ORIGINAL ARTICLE

Vasospasm Post Pituitary Surgery: Systematic Review and 3 Case Presentations

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ABSTRACT: ***Background:*** Vasospasm is a known complication of aneurysmal subarachnoid hemorrhage and is a major cause of neurological morbidity and mortality. It is infrequently associated with pituitary adenoma surgery. We report three cases and present a systematic review of the literature with a view towards guiding neurosurgeons in the prevention and management of this complication. ***Results:*** Including our experience, vasospasm complicating pituitary adenoma surgery has been documented in 29 patients (mean age of 45). All cases occurred in the setting of a postoperative hemorrhage: 21 had a subarachnoid hemorrhage and 10 had a postoperative hematoma requiring evacuation. Initial clinical appearance of delayed cerebral ischemia attributable to vasospasm occurred from postoperative Days 2-13 (most commonly Day 5). Digital subtraction angiography and medical management were the most common diagnostic and therapeutic strategies, respectively. Glasgow Outcome Scores were ≤3 in 59% of cases. Univariate logistic regression identified later diagnosis of vasospasm and surgery for hematoma evacuation to be independently associated with better outcomes. ***Conclusion:*** Vasospasm should be considered in the differential diagnosis of patients demonstrating altered mental or neurological status following pituitary surgery, particularly if there has been postoperative hemorrhage of any degree. Prompt treatment should be instituted to optimize outcome.

RÉSUMÉ: Le vasospasme après la chirurgie pituitaire : une revue systématique et présentation de 3 observations. ***Contexte :*** Le vasospasme est une complication bien connue de l'hémorragie sous-arachnoïdienne anévrismale et constitue une cause majeure de morbidité neurologique et de mortalité. Il est rarement associé à la chirurgie de l'adénome pituitaire. Nous rapportons 3 observations et nous présentons une revue systématique de la littérature dans l'intention de guider les neurochirurgiens concernant la prévention et le traitement de cette complication. ***Résultats :*** Le vasospasme comme complication de la chirurgie pour un adénome pituitaire a été documenté chez 29 patients (âge moyen 45 ans), incluant nos observations cliniques. Toutes ces complications sont survenues dans le cadre d'une hémorragie postopératoire : 21 hémorragies sous-arachnoïdiennes et 10 hématomes postopératoires nécessitant une évacuation de l'hématome. Au point de vue clinique, une ischémie cérébrale retardée attribuable au vasospasme a été observée entre le 2e jour et le 13e jour après la chirurgie (le plus souvent au 5e jour). L'angiographie digitale de soustraction et le traitement médical ont été les stratégies diagnostique et thérapeutique les plus fréquemment utilisées. Le score de Galsgow Outcome Scale était de ≤ 3 chez 59 % des patients. L'analyse de régression logistique univariée a montré qu'un diagnostic subséquent de vasospasme et une chirurgie pour évacuation d'un hématome étaient associés de façon indépendante à de meilleurs résultats. ***Conclusion :*** Le vasospasme devrait être inclus dans le diagnostic différentiel de patients dont l'état mental ou l'état neurologique est altéré après la chirurgie pituitaire, particulièrement s'ils ont présenté une hémorragie postopératoire, quelle qu'en soit l'importance. Un traitement rapide devrait être institué afin d'optimiser le résultat.

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Pituitary adenomas are among the most common primary adult intracranial tumors[1]. Surgical treatment of non-functional adenomas is typically reserved for cases that are symptomatic secondary to mass effect[2]. The surgical approach to these tumors includes the transsphenoidal or transcranial route. Complications commonly associated with pituitary adenoma surgery include diabetes insipidus, cerebral spinal fluid (CSF) leak, transient or permanent visual loss, hypopituitarism, epistaxis, and meningitis[3]. While the risk of hemorrhagic stroke secondary to damage of surrounding vascular structures is well known[4], the occurrence of vasospasm following pituitary adenoma resection has rarely been documented. We describe three cases of vasospasm following pituitary adenoma surgery from our institution. Further, a summary of cases in the literature is provided with the goal of determining the optimal approach for preventing, diagnosing, and managing this complication.

Methods

A systematic search of the literature was performed in November of 2011 using the MEDLINE (1946-2011) and EMBASE (1947-2011) databases to identify relevant cases of vasospasm following pituitary adenoma resection. The following search terms were employed: ['*Pituitary*' and

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'adenoma'] and ['*vasospasm*' or '*complication*' or 'delayed cerebral ischemia' or 'angioplasty'] and ['surgery' or 'transcranial' or 'transsphenoidal']. This was determined to be the most inclusive strategy while avoiding an overly non-specific search. The search was limited to cases involving human subjects; there were no limitations on language or publication date. Further cases were identified through hand searching. Cases describing a delayed neurological deficit (within the same admission) following any surgical procedure for the resection of a pituitary adenoma were analyzed (including repeat procedures). Only cases with clinical and radiological evidence of vasospasm (either through digital subtraction angiography, computed tomography (CT) perfusion analysis, computed tomography with angiography (CTA) / magnetic resonance angiography (MRA), or transcranial doppler (TCD)) were included in the study. Cases of vasospasm or cerebral ischemia following pituitary apoplexy were not included. No limits were set for the length of follow-up post diagnosis.

The abstracts of the articles identified were independently assessed for appropriateness by two reviewers (AM and AF). Discrepancies in articles identified were resolved through personal discussion. The following variables were extracted for qualitative and quantitative analysis: Date of publication, patient age at time of surgery, gender, tumor type and size, operative approach, initial clinical symptoms (timing of onset of symptoms), method of diagnosis, time to diagnosis (radiological), vessels affected by spasm, treatment strategy, and outcome. For the purpose of statistical analysis the reported outcomes, expressed as a Glasgow Outcome Score (GOS) value, were dichotomized into groups of GOS ≥4 (mild to no deficit) or GOS ≤3 (significant deficit, vegetative state or death).

Statistical analysis

Univariate regression was performed to identify predictors associated with a dichotomized outcome (GOS 1-3 representing a poor outcome compared to GOS 4-5 representing a good outcome). Independent variables with five or fewer events or those that were biologically implausible to affect outcome were excluded. Any statistically significant predictor of outcome was expressed as an odds ratio with 95% confidence interval. We also performed multivariable regression, however, the small sample size made robust estimates of parameters for this so unstable that it was abandoned. All statistics were performed on IBM SPSS Statistics 20.

Case 1

Background

A 29-year-old right-handed woman presented with a history of progressive headaches, diplopia, visual loss, and amenorrhea. magnetic resonance imaging (MRI) demonstrated a 6.0 x5.0 x6.0 cm enhancing mass that extended from the sella into the right middle cranial fossa, anterior cranial fossa, and posterior cranial fossa. A two-stage plan was constructed beginning with a subtotal resection through a right fronto-temporal craniotomy for the lateral tumour followed by a purely endoscopic transsphenoidal approach for the midline and sphenoidal lesion. The lateral wall of the cavernous sinus was opened widely and significant amounts of a very vascular tumour were evacuated, contaminating the CSF with blood as well. Pathological analysis revealed a pleomorphic atypical aggressive adenoma producing primarily alpha-subunit and smaller amounts of prolactin and beta-TSH.

Symptom presentation

Immediate postoperative course was unremarkable. On post-operative Day 5, the patient suddenly developed left-sided hemiplegia and altered level of consciousness. Laboratory studies were normal. Computed tomography scan showed subarachnoid blood, hydrocephalus, and evidence of a right middle carotid artery (MCA) territory infarct. Angiography demonstrated severe diffuse vasospasm involving the supraclinoid segment of the right internal carotid artery (ICA) with narrowing of the right A1 and no filling of the distal right MCA beyond the M1 segment.

Management

The patient was treated aggressively with hypervolemia, vasopressor-induced hypertension, and nimodipine, with a gradual improvement of her symptoms. A residual hemiparesis was evident upon discharge which has completely resolved. At 16 years follow-up she has no residual hemiparesis and normal cognitive function (GOS=5).

Case 2

Background

A 43-year-old right-handed woman presented with progressive diplopia, bitemporal hemianopsia and signs of early Cushing's syndrome. Computed tomography showed a large sellar tumor invading the left cavernous sinus with encasement of the cavernous portion of the left ICA. Portions of the tumor had extended into the prepontine and interpeduncular cisterns. The index operation resulted in a subtotal resection of the tumor which was found to be an aggressive adrenocorticotropic hormone (ACTH) cell adenoma of the Crooke's cell variety. The patient was followed closely with frequent imaging and a second operation was performed six months following the first attempt, which also resulted in a subtotal resection with inadequate decompression of the left optic nerve. The patient then returned to the operating room for a left orbito-fronto-temporal craniotomy for further tumor resection. At surgery, the tumor was found to have invaded the pia of the left optic nerve.

Symptom presentation

Immediate postoperative course was unremarkable until post-operative day (POD) seven, when she developed headache, vomiting and a mild mixed aphasia. Magnetic resonance imaging showed local edema in and around the frontal and temporal opercula on the left side. Angiogram on POD eight confirmed a mild-to-moderate degree of vasospasm in the left A1 and M1 segments.

Management

A moderate course of "Triple-H" therapy (hypertension, hypervolemia, and hemodilution) along with nimodipine was instituted and she demonstrated improvement over the course of the next four days.

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Table 1: Summary of data points obtained through a systematic review of literature on the incidence of vasospasm following pituitary adenoma surgery

1st author (year)	Age (sex)	Type	Size	Approach	Symptoms	Onset (POD)	SAH (Y/N)	Hematoma* (Y/N)	Method of diagnosis	Vessels affected	Treatment	Outcome (GOS)
Krayenbuhl (1960)**	N/A (F)	NF	N/A	Subfrontal TC	L hemi- paresis	4	N/A	N	Angiogram	N/A	Papaverine	Resolution (5)
Tsunoda (1972)******	16 (F)	NF	Suprasellar	TC	Hemi- plegia	4	N/A	N/A	N/A	N/A	N/A	N/A
	50 (F)	NF	Suprasellar	TC	Hemi- paresis	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Takao (1979)******	46 (M)	NF	Suprasellar	TC	Hemi- paresis	5	N/A	N/A	N/A	N/A	N/A	N/A
Mawk (1979)	15 (F)	NF	Extension into SOF, Hypothalamus, Clivus	R Frontal TC GTR	Awoke with dense L hemi- paresis Lethargy POD4	6	N/A	N	Angiogram	R ICA	Conservative	Mild affectual disturbance (5)
	42 (M)	NF	Suprasellar	R Frontal TC GTR	Confusion POD3 R hemi- paresis + obtunded POD5	3	N/A	Y	Angiogram	L MCA/ACA	Dex	Death (1)
	23 (M)	NF	N/A	R Frontal TC STR	Dense L hemi- plegia	10	N/A	POD8	Angiogram	R MCA/ACA	Dex	Resolution (5)
Mawk (1980)	22 (M)	NF	5x5x6cm Extension into R cavernous sinus and clivus	L Subfrontal STR	L hemiparesis	3	N	N	Angiogram	R ICA	Hypervolemic Therapy	Death (1)
Camp (1980)	33 (F)	NF	Large sellar	TS (repeat TS for CSF leak 1 week later)	Orientation + L hemi- paresis L CN VI/ VII palsy L decerebrate posturing	6	N	N	Angiogram	Diffusely in proximal portion of vessels	HHH + Antibiotics	Death (1)
Ono (1981)******	48 (M)	NF	Suprasellar	TC	Lethargy + hemi- paresis	7	N/A	N/A	N/A	N/A	N/A	N/A
Hyde-Rowan (1983)	30 (F)	GH + PRL	N/A	TS 1400ml blood loss intra-op	MI Comatose + decorticate posturing: awoke POD5 Apnea + aphasia + obtunded POD6	2	Y POD2 (LP)	N	Angiogram	B/L supraclinoid ICAs	Conservative	Death (1)
Barrow (1990)	50 (M)	PRL	Suprasellar L frontal lobe	L Frontal TC STR (Second stage TS STR)	R hemi- paresis + R sided focal seizure + L eye blindness + dysphasia	7 (POD 2 after second stage TS)	N	N	Angiogram (POD9)	L ACA + ICA (supra- clinoid)	HHH	Gradually better L eye blind (3)
Aoki (1995)	51 (F)	NF	Suparsellar L cavernous sinus	L Cranio- orbito- zygomatic STR	"Clinical deterioration"	5	N/A	N/A	CTA	B/L ICAs	HHH	Resolution (5)
Cervoni (1996)	51 (M)	NF	Suprasellar	TS	Orientation + L hemi- paresis	4	Y POD4	N/A	TCD	R MCA/ACA	HHH + nimodipine	Resolution (5)
	48 (F)	NF	Suprasellar	R Fronto- temporal TC	Progressive L hemi- paresis	5	Y POD5	N/A	TCD	R MCA	HHH + nimodipine	Death from MI (1)
Friedman (2001)	41 (M)	GH	N/A	TS GTR	- Drowsy POD10 - Mild aphasia - R arm weaknessPOD11	10	N	N	Angiogram	Severe L supraclinoid ICA	Angioplasty	Resolution (5)
Nishioka (2001)	41 (M)	FSH	N/A	TS	Orientation L hemi- paresis POD12 Aphasia + R hemi- paresis POD 17	12	Y POD0	N	Angiogram	R MCA/ACA/ diatal ICA	Papaverine POD1 HHH 4 weeks later	Hypo- pituitarism (5)
Kasliwal (2008)	34 (F)	NF	Suprasellar	TS STR	R sided hemi-paresis, focal convulsions	13	N	Y	Angiogram + TCD	L ICA bifurcation	Hypervolemic Therapy	Death (1)
Puri * (2010)**	N/A	NF	N/A	TS	Global aphasia	5	Y	Y	Angiogram	Diffuse (worse in ACAs)	Verapamil	B/L L/E weakness (3)
	N/A	NF	N/A	TS	Behavioral changes	9	Y	Y	Angiogram + CTA	Diffuse	Verapamil	"Lasting deficit" (3)
	N/A	NF	N/A	TS	Depressed mental status	5	Y	Y	Angiogram + CTA	Diffuse	Verapamil	Death (1)
Popugaev (2011)	45 (M)	NF	Suprasellar	TS	Meningismus	4	Y POD4	N	TCD (POD4) Angiogram (POD23)	B/L ICA + MCA	IV Antibiotics started POD7	GOS 4
	52 (F)	NF	Suprasellar	TS STR	Delirium Respiratory insufficiency	4	N/A	N/A	TCD	L MCA	IV Antibiotics started POD4	GOS 5
Zada (2011)	59 (M)	NF	4x2.9cm Suprasellar Floor of third Encasing ACAs	TS STR	Drowsy + R pupil dilation POD2 Global aphasia + B/L leg weakness POD5	2	Y POD2	Y POD2	Angiogram + CTA	Diffuse (ACAs severe)	Verapamil x 3	Short- term memory and VF deficit (4)
	66 (M)	NF	4.9x3.6cm Suprasellar Frontal lobe	TS STR	Decreased LOC R pupil dilation POD5 Obtunded POD8	8	N	Y POD5	Angiogram + MRA	Severe B/L ACA + L PCA	Verapamil	Death (1)
	36 (F)	FSH	2.9x2.1cm Suprasellar	TS- GTR (Previous STR via TS)	Agitation Expressive aphasia	9	Y POD 0	N	CTA	Diffuse (infarct in B/L ACA territories)	HHH + verapamil x 4	Stable pan- hypo- pituitarism (5)
Toronto (2011)	29 (F)	GH + PRL	6x 5 x 6cm R mid skull base Ant.& post. fossa	Fronto- temporal TC	L sided hemi- plegia	5	Y	N	Angiogram	R ICA/MCA/ ACA	HHH + nimodipine	Resolution (5)
	45 (F)	ACTH	Cavernous sinuses Middle cranial fossa	Orbito- fronto- temporal (3 previous TS surgeries) All = STR	Dysphasia	7	Y	Y	Angiogram (POD8)	L A1/M1	HHH + nimodipine	Mild speech deficits (4)
	75 (M)	NF	2x 1.7 x 2.8 cm Floor of 3rd	TS	Decreased level of consciousness + R sided hemi- paresis	7	Y	Y	CT perfusion	L ICA/MCA	Permissive HTN	Difficulty ambulating (3)

‡ Abbreviations: GH, Growth Hormone; FSH, Follicle Stimulating Hormone; PRL, Prolactine; ACTH, Adrenocorticotrophic Hormone; NF, Non-Functional; TS, Transsphenoidal; TC, Transcranial; STR, Sub Total Resection; GTR, Gross Total Resection; POD, Postoperative Day; SAH, Subarachnoid Hemorrhage; CTA, Computed Tomography with Angiography; MRA, Magnetic Resonance Angiography; TCD, Transcranial Doppler; ICA, Internal Carotid Artery; MCA, Middle Cerebral Artery; ACA, Anterior Cerebral Artery; PCA, Posterior Cerebral Artery; B/L, Bilateral; L/E, Lower extremity; HHH, Hypertension-Hypervolemia-Hemodilution therapy; HTN, Hypertension; GOS, Glasgow Outcome Scale.
* Indicates hematoma significant enough to require evacuation; ** Indicates article in German; *** Indicates publication type as abstract only; **** Indicates articles in Japanese

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Outcome

Following discharge, the patient underwent adjuvant therapy with radiation and temozolomide. However, the tumor recurred once again and a further transsphenoidal approach was necessary. A near-total resection of the tumor was obtained. On most recent follow-up the patient demonstrated mild deficits in medial and lateral movements of the left eye, intermittent headaches, and mild speech difficulties (GOS=4).

Case 3

Background

A 75-year-old right-handed man presented with a one year history of decreased peripheral vision, visual blurring, and a three to four week history of new-onset headaches. Magnetic resonance imaging showed a pituitary macroadenoma measuring 2.0 x 1.7 x 2.8 cm extending superiorly into the suprasellar cisten with mass effect on the chiasm and floor of the third ventricle. Displacement of cavernous ICAs with bilateral invasion of the cavernous sinuses was also noted. An endoscopic extended transsphenoidal resection of the tumor was undertaken. The optic chiasm and the right optic nerve were decompressed. Significant amount of venous bleeding from the left cavernous sinus was noted but hemostasis was obtained with gel foam and irrigation. A small perforation was inadvertently created in the arachnoid veil resulting in an immediate CSF leak which was managed intraoperatively.

Symptom presentation

In the immediate postoperative period the patient was cogent and reported an improvement in his visual acuity. Twenty four hours after surgery the patient developed a decrease in the level of consciousness. Computed tomography showed acute hemorrhage in the suprasellar space, just anterior to the genu of the corpus callosum, along with the interpeduncular fossa, the right pre-pontine cistern, and in the third and lateral ventricles. Hydrocephalus was also noted. The CTA did not reveal evidence of vascular injury or vasospasm.

The patient was taken back to the operating room for endoscopic transsphenoidal evacuation of the suprasellar hematoma. An external ventricular drain was inserted at the same setting. The patient gradually improved until POD seven when he once again became somnolent and developed a right-sided hemiplegia. The CT perfusion imaging demonstrated a significant narrowing of left supraclinoid ICA with focal narrowing extending to level of the left MCA resulting in hypoperfusion of the left hemisphere.

Management

The patient was managed via permissive hypertension and hypervolemia. A CT scan on POD ten showed evidence of infarcts in the left globus pallidus and genu of internal capsule. These infarcts were confirmed by MRI three weeks later.

Outcome

Over the course of the next month he demonstrated gradual improvement, but remained significantly impaired. While able to follow simple commands, he required assistance with ambulation. At three month follow-up, he was found to have a mild residual hemiparesis, but displayed severe abulia (GOS = 3).

Table 2: Demographics and pre/post-operative tumor information

	Frequency (Percentage)
Gender	
Male	13 (50%)
Female	13 (50%)
Not specified	3
Publication date range	
1960-1969	1 (3%)
1970-1979	6 (21%)
1980-1989	4 (14%)
1990-1999	4 (14%)
2000-2011	14 (48%)
Type of tumor	
Non-functional	22 (76%)
Functional	7 (24%)
Surgical approach	
Transsphenoidal	15 (52%)
Transcranial	14 (48%)
Operative outcome	
Sub-total resection	12 (60%)*
Gross-total resection	8 (40%)*
Not specified	9 (N/A)

* Indicates percentage of those reported

Results

The initial search yielded 844 articles; after review of abstracts for appropriateness, 20 cases (12 articles) were identified as relevant. Six additional cases (five articles) were identified by searching through the references of the above articles. Including the three cases from our institution, there have been a total of 29 cases of vasospasm following pituitary adenoma resection reported in the literature (Table 1)[5-21]. Patient demographics, preoperative tumor information, along with operative approach and outcome have been summarized in Table 2. Nearly half of the cases were reported within the past decade. Patient age at presentation ranged from 15 to 75 with a mean age of 45 at time of surgery. Gender, operative approach, or extent of surgical resection were not predictive of the risk of vasospasm. Initial signs and symptoms of deterioration such as changes in mental status (56%), motor deficits (62%), and speech difficulties (28%) were detected on POD 2-13; the majority of cases were detected on POD 5. Among reports commenting on the presence of subarachnoid hemorrhage (SAH), 70% (14/20) of vasospasm cases were associated with SAH while 34% had developed postoperative hemorrhage significant enough to require surgical evacuation. A GOS score of ≤3 was observed in half of the patients with evidence of SAH.

A variety of diagnostic and treatment modalities were utilized (Table 3). Angiography was used to diagnose vasospasm in 77% of cases (used as the only tool in 54% and as an adjunct in 23% of cases). The majority of cases (68%) employed medical measures such as “Triple H”, nimodipine, intra-arterial

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verapamil, and IV papaverine. Conservative measures (28% of cases) included the use of antibiotics for suspected meningitis, dexamethasone, permissive hypertension or clinical monitoring. Only one case reported the use of angioplasty as a treatment strategy and with good success (GOS≥4). More than half of the cases overall were associated with a GOS score of ≤ 3 (60%); eight cases (32%) ultimately resulted in patient death. Sub-analysis in this group did not suggest a definitive association of mortality with the presence of SAH or extensive hematoma.

On univariate analysis a trend was observed for patients with "Hematoma requiring evacuation and a good outcome with an OR of 5.5 (p = 0.08). We were unable to perform multivariate analysis to identify independent predictors of outcome due to the low sample size.

Table 3: Summary of diagnostic methods, management approaches, and outcomes

	Frequency (Percentage)
Diagnostic modality	
Angiography	14 (54%)
CT perfusion/ CTA/MRA	3 (11.5%)
Trans-cranial Doppler	3 (11.5%)
Angiography + other diagnostic modality	6 (23%)†
Not specified	3
Treatment approach	
Endovascular	1 (4%)
Medical	17 (68%)
Conservative	7 (28%)
Not specified	4
Outcome	
GOS≥4	10 (40%)
GOS≤3	15 (60%)
Not specified	4

†4 involved the use of CTA/MRA while 2 involved the use of TCD

Discussion

The incidence of vasospasm following SAH is well-described[22,23]. While SAH-related vasospasm is most commonly associated with rupture of an intracranial aneurysm, the literature contains reports of cases associated with surgical resection of skull base tumors as well[7,12,14,24,25]. Further, there have been a limited number of published cases of vasospasm following pituitary surgery. In this study, we have reported findings from three cases at our institution and have systematically reviewed the literature and identified an additional 26 cases. Through this approach we have been able to gain further insight into the phenomenon of vasospasm following pituitary surgery.

Clinical presentation

The presenting symptoms noted in our case series were generally reflective of those commonly encountered in patients developing vasospasm. However, the differential diagnosis for such presenting symptoms in the postoperative period following pituitary surgery is broad and includes multiple other etiologies: metabolic (hyponatremia, hypernatremia, hypocortisolemia), systemic (hypotension, hypoxia, hypercarbia), infectious (meningitis, sepsis), and neurologic (stroke, hydrocephalus, mass effect from hemorrhage or edema, seizure)[26]. Given that these diagnoses are more common following pituitary adenoma surgery emphasizes the importance of maintaining a high index of suspicion for vasospasm, particularly following anatomically challenging cases or those associated with hemorrhage.

Putative mechanisms

Clinical vasospasm associated with aneurysmal rupture portends a poor prognosis, with reported death in 7% of cases and a severe, lasting deficit in an additional 7%[27]. The overall rate of severe deficit and mortality in our series was substantially higher, at 59% and 28%, respectively. This is attributable to our data including extreme cases and the probability of mild cases being undiagnosed is high. Aside from SAH, other factors relevant to pituitary surgery that can contribute to the development of vasospasm include mechanical intraoperative manipulation of cerebral arteries[28], meningitis[11], irritation of vessels by packing material[13] or the release of vasoactive peptides and hormones from the hypothalamus following surgery within the sellar/suprasellar region[29]. Anatomy may also play a role. Hemorrhage from pituitary surgery is also most likely to maximally affect the basal cisterns of the entire Circle of Willis. Thus the likelihood of diffuse vasospasm involving anterior and middle cerebral arteries bilaterally would be higher than a localized SAH, say around a single middle cerebral artery.

Diagnostic modalities

In our series, conventional angiography was the primary diagnostic tool, followed by CTA, TCD, MRA, and CT perfusion studies. Angiography has been established as the gold standard for the diagnosis of vasospasm; however, CTA and MRA have a reasonable specificity and sensitivity for detection of vasospasm and can often be sufficient for diagnosis[30,31]. If CTA or MRA are not suggestive of vasospasm but there is radiographic evidence of SAH and clinical suspicion of vasospasm, early angiography should be performed in patients with a delayed neurological decline as a delay in diagnosis may have an effect on outcome.

Therapeutic approaches

As in vasospasm associated with aneurysmal SAH, a variety of therapeutic strategies can be utilized for the management of vasospasm complicating pituitary surgery. In our series, the majority of cases involved the use of "Triple-H" therapy, typically in conjunction with nimodipine, followed by intra-arterial delivery of an antispasmodic such as verapamil or papaverine or mechanical angioplasty if needed. "Triple-H" resulted in a good outcome in 7 of 11 patients. In the remaining four cases, however, mortality was the outcome; one of these was from a myocardial infarct. In certain cases where meningitis was presumed to be the underlying cause of vasospasm, appropriate antibiotic therapy resulted in a good outcome. In other cases, however, conservative management had a higher association with poor outcome. Mechanical angioplasty was performed in one case with a resultant good outcome. While our study was under-powered for the identification of the superiority of one management approach over another, the prompt

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institution of appropriate therapy for vasospasm in a monitored neurosurgical ICU setting, with consideration of patient co-morbidities, seems prudent.

In our analysis, an unexpected trend was observed correlating surgical evacuation of hematoma within the tumor bed and an overall good patient outcome. It is possible that this was a spurious finding that occurred by chance as evidenced by the wide confidence interval. However, it is possible that early relief of mass effect can result in better outcomes; the size of the hematoma was often not reported. In addition, other unknown underlying mechanisms could be contributing to this finding, and may be independent of any effect on vasospasm. Regardless of mechanism, early evacuation of a hematoma in a patient with an altered level of consciousness is a variable that should be considered and further analyzed in future studies.

Limitations

Although our search of the literature was able to identify several cases, the small number of cases identified was not sufficient to achieve adequate statistical power to identify clinically important associations. It is likely that the incidence of vasospasm following pituitary surgery is higher than we have indicated, and that only the most severe cases have been reported in the literature (i.e. publication bias). Furthermore, our data points were extracted from case reports and case series. Therefore, our study is limited by a high level of reporting bias. Among the cases identified, incomplete reporting of data such as presence and amount of SAH, degree of spasm, outcomes in terms of GOS, and follow-up further complicated our study. This limitation was particularly important for GOS, where inferences were made based on the reported descriptors of patient outcome. In addition, specific information regarding the treatment center is also missing; institutions with a dedicated neurosurgical ICU with the expertise to manage aneurysmal SAH and vasospasm are likely to have better outcomes.

Overall, this is the first attempt in the neurosurgical literature to summarize the reported cases of vasospasm following pituitary adenoma surgery. Our study enabled the observation of trends and patterns in this patient population and served as a hypothesis-generating exercise for further studies. Future directions would include the accumulation of additional studies to garner higher statistical power. Also, while there are theories regarding the underlying pathophysiology of vasospasm following pituitary adenoma surgery, further research is necessary for better characterization.

Conclusion

Through this systematic review, we have been able to gain further insight into the phenomenon of vasospasm following pituitary surgery. Given the relatively high morbidity and mortality rates observed in this series, a high level of vigilance for vasospasm is necessary in patients undergoing an extensive resection of a pituitary adenoma. Although the differential diagnosis for an altered level of consciousness or deficits in motor functions and speech is broad, vasospasm is a rare but important diagnosis to consider during the immediate postoperative period. The astute clinician will consider the diagnosis in the setting of pituitary surgery complicated by hemorrhage and remain vigilant and institute preventive measures to avoid potentially fatal or disabling complications seen in these patients.

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