Pecorari IL, et al., Archiv Surg S Educ 2023, 5: 050
DOI: 10.24966/ASSE-3126/100050

HSOA Archives of Surgery and Surgical Education

Research Article

Cavernous sinus invasion: imaging versus clinical outcomes of pituitary adenomas

Isabella L. Pecorari*, Mousa K. Hamad and Vijay Agarwal

Department of Neurological Surgery, Albert Einstein College of Medicine, Bronx, NY, USA; Department of Neurological Surgery, Montefiore Medical Center, Bronx, NY, USA

Abstract

Introduction

Pituitary adenomas are a common neoplasm of the skull base. While magnetic resonance imaging (MRI) is used to visualize the size and extent of local tumor growth, its use in accurately assessing invasion into the cavernous sinus (CS) may be unreliable. The goal of this study was to determine the relationship between MRI reports suggestive of pituitary invasion into the cavernous sinus and confirmation of invasion during surgical resection.

Methods

A retrospective review of patients who underwent surgical resection of pituitary adenomas between 2018 – 2023 was conducted. Medical records were reviewed to obtain demographic information and pre-operative MRI reports were analyzed for documentation of parasellar extension. Tumor invasion into the cavernous sinus was confirmed intra-operatively.

Results

Forty-seven patients were included in the analysis (21 males, 26 females). The average patient age was 55.2 ± 14.7 years. MRI reports for 33 patients (70.2%) documented evidence of pituitary tumor extension into the cavernous sinuses, with intraoperative verification of invasion in only 3 cases (9.1%). Patients with surgically confirmed cavernous invasion were significantly more likely to be of younger age ($p = 0.002$; mean age: 31 years). Pituitary tumors without CS invasion were more likely to have a low Ki-67 index and a greater cranio-caudal tumor dimension compared to laterally invasive tumors ($p = 0.043$; $p < 0.001$, respectively).

Conclusion

While MRI reports are widely used to assist with neurosurgical planning, radiographic evidence of CS invasion does not always correlate to intraoperative findings. However, there should remain a high index of suspicion of true invasion, as indicated by imaging reports, for patients who are of younger age. Furthermore, while tumors that lack extension into the CS express lower levels of proliferative biomarkers, they also demonstrate increased vertical growth compared to those tumors that are laterally invasive.

Keywords: Cavernous sinus; Cavernous sinus invasion; MRI; Pituitary adenoma

Introduction

Pituitary adenomas are one of the most commonly diagnosed brain tumors, constituting approximately 10-15% of all intracranial neoplasms [1]. Despite being considered a benign growth, these tumors can impart an array of clinical side effects and endocrine abnormalities. These include symptoms resulting from mass effect, such as headaches and visual field abnormalities, and hormone dysregulation, including hyperthyroidism, hyperprolactinemia, Cushing disease, acromegaly, infertility, and hypopituitarism [2]. Often classified based on size as a microadenoma (<10mm) or macroadenoma (≥10mm), those of larger dimensions often invade into nearby intracranial structures, such as the cavernous sinus.

The cavernous sinuses are an interconnected network of venous plexuses situated on both sides of the sella turcica and sphenoid sinus. Extension of pituitary adenomas into this region can disrupt the function of any of the structures residing within them. This includes the internal carotid artery and abducens nerve, which are situated medially within the sinuses, as well as the oculomotor, trochlear, ophthalmic, and maxillary nerve, located laterally [3]. Local invasion of tumors into this region increases the difficulty of achieving gross total resection, allowing for residual tumor to cause continued hormone dysregulation, higher rates of tumor recurrence, and the need for continued post-operative medical therapy [4].

At this time, MRI is used to delineate the extent of pituitary tumor extension and to classify whether invasion into the cavernous sinus has occurred. The Knosp grading system was specifically designed to categorize the degree of spread into this area, with higher grades associated with larger tumors, higher rates of surgical complications, and decreased biochemical remission after resection [5]. Unfortunately, the use of pre-operative imaging in predicting true CS invasion has shown to be unreliable, even among tumors labeled with higher Knosp grades [6]. While current studies are focused on developing more reliable imaging techniques to predict expansion of tumors into the parasellar space, understanding the factors that may correlate to true CS invasion can be useful in the surgical planning and management of pituitary tumors.

***Corresponding author:** Isabella L. Pecorari, The University Hospital for the Albert Einstein College of Medicine, Montefiore Medical Center, USA. Tel: 718-920-4216. E-mail: isabella.pecorari@einsteinmed.edu

Citation: Pecorari IL, Hamad MK, Agarwal V (2023) Cavernous sinus invasion: imaging versus clinical outcomes of pituitary adenomas. Archiv Surg S Educ 5: 050.

Received: November 10, 2023; **Accepted:** November 23, 2023; **Published:** November 30, 2023

Methods

A retrospective review of patients who underwent surgical resection of pituitary adenomas by one neurosurgeon at a single institution was completed between 2018 and 2023. Each patient's electronic medical record was reviewed to collect relevant demographic information, including age, sex, and body mass index (BMI). Pre-operative MRI scans were read by a neuroradiologist, who documented if there was radiographic evidence of cavernous sinus invasion. The presence or absence of tumor extension into the cavernous sinus was confirmed intra-operatively. Institutional review board approval was obtained prior to study initiation (2018-9379).

Statistical analysis was completed using means and standard deviations for continuous variables. Cases with and without confirmed cavernous sinus invasion were compared using an independent samples t-test. Categorical variables were summarized using frequencies and compared between the two groups using chi-square or Fisher exact tests. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for MRI reports. Significance was defined as p-value <0.05. All analyses were performed using SPSS Statistics Version 29.0.0.0 (IBM Corp., Armonk, N.Y., USA).

Results

Descriptive Statistics

A total of 47 patients were included in the analysis, consisting of 21 males (44.7%) and 26 females (55.3%) [Table 1]. Average patient age was 55.2 ± 14.7 years (range: 26 to 84 years) and the mean body mass index (BMI) was 32.3 ± 7.2 kg/m^2. An elevated Ki67 index was identified in 6 patients (12.8%). Mean pituitary tumor dimensions were 3.3 cm (craniocaudal [CC]), 2.6 cm (anterior-posterior [AP]), and 2.9 cm (transverse [TV]).

Characteristic	Total (n = 47)
Age (years) [mean ± SD]	55.2 ± 14.7
Sex	
Male	21 (44.7%)
Female	26 (55.3%)
BMI (kg/m2) [mean ± SD]	32.3 ± 7.2
Elevated Ki67 index	6 (12.8%)
Mean tumor dimensions	
Cranio-caudal	3.3
Anterior-posterior	2.6
Transverse	2.9

Table 1: Descriptive Statistics of Patients.

SD: standard deviation; BMI: body mass index

Radiographic versus Operative Findings

Thirty-three patients had MRI reports suggestive of pituitary tumor invasion into the cavernous sinus, with surgical confirmation of CS invasion occurring in only 3 cases (PPV, 9.1%; P = 0.544) [Table 2]. Out of the 14 cases without radiographic evidence of invasion, all of them were confirmed to lack CS involvement intra-operatively (NPV, 100%, P = 0.544).

	Intra-operative Findings		
MRI Findings	Invasion	No Invasion	p-value
Invasion	3	30	0.544
No Invasion	0	14	
Sensitivity (%)	100		
Specificity (%)	31.8		
PPV (%)	9.1		
NPV (%)	100		

Table 2: CS invasion: Radiographic versus Operative Findings.

CS: cavernous sinus

Comparative Analysis of Patients with and without Surgically Confirmed CSI

Analyzing cases with and without verified CS invasion of pituitary tumors revealed that patients with true invasion, as indicated intra-operatively, were significantly younger than patients who did not have lateral tumor growth (P <0.002) [Table 3]. A statistically significant relationship was also observed between CS invasion and the Ki-67 index of pituitary tumors, with those tumors lacking CS involvement being found to have low levels of Ki-67 expression (P = 0.043). Furthermore, comparing the mean tumor dimensions between cases revealed that pituitary adenomas that did not exhibit lateral expansion into the CS had a significantly greater cranio-caudal dimension compared to tumors with growth into the CS. No significant relationships between cavernous sinus invasion and sex, BMI, eccentric tumor growth, and anterior-posterior or transverse tumor dimensions were observed.

	With CSI (n=3)	Without CSI (n=44)	p-value
Age	31.0	56.9	0.002*
Sex			1.000
Male	1	20	
Female	2	24	
BMI	36.3	32.1	0.478
Ki67 index			0.043*
>3%	2	4	
≤3%	1	38	
Mean tumor dimensions			
Cranio-caudal	1.7	3.4	<0.001*
Anterior-posterior	2.1	2.6	0.213
Transverse	2.3	2.9	0.249
Eccentric tumor growth			1.000
Yes	2	23	
No	1	21	

Table 3: Comparative Analysis of Patients with and without Confirmed CSI.

CSI: cavernous sinus invasion; BMI: body mass index

Discussion

Despite the benign nature of pituitary adenomas, invasion into the cavernous sinus is a common occurrence, reported in approximately 10% of operative cases [7]. While lateral extension of such tumors can disrupt the function of nearby structures and result in significant

clinical consequences such as cranial nerve dysfunction, growth into the parasellar region can increase the risk of operative complications and unfavorable outcomes, such as cerebrospinal fluid leaks, damage to the optic chiasm, cerebrovascular injury, and persistent endocrine dysregulation [3]. Additionally, involvement of the CS has been found to be associated with lower rates of gross total resection and can increase the need for further treatment, including re-resection, radiation therapy, or medical management [4]. Since CS invasion can significantly affect patient outcomes, the ability to recognize true tumor extension or invasion into this area is important for surgical planning and long-term patient management.

While pre-operative imaging is widely used to quantify tumor size and extent of growth, its use in identifying true cavernous sinus invasion has not always proven to be accurate. Prior studies have focused on developing classification schemes for predicting CS invasion based on MR imaging, with percent of ICA encasement and Knosp grading considered to be potential predictive factors. Cottier et al., for example, reported that ICA encasement of at least 67% was consistently associated with true tumor invasion (100%, PPV), whereas encasement of 25% or less confirmed lack of tumor extension into the CS (100% NPV) [8]. However, given that other studies have reported lower degrees of ICA encasement to be predictive of true invasion, it remains unclear what percent can be accurately used in clinical practice [9]. Other reports have analyzed the utility of the Knosp grading system, widely used in radiographic reports to describe CS invasion, in accurately predicting lateral tumor expansion. However, these results have proven to be variable, as well. While one report identified Knosp grades 3 and 4 to be associated with CSI at a rate of 85% and 100%, respectively, a retrospective review by Fang et. al demonstrated the rates of surgically confirmed CSI to be 37.5%, 54.5%, and 88.9% for grades 3a, 3b, and 4 [8, 10]. In this study, MRI reports suggestive of pituitary tumor invasion into the CS had a low PPV (9.1%) and high NPV (100%), although the relationship between MRI results and surgical findings were not statistically significant. Given that radiographic studies demonstrate greater ability to consistently rule out, rather than confirm true CS invasion, the development of more accurate imaging techniques would be advantageous.

Aside from the use of imaging reports, identifying other patient factors that may be associated with true CS invasion could prove useful. In this study, younger age was significantly associated with lateral expansion into the cavernous sinus. Among patients with pituitary tumors, younger age has been found to be associated with greater expression of proliferative tumor markers, such as Ki-67 [11]. Given that the average age at diagnosis of pituitary tumors in the United States is approximately 49 years, evidence of increased cavernous sinus invasion among younger patients may be suggestive that such individuals may be harboring more aggressive tumors with increased risk of extension into the parasellar space [12]. Therefore, despite the low specificity of MR imaging, there should remain a higher degree of suspicion for true CS invasion among younger patients where MR imaging is suggestive of such growth.

Among those cases that demonstrated lack of CS invasion on surgical reports, pituitary tumors were found to be more likely to express a low level of the Ki-67 index marker, a nuclear antigen found to be more strongly expressed in cells exhibiting high rates of cell division and proliferation [13]. Previous reports have suggested a value above 3% to be indicative of tumors having invasive and aggressive characteristics [14]. Therefore, it is unsurprising that in this study a low Ki-67 index level was found among those pituitary adenomas that did not invade into the CS. Interestingly, those tumors that did not invade laterally into the parasellar region were found to be significantly larger in the cranio-caudal direction compared to those tumors that exhibited CS involvement. Since the pituitary gland is bordered inferiorly by the sella turcica of the sphenoid bone and laterally by dura mater, a dense, fibrous layer of connective tissue encasing the CS, pituitary tumors with low invasive potential are more likely to exhibit vertical, rather than horizontal, growth. This vertical pathway between the diaphragma sella and the pituitary infundibulum offers a low resistance pathway, providing a more accessible route for non-aggressive and slow growing tumors. Therefore, while greater vertical growth may not be diagnostic of lack of CS invasion, increasing tumor size in the cranio-caudal direction may be suggestive of a less aggressive and invasive adenoma.

Conclusion

While MR imaging is not always accurate in the diagnosis of true cavernous sinus invasion, the presence of certain clinical characteristics may strengthen the suggestive power of radiographic reports. In this study, younger age was significantly associated with true CS invasion, as confirmed on operative notes. Additionally, a low Ki-67 index and increased vertical tumor growth was found to correspond to tumors with low invasive potential into the lateral parasellar space.

Declarations of interest

None

Funding

None.

References

1. Jesser J, Schlamp K, Bendszus M (2014) [Pituitary gland tumors]. Radiologe 10: 981-988.
2. Molitch ME (2017) Diagnosis and Treatment of Pituitary Adenomas: A Review. JAMA 317: 516-524.
3. Mahalingam HV, Mani SE, Patel B, Prabhu K, Alexander M, et al. (2019) Imaging Spectrum of Cavernous Sinus Lesions with Histopathologic Correlation. RadioGraphics 39: 795-819.
4. Ajlan A, Achrol AS, Albakr A, Feroze AH, Westbroek EM, et al. (2017) Cavernous Sinus Involvement by Pituitary Adenomas: Clinical Implications and Outcomes of Endoscopic Endonasal Resection. J Neurol Surg B Skull Base 78: 273-282.
5. Araujo-Castro M, Acitores Cancela A, Vior C, Pascual-Corrales E, Rodríguez Berrocal V (2021) Radiological Knosp, Revised-Knosp, and Hardy-Wilson Classifications for the Prediction of Surgical Outcomes in the Endoscopic Endonasal Surgery of Pituitary Adenomas: Study of 228 Cases. Front Oncol 11: 807040.
6. Buchy M, Lapras V, Rabilloud M, Vasiljevic A, Borson-Chazot F, et al (2019) Predicting early post-operative remission in pituitary adenomas: evaluation of the modified knosp classification. Pituitary 22: 467-475.
7. Ahmadi J, North CM, Segall HD, Zee CS, Weiss MH (1986) Cavernous sinus invasion by pituitary adenomas. AJR Am J Roentgenol 146: 257-262.
8. Cottier JP, Destrieux C, Brunereau L, Bertrand P, Moreau L, et al (2000) Cavernous sinus invasion by pituitary adenoma: MR imaging. Radiology 215: 463-469.

9. Vieira JO Jr, Cukiert A, Liberman B (2006) Evaluation of magnetic resonance imaging criteria for cavernous sinus invasion in patients with pituitary adenomas: logistic regression analysis and correlation with surgical findings. Surgical Neurology 65: 130-135.

10. Fang Y, Wang H, Feng M, Chen H, Zhang W, et al. (2022) Application of Convolutional Neural Network in the Diagnosis of Cavernous Sinus Invasion in Pituitary Adenoma. Frontiers in Oncology 12.

11. Trott G, Ongaratti BR, de Oliveira Silva CB, Abech GD, Haag T, et al. (2019) PTTG overexpression in non-functioning pituitary adenomas: Correlation with invasiveness, female gender and younger age. Annals of Diagnostic Pathology 41: 83-89.

12. Chen C, Hu Y, Lyu L, Yin S, Yu Y, et al. (2021) Incidence, demographics, and survival of patients with primary pituitary tumors: a SEER database study in 2004-2016. Sci Rep 11: 15155.

13. Li LT, Jiang G, Chen Q, Zheng JN (2015) Ki67 is a promising molecular target in the diagnosis of cancer (Review). Mol Med Rep 11: 1566-1572.

14. Thapar K, Kovacs K, Scheithauer BW, Stefaneanu L, Horvath E, et al. (1996) Proliferative activity and invasiveness among pituitary adenomas and carcinomas: an analysis using the MIB-1 antibody. Neurosurgery 38: 99-106.

HERALD

Advances In Industrial Biotechnology | ISSN: 2639-5665

Advances In Microbiology Research | ISSN: 2689-694X

Archives Of Surgery And Surgical Education | ISSN: 2689-3126

Archives Of Urology

Archives Of Zoological Studies | ISSN: 2640-7779

Current Trends Medical And Biological Engineering

International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X

Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276

Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292

Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370

Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594

Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X

Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562

Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608

Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879

Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397

Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751

Journal Of Aquaculture & Fisheries | ISSN: 2576-5523

Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780

Journal Of Biotech Research & Biochemistry

Journal Of Brain & Neuroscience Research

Journal Of Cancer Biology & Treatment | ISSN: 2470-7546

Journal Of Cardiology Study & Research | ISSN: 2640-768X

Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943

Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771

Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844

Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801

Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978

Journal Of Cytology & Tissue Biology | ISSN: 2378-9107

Journal Of Dairy Research & Technology | ISSN: 2688-9315

Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783

Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X

Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798

Journal Of Environmental Science Current Research | ISSN: 2643-5020

Journal Of Food Science & Nutrition | ISSN: 2470-1076

Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X

Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566

Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485

Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662

Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999

Journal Of Hospice & Palliative Medical Care

Journal Of Human Endocrinology | ISSN: 2572-9640

Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654

Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493

Journal Of Light & Laser Current Trends

Journal Of Medicine Study & Research | ISSN: 2639-5657

Journal Of Modern Chemical Sciences

Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044

Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X

Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313

Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400

Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419

Journal Of Obesity & Weight Loss | ISSN: 2473-7372

Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887

Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052

Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X

Journal Of Pathology Clinical & Medical Research

Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649

Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670

Journal Of Plant Science Current Research | ISSN: 2639-3743

Journal Of Practical & Professional Nursing | ISSN: 2639-5681

Journal Of Protein Research & Bioinformatics

Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150

Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177

Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574

Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060

Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284

Journal Of Toxicology Current Research | ISSN: 2639-3735

Journal Of Translational Science And Research

Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193

Journal Of Virology & Antivirals

Sports Medicine And Injury Care Journal | ISSN: 2689-8829

Trends In Anatomy & Physiology | ISSN: 2640-7752