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Decision-Making in Clival Mass Lesions: Risk Factors for Malignant Disease and an Illustrative Case Example

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Abstract

Introduction Clival tumors are rare and heterogeneous. Although some benign prototypical sellar lesions may present as clival tumors, the likelihood of malignant disease is higher. Here we define a novel algorithm for the workup and management of clival masses through an illustrative case of colorectal adenocarcinoma metastasis to the clivus.

Methods In this case report, the best practice guidelines for managing clival masses are described through a literature review and refined by senior author consensus. We conducted a focused systematic review to characterize the present case in the context of clival metastasis from gastrointestinal malignancy.

Results An 83-year-old woman presented with 4 weeks of headaches and blurry vision. Examination revealed partial right abducens and left oculomotor palsies. Magnetic resonance imaging (MRI) identified a large, weakly enhancing sellar and clival mass with sphenoid sinus extension. An aggressive subtotal endoscopic endonasal resection was performed with removal of all sphenoid, clival, and sellar disease without cavernous sinus wall resection. Pathology confirmed colorectal adenocarcinoma; computed tomography (CT) imaging identified an ascending colon mass with metastases to the liver and mesenteric nodes. Palliative oncologic therapies were recommended, but she elected hospice, and died 3 months after initial presentation. Gastrointestinal clival metastases are exceedingly rare among sellar and clival pathologies, with eight prior cases reported, most of which presented with diplopia from abducens nerve involvement.

Conclusion Clival masses are uncommon skull base lesions that are associated with more aggressive diseases. We present a consolidated framework for decision-making in these challenging patients, alongside an unusual case example that illustrates the importance of increased suspicion for malignant clinical entities in this setting.

Keywords
- clivus
- sella
- metastasis
- colorectal adenocarcinoma

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Introduction

Tumors involving the clivus are rare, representing approximately 0.1% of all intracranial tumors.[1] Chordoma and chondrosarcoma—both uncommon diagnoses unto themselves—represent the majority of clival lesions, followed by a range of rare entities. Given the unusual distinction of the clivus as an anatomical location with a strong predilection for atypical entities, the goal of the current study was to report a preliminary clinical protocol for the diagnosis and management of a suspected clival neoplasm, described through the lens of an illustrative case of metastatic colorectal cancer presenting with isolated cranial abducens and oculomotor palsies. We further emphasize the importance of an aggressive approach toward the evaluation of clival lesions, given the high prevalence of malignant diseases within this rare subset of skull base tumors.

Methods

Case history and pertinent details for the illustrative case example were abstracted from the electronic medical record via a retrospective chart review. A systematic review of the literature for gastrointestinal malignancies to the clivus was conducted via a PubMed search conducted in January 2023 using the following keywords alone and in combination: "clivus," "gastrointestinal cancer," "adenocarcinoma," "colorectal," "gastric." Inclusion criteria were original articles published in English since 2000 documenting cases or series of patients with gastrointestinal metastases to the clivus. Following abstract screening, eligible records underwent full-text review, followed by study inclusion as indicated. Data abstracted from included manuscripts were primary pathological diagnosis, age, sex, presenting symptoms, cancer history including chronicity of clival and general diagnoses with lead time for metachronous diagnosis, and treatment histories. A general review of management principles for clinical care of patients with clival lesions was performed by the study team and used to provide preliminary recommendations for a management algorithm, which was in turn further refined by serial collaborative revisions among the senior authors (I.F.D., C.S.G.). All pertinent aspects of the current study were conducted under the approval and supervision of our institutional review board.

Illustrative Case Example

Presentation

An 83-year-old woman with multiple chronic medical conditions presented to an outside emergency department (ED) complaining of headache and blurry vision, worsening over the preceding 4 weeks. Computed tomography (CT) imaging of the head identified a skull base mass centered in the clivus with erosion into the sella and sphenoid sinus (►**Fig. 1**). Laboratory studies were unremarkable, apart from stable findings consistent with the patient's known chronic hypothyroidism. Given the high clinical suspicion for benign etiology of the mass, the decision was made to observe the patient on an outpatient basis.

Two weeks later and prior to outpatient evaluation, the patient returned to the ED with a new syncopal episode followed by progressive visual decline, concerning for apoplexy. On examination by our service, she was found to have right lateral gaze restriction and left ptosis with anisocoria and subjectively decreased visual acuity. Magnetic resonance imaging (MRI) of the brain demonstrated a 2.6 cm × 2.7 cm × 3.5 cm T1-hypointense, T2-hypointense, modestly enhancing clival and sellar mass with ventral extension into the sphenoid sinuses (►**Fig. 2**), suggestive of pituitary macroadenoma.

Treatment

The patient underwent an endoscopic endonasal transsphenoidal approach to the sella. A soft, friable, well-encapsulated mass was encountered within the sphenoid, clivus, and sella, without intradural or intracavernous extension. A gross total resection (GTR) was readily achieved in a piecemeal fashion through a combination of suction and blunt dissection techniques. Intraoperative pathology was concerning for carcinoma. Consideration was given to resection of the diaphragm sellae or medial cavernous sinus walls, but ultimately deferred due to the significant risk of deficit without

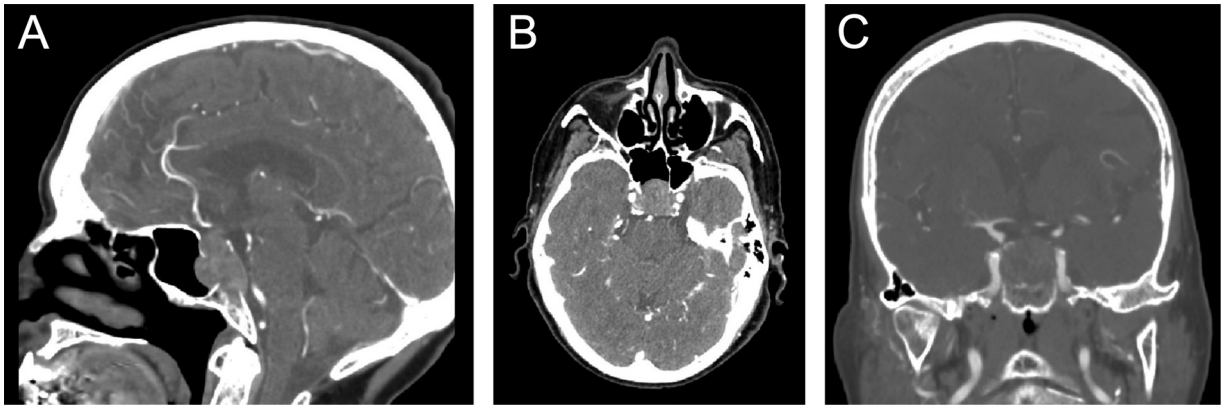

Fig. 1 Initial (**A**) sagittal, (**B**) axial, and (**C**) coronal computed tomography scan of the brain demonstrating a soft-tissue lesion in the sella with erosion into the clivus and sphenoid sinus.

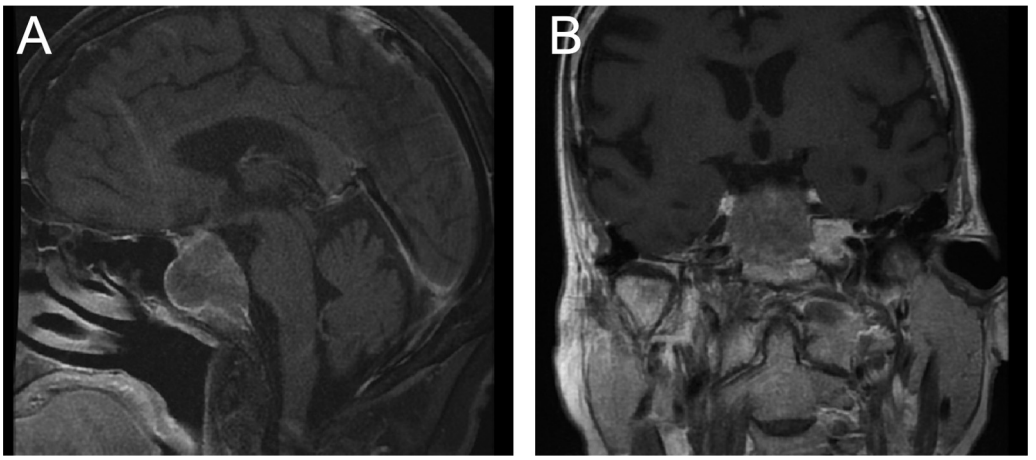

Fig. 2 Preoperative (**A**) sagittal and (**B**) coronal T1 magnetic resonance imaging with contrast of the pituitary demonstrating the 2.6 cm × 2.7 cm × 3.5 cm mass involving the sella extending into the right sphenoid sinus and superior clivus.

defined benefit. The skull base was then reconstructed with a free mucosal graft followed by routine nasal packing, and the patient completed an uneventful postoperative recovery.

Outcome

Postoperative MRI demonstrated GTR of the lesion without disruption of the normal pituitary gland with presumed normal-appearing pituitary tissue in the sella. The patient's left incomplete oculomotor palsy and right abducens palsy persisted following surgery. Final pathology of the mass demonstrated an enteric-type adenocarcinoma comprising well-formed glands and tubules with dirty necrosis (►**Fig. 3**). The tumor cells demonstrated immunoreactivity to CDX2, villin, and cytokeratin 20, and were nonreactive with cytokeratin 7, thyroid transcription factor-1 (TTF-1), Napsin-A, and synaptophysin. The histomorphology and immunohistochemical profile were consistent with an adenocarcinoma of the gastrointestinal tract. Primary intestinal-type sinonasal adenocarcinoma, a similar-appearing tumor arising from the sinonasal region, was excluded in this case given that there was no involvement of the sinonasal cavity on imaging studies. Subsequent CT of the chest, abdomen, and pelvis revealed an ascending colon mass with numerous hepatic metastases and early mesenteric lymph node involvement (►**Fig. 4**). The patient was referred to oncology to discuss treatment, but ultimately elected to proceed with hospice with symptomatic palliation and died approximately 1 month postoperatively.

Discussion

Due to their close relationships to critical skull base structures, mass lesions involving the clivus or sella may result in major neurological deficits. Clival masses are frequently

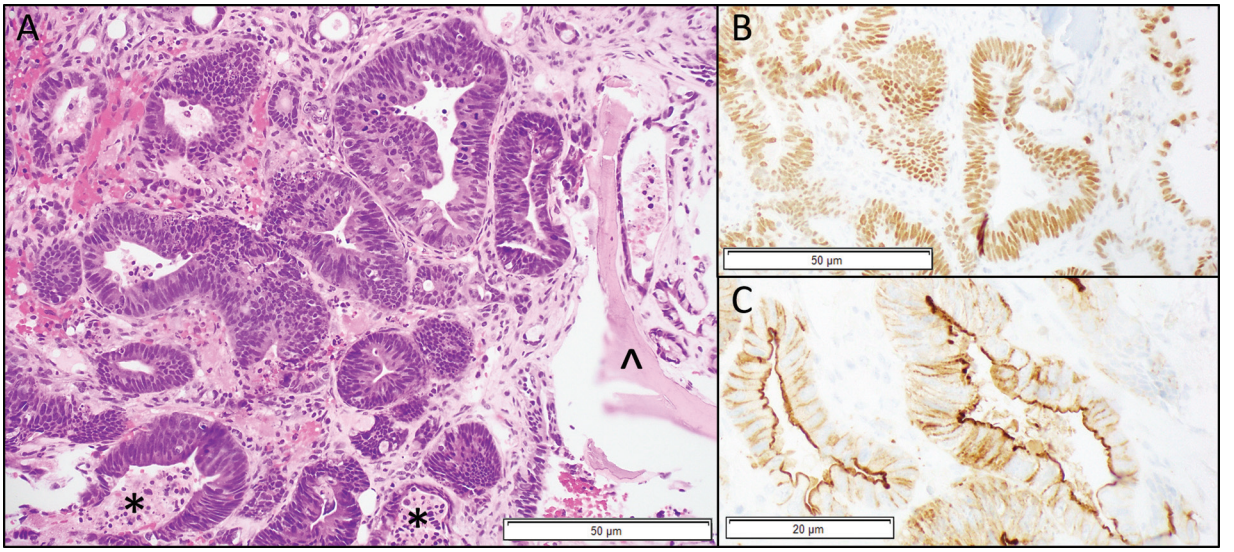

Fig. 3 (**A**) Hematoxylin and eosin stained slide (×200 magnification) demonstrating well-formed glands and simple tubes with dirty necrosis (*) adjacent to bone (^). Immunohistochemically stained slides for (**B**) CDX2 (×200 magnification) demonstrating nuclear staining in tumor cells and (**C**) villin (×400 magnification) demonstrating staining in the tumor cells at the apex of the cells, around the lumen of the gland (luminal staining).

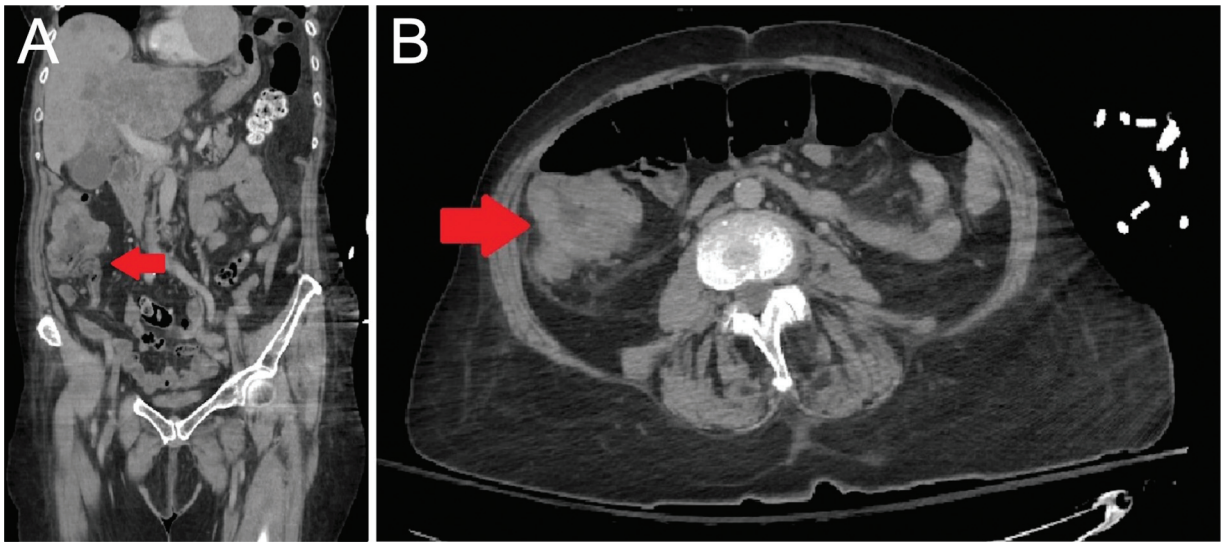

Fig. 4 (A) Coronal and (B) axial computed tomography scan with/without contrast of the abdomen and pelvis demonstrating a prominent thickening of the proximal ascending colon (red arrow) suspicious for colorectal cancer.

identified incidentally on imaging; when symptomatic, they present clinically with headache or cranial nerve palsy, most likely involving the abducens nerve or another element of the cavernous sinus.[2] Sellar masses more frequently present with visual field deficits or endocrinopathy due to compression of the optic chiasm or pituitary gland.[3]

The list of common clival tumors includes a surprisingly wide swath of rare diseases, the most common of which include chordoma, chondrosarcoma, plasmacytoma/multiple myeloma, and metastatic disease (►**Fig. 5**). In contrast to the predominantly malignant pathologies encountered in the clivus, the differential for sellar lesions is predominantly populated by benign entities, such as pituitary adenoma, craniopharyngioma, and meningioma. Given the close relationship of the sella and clivus, some overlap exists in the differential between the two regions in particular for invasive diseases that may involve both regions.[4]

Metastatic tumors involving the clivus are estimated to account for less than 0.02% of all intracranial tumors.[5] Although chordomas comprise the majority of clival tumors, clival masses in patients with a known cancer diagnosis are nevertheless more likely to be of metastatic origin.[6,7] A recent meta-analysis by Jozsa and Das showed that, by incidence, metastatic tumors to the clivus most frequently arose from the prostate, kidney, and lung primaries.[5] Brain metastases from gastrointestinal (GI) malignancies have an estimated incidence of 1 to 3%,[8] which may be increasing over time as more effective treatments have continued to prolong overall survival.[9] Nonetheless, gastrointestinal metastasis to the clivus is exceedingly uncommon, with only

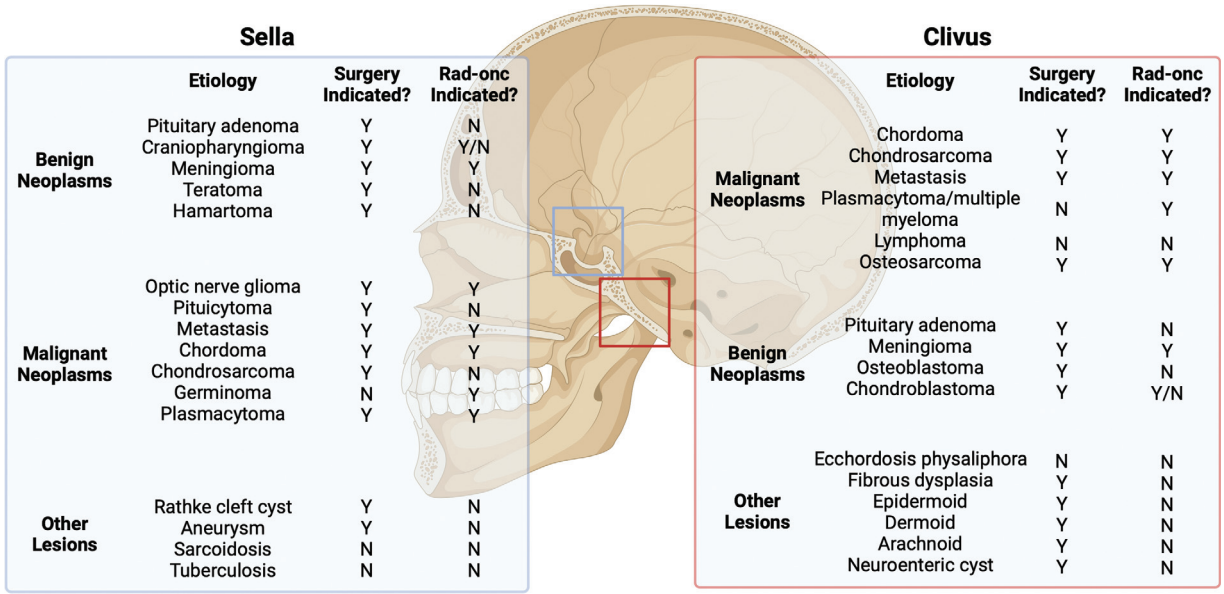

Fig. 5 Summary figure of differential diagnoses for sellar and clival pathologies. The etiologies are listed in order of approximate relative incidence.

Table 1 Literature review of previous gastrointestinal malignancy cases (within 20 years)

Study	Primary cancer	Age (y), sex	Symptoms at presentation	Known cancer diagnosis before clival metastasis presentation?	Lead time to clival metastasis presentation (y)
This report	Lower gastrointestinal adenocarcinoma	83, F	H/A, N/V, diplopia, R CN VI, and incomplete L CN III palsies	No	NA
Lee et al[19]	Gastric adenocarcinoma	42, F	H/A, N/V, diplopia, bilateral CN III and VI palsies	No	NA
Lee et al[20]	Upper gastrointestinal adenocarcinoma	78, M	H/A, diplopia, R facial pain, altered taste, R CN V, VI, VII, and XII palsies	No	NA
Dekker et al[21]	Duodenal adenocarcinoma	67, M	H/A, diplopia, and bilateral CN VI palsy	Yes	1
Yoshikawa-Kimura et al[22]	Gastric carcinoma	73, M	H/A, tongue deviation, and CN IX and XII palsies	Yes	2
Kendre et al[23]	Rectal signet cell carcinoma	34, M	Diplopia and bilateral CN VI palsy	Yes	2
Fukushima et al[24]	Gastric signet cell carcinoma	64, M	H/A, diplopia, and bilateral CN VI palsy	Yes	10
Baeg et al[25]	Gastrointestinal stromal tumor	70, M	Diplopia and R CN VI palsy	No	NA
Barrière et al[26]	Rectal stroma tumor	57, M	Diplopia and R CN VI palsy	No	NA

Abbreviations: CN, cranial nerve(s); F, female; H/A, headache; L, left; M, male; NA, not applicable; N/V, nausea and vomiting; R, right.

eight cases reported in the last 20 years (►**Table 1**). Notably, five of the nine cases (including our patient) were diagnosed via the clival lesion, which itself was identified due to diplopia.

Clinical Pearls and Preliminary Management Algorithm

Management of clival tumors should consider several factors, including suspicion of malignancy, presence of symptoms, and the potential to safely achieve a GTR. Clinical and radiographic findings populate and refine the differential diagnosis, which in turn guides decision-making (►**Fig. 6**).

A critical early branch point in the clinical logic is the potential for malignancy. When benign disease is suspected, the decision to either observe or resect should be made in consideration of risk of morbidity on progression as compared with proactive resection, taken in the context of active symptoms and the potential for intervention to provide relief. For most patients, symptomatic mass effect or high risk of progression increasing treatment morbidity should prompt consideration for early resection. Alternatively, asymptomatic benign diseases that progress in an indolent fashion will be more amenable to front-line observation. In ambiguous circumstances, recommendations should be made with allowances for individual patient preferences and risk tolerance.

Where malignant or aggressive disease is suspected, management is guided in part by the potential to achieve a GTR. When GTR is possible, resection is likely warranted, assuming the patient's performance status and systemic disease burden are aligned with sustaining a major operation. Ambiguous presentations from either a diagnostic or prognostic perspective warrant an operative biopsy to obtain a pathologic diagnosis via the endonasal approach. Patients who are not surgical candidates or who defer resection will likely be eligible for palliative chemotherapy or irradiation, guided by the biopsy findings.

Radiographic Assessment of Clival and Sellar Lesions

Although histopathological analysis is required for definitive diagnosis, imaging features of clival lesions provide crucial insight in refining the differential and formulating a plan.[10] CT imaging defines bony anatomy, which in turn highlights whether the tumor behavior has been lytic, blastic, erosive, invasive, or simply expansile, among other less common but important changes.[2] MRI is more sensitive than CT for evaluating bone marrow signal abnormalities in the skull base and adjacent soft tissues, as well as the presence and extent of any intracerebral involvement.[2]

Common Lesions of the Sella

Pituitary adenomas are the most common sellar lesions, and typically present with characteristically weak but homogeneous contrast enhancement and isodense/isointense signal, relative to gland.[3,10] On T2-weighted imaging, they typically appear isointense or hyperintense.[2] Pituitary adenomas

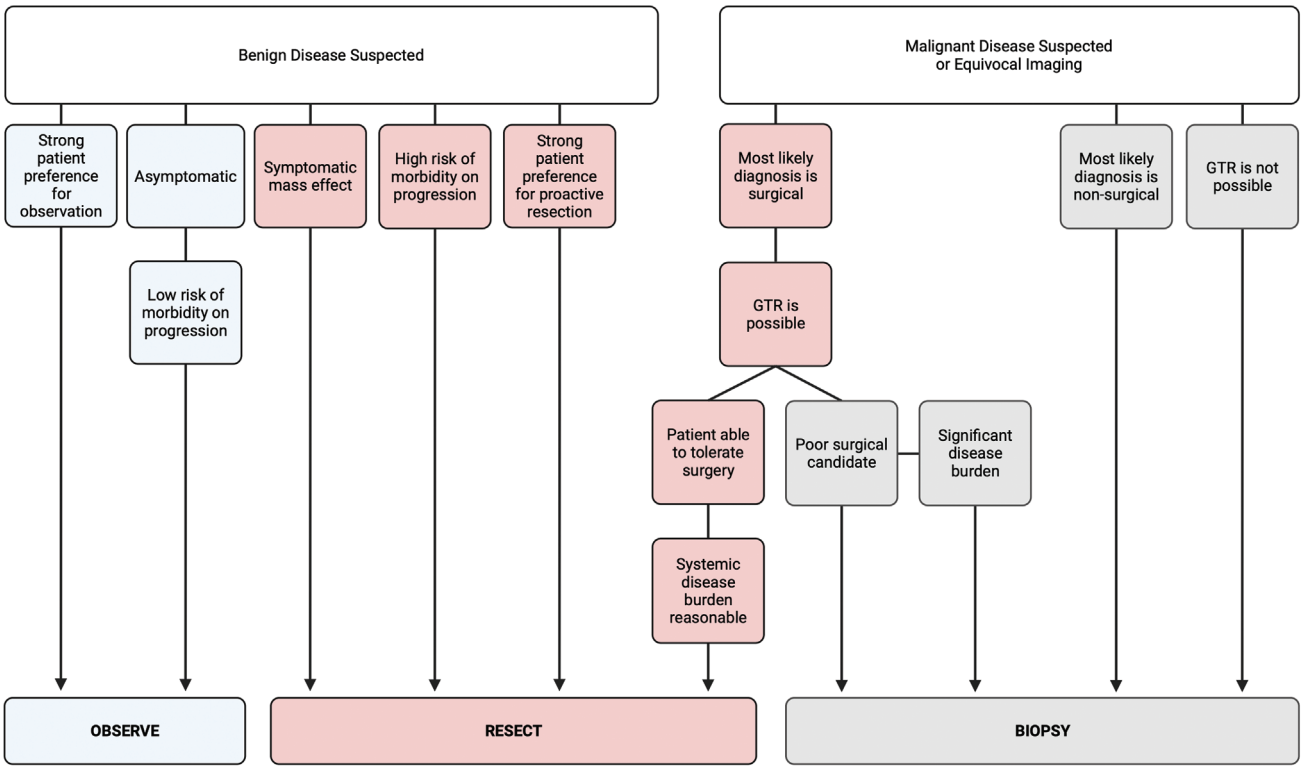

Fig. 6 Overview algorithm for decision-making between observation, resection, and biopsy of clival and sellar mass lesions.

smoothly expand the bony sella and lack calcification, which are key distinguishing features from a sellar meningioma.[10,11] Macroadenomas (>10 mm) are more prevalent than microadenomas, and invade into the cavernous sinus in up to 10% of cases, which increases the risk of surgical morbidity.[10] Secreting pituitary tumors represent a minority of microadenomas, and present with distinct clinical and laboratory features that are often diagnostic.[12]

Meningiomas are the most common benign primary central nervous system neoplasm, and frequently demonstrate iso- to hyperdense CT and iso- to hypointense T1- and T2-weighted MRI findings.[10] Characteristic features of meningiomas include the presence of a wide dural base with an enhancing dural tail, hyperostosis of adjacent bone, and unambiguous differentiation from pituitary gland tissue.[10]

Rathke's cleft cysts (RCC) and craniopharyngiomas are congenital and neoplastic lesions arising from remnants of the Rathke pouch, respectively. Both of these entities have the potential to appear as suprasellar lesions, but differ in their complexity,[3,13] with RCCs appearing as simple, typically non-enhancing cysts, in comparison to the polycystic, heterogeneous, often partially intraventricular appearance of craniopharyngiomas.[3,10] Despite their histologically benign grade, craniopharyngiomas have the potential to cause significant morbidity due to the involvement of regional neurovascular structures and the challenge of obtaining a complete resection without deficits.[3,13] Nuanced management of craniopharyngiomas is beyond the scope of the review, in particular given the profound advances recently reported in the application of proton beam therapy[14] and BRAF inhibitors[15] for the treatment of appropriately selected lesions.

Common Lesions of the Clivus

Clival chordomas appear on CT as midline soft-tissue lesions with bony destruction and sharp margins; MRI signal intensity is variable, but most often T1 hypointense and T2 hyperintense with a possible T2 "lightbulb" sign.[2,7] Chordomas almost universally arise in the midline, medial to the petroclival synchondrosis, which is a key distinguishing feature from chondrosarcomas, which have similar MRI signal patterns but are prototypically centered on the synchondrosis itself.[1,6,10] Calcification is unusual in chordomas but commonplace in chondrosarcomas, appearing in approximately 41% of such lesions.[10]

Plasmacytoma describes the singular form of multiple myeloma and appears iso- to hyperintense on T1- and T2-weighted MRI with robust engagement.[1] In contrast to chordomas, plasmacytomas are typically generally centered within the bone, although exophytic lesions or tumors involving the skull base foramina have been reported.[10,16] Multiple comorbid vertebral lesions and positive ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) in the setting of suspected plasmacytoma are consistent with multiple myelomas.[17]

Clival metastases are radiographically diverse, due to the heterogeneous behavior of the primary malignancies. CT typically reveals areas of lytic bone destruction, although prostate metastasis is associated with osteoblastic lesions.[2] While a limited number of studies have reported a range of intensity from hypo- to hyperintense on both T1- and T2-weighted images,[18] metastasis is most commonly characterized as hypointense on T1-weighted images with heterogeneous contrast enhancement.[1] Notably, metastatic lesions may be hypointense on T2-weighted images,[7] thus providing

a potential differentiating factor from T2-hyperintense chordomas and chondrosarcomas. Although MRI may help differentiate between various clival tumors preoperatively, it is rarely definitive, particularly when heterogeneous entities like metastatic disease are suspected.[18]

From Case to Concept: When to Look for Zebras

Metastasis to the clivus is a rare occurrence, and the current study highlights how unique each of such cases may be—whether in terms of the rarity of the primary in that location, the presentation, or the imaging findings. The case of our patient is one of the only reported instances of colorectal adenocarcinoma metastatic to the clivus, which presented with subjective visual blurring ultimately found referable to differential left- and right-sided cranial neuropathies. Although an identical case presentation may not be seen in the foreseeable future, the core lesson remains critical: unusual skull base presentations warrant an aggressive stance, in particular toward the establishment of a tissue diagnosis when any potentially malignant features are observed. At a minimum, atypical imaging findings or neurological deficits should prompt comprehensive diagnostic imaging to assess for possible malignancies with very close clinical follow-up.[5]

Conclusion

Clival tumors are rare and often benign, but given the wide swath of potential diagnoses, a high index of suspicion for malignant or aggressive diseases is warranted. Tissue pathology is frequently needed to establish a definitive diagnosis and treatment plan, and equivocal presentations should be approached with a relatively aggressive posture. Atypical entities are found more frequently here than elsewhere in the skull base, and a healthy degree of clinical suspicion will likely benefit patients and surgeons alike.

Conflict of Interest
CSG serves as Editor-in-Chief for the *Journal of Neurological Surgery Reports*.

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