operated on four blind patients at different timing, and all of them improved. They concluded that early surgery within the first week leads to excellent visual outcome compared to surgeries performed at the later stage.[25]

CONCLUSION

In conclusion, there is no dominant consensus in the literature on the best timing to operate on pituitary tumor apoplexy patients. This paper is an addition to several studies that advocate early surgery for pituitary apoplexy cases with neuro-ophthalmologic involvement. The earlier to remove the compressive pathology, the better the outcome is. However, some publications reported varying degree of improvement at the delayed intervention. The final decision will be based on multidisciplinary discussion, institutional experience, and reported outcome. Prospective studies are needed to propose evidence-based guidelines.

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Conflicts of interest
There are no conflicts of interest.

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