



Case report

Cavernous sinus syndrome associated with metastatic colorectal cancer and perineural spread along the trigeminal nerve



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ABSTRACT

Purpose: We report the case of a patient with cavernous sinus syndrome associated with biopsy-confirmed metastasis from colorectal cancer.

Observations: A patient known for laryngeal carcinoma and metastatic colorectal carcinoma presented with symptoms of left trigeminal neuralgia and progressive, near-complete ophthalmoplegia. Magnetic resonance imaging (MRI) revealed a mass in the left cavernous sinus, extending into Meckel's cave with perineural spread along the mandibular branch of the left trigeminal nerve. A transsphenoidal biopsy was performed and demonstrated metastatic colon adenocarcinoma. We review the existing literature on colorectal cancer associated cavernous sinus syndrome.

Conclusions and importance: Cavernous sinus metastasis from colorectal cancer is exceedingly rare. We report the second case of this entity with histopathologic confirmation, and the first case with concurrent perineural spread involving the trigeminal nerve. Cavernous sinus metastasis may represent a poor prognostic factor in colorectal cancer.

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Introduction

Cavernous sinus syndrome, also known as parasellar syndrome, is characterized by unilateral ophthalmoplegia of varying degree that may be associated with pain, pupillary changes and trigeminal nerve dysfunction. A variety of etiological processes have been associated with cavernous sinus syndrome including neoplastic, vascular, infectious and inflammatory pathologies. Neoplastic lesions are the most common, and can range from benign to locally invasive and metastatic disease.^{1,2} While metastases to the cavernous sinus are often attributed to primary breast and lung malignancies, gastrointestinal cancers are rarely associated with such lesions.³ Cavernous sinus metastasis associated with colorectal cancer is exceedingly rare with less than a handful of documented cases in the literature.^{4–6} We report the clinical course and pathology of a patient with biopsy-confirmed cavernous sinus syndrome resulting from metastatic adenocarcinoma of the colon.

Case report

An 82-year-old man presented to our ophthalmology service for diplopia in the context of a known cavernous sinus mass. The patient was also known for a history of laryngeal cancer and metastatic colorectal cancer. He was diagnosed with laryngeal invasive basaloid squamous cell carcinoma 2 years prior to presentation (Fig. 1D), and within the same month, he was also found to have a T3, N1 invasive adenocarcinoma of his descending colon (Fig. 1A). The patient received radiotherapy for laryngeal cancer and underwent a hemicolectomy with adjuvant chemotherapy for his colorectal carcinoma. Over one year later on positron emission tomography (PET) screening, a spiculated lesion was noted in the right lung apex. A transthoracic needle biopsy was performed and pathology with immunohistochemistry (positive for CK20, negative for CK7, TTF1 and Napsin A) showed moderately differentiated adenocarcinoma consistent with metastasis from the colon (Fig. 1B). At the time of presentation, the patient was receiving chemotherapy for metastatic disease.

The patient initially presented to ENT with headache and left-sided numbness in both the V2 and V3 distributions of the trigeminal nerve. Magnetic resonance imaging (MRI) of the head demonstrated a gadolinium-enhancing lesion exhibiting perineural spread extracranially along V3 (Fig. 2A) and extending posteriorly

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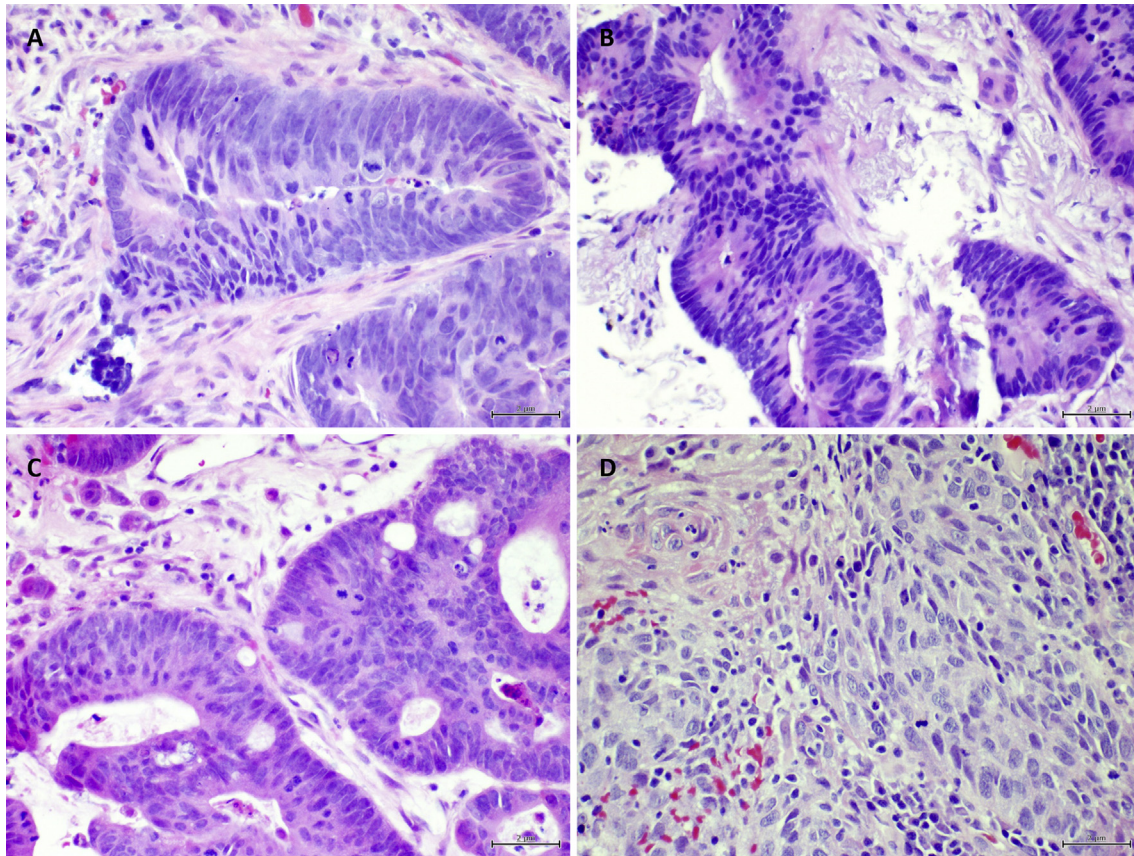


Fig. 1. Representative microphotographs of hematoxylin and eosin stained histological slides, magnification $\times 400$. A, initial adenocarcinoma from the colon. B, lung metastatic adenocarcinoma showing the same characteristics as the colon tumor. C, left cavernous sinus tumor showing an adenocarcinoma with presence of glandular differentiation consistent with a metastasis of the colon adenocarcinoma. D, tongue/larynx tumor showing a squamous cell carcinoma.

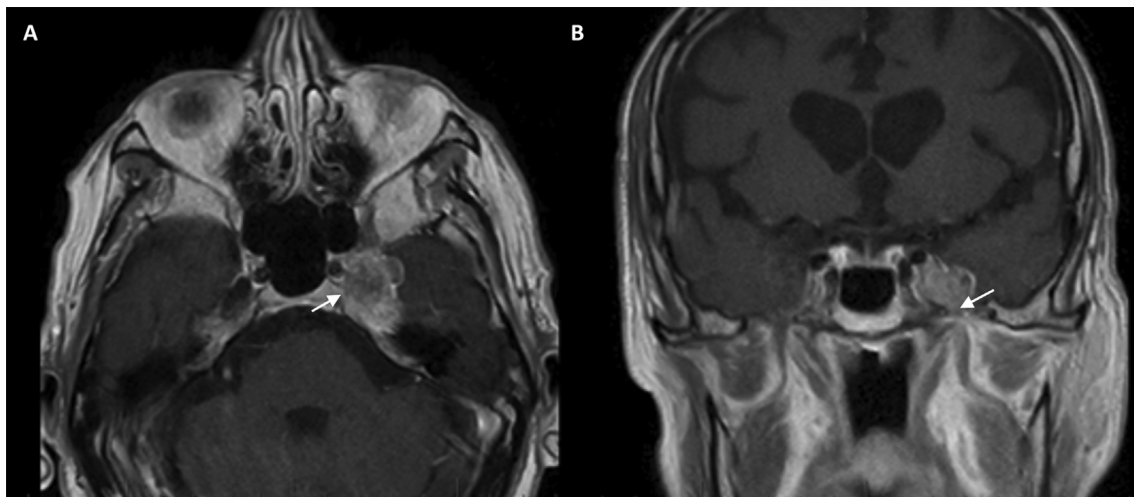


Fig. 2. Gadolinium-enhanced T1-weighted magnetic resonance imaging demonstrating left cavernous sinus mass. A, axial section showing posterior extension into Meckel's cave (white arrow). B, coronal section showing perineural spread into the left foramen ovale (white arrow) along the mandibular branch (V3) of the trigeminal nerve.

into Meckel's cave and in the subarachnoid space, anteriorly in the cavernous sinus, laterally into the left middle fossa, and inferiorly through the foramen ovale (Fig. 2B). An endoscopic trans-sphenoidal biopsy of the cavernous sinus lesion was performed showing adenocarcinoma with the presence of glandular differentiation (Fig. 1C). The samples were positive for cytokeratin 19/20

and CDX2, and negative for cytokeratin 5/6/7. These markers supported the diagnosis of metastatic colon adenocarcinoma, and no histological features suggestive of squamous cell carcinoma were noted.

Two months afterwards, the patient developed diplopia and presented to ophthalmology. Examination showed visual acuity of

20/50 OD and 20/60 OS with normal intraocular pressures. Pupils were equal and reactive with no relative afferent defect. Extraocular movements were full in the right eye, while a near complete ophthalmoplegia was present in the left eye. Decreased left corneal sensation was noted with a mild neurotrophic keratitis and accompanying numbness in V1–V3 distributions. Slit lamp and dilated fundus examination were otherwise unremarkable. Topical lubricants were prescribed for the left eye and patient was observed initially. Eventually during the course of follow up, the patient developed complete left-sided ptosis and ophthalmoplegia. Subsequently, with complete occlusion of his left eye, he had resolution of his diplopia. Further discussion with radiation and medical oncology concluded that the patient was not eligible for further chemotherapy or radiotherapy. The focus of care became palliative and the patient passed away several months later.

Discussion

Colorectal cancer with metastasis to the cavernous sinus has thus far only been reported in 3 cases.^{4–6} Thus far, only one case includes histopathologic confirmation of the diagnosis. The remaining cases consist of clinical and radiological diagnoses in the context of existing metastatic disease only. Given the sparsity of available data, our report contributes to and expands the clinical and pathological characteristics of cavernous sinus syndrome associated with colorectal cancer.

Although the limited number of reports precludes a definitive association, the presence of cavernous sinus metastases appears to accompany poor prognosis in colon carcinoma. In all currently documented cases, metastatic disease was present in other organ systems at the time of diagnosis of cavernous sinus syndrome.^{4–6} Furthermore, survival from diagnosis of cavernous sinus involvement ranged from 2 months to 1 year in these cases – a similar prognosis exists with respect to brain metastasis in colorectal carcinoma in which mean survival has been reported to be 4 months (ranging from 1 to 13 months).⁷ Our patient passed away 6 months after the onset of his symptoms.

The differential diagnosis of cavernous sinus tumours includes multiple entities, which vary in prognosis and management. Several factors confounded the clinical diagnosis of our patient's cavernous sinus mass and contributed towards the need for a histopathological diagnosis. First, a history of laryngeal cancer in addition to colorectal cancer was present at the time of diagnosis of the cavernous sinus lesion. Central nervous system (CNS) involvement in nasopharyngeal carcinoma is not uncommon, however it often occurs through direct invasion.⁸ In contrast, only 11 cases are reported documenting cavernous sinus metastasis from laryngeal carcinoma, with a mean survival of 4.7 months.^{9–15} Furthermore, given that the patient's MRI demonstrated perineural spread, a diagnosis of lymphoma could not be ruled out as it has also been shown to demonstrate this feature.¹⁶ Primary cavernous sinus lymphoma is a rare entity with 8 cases described in the literature – however, these lesions are amenable to systemic chemotherapy and the prognosis of cavernous sinus lymphoma with treatment is far better than that of metastasis from colorectal carcinoma with an average survival greater than 18 months.^{17–22} Meningioma is the most common CNS tumor (40%)²³ and should be ruled out in any cavernous sinus mass. When arising in the cavernous sinus, meningioma can be managed with a combinations of observation, microsurgical resection and stereotactic radiosurgery (SRS), and generally carries an excellent prognosis with 90% demonstrating tumor control after 5 years.²⁴ As such, biopsy and histological diagnosis of cavernous sinus tumours is pivotal in directing treatment and conferring prognosis.

The treatment of brain metastasis by whole brain radiotherapy (WBRT), SRS or surgical resection has been historically indicated in patients with positive prognostic factors; particularly a Karnofsky Performance Status (KPS) > 70, controlled primary tumor, age less than 60 years, and metastatic spread limited to the brain.²⁵ In particular, brain metastasis secondary to colorectal carcinomas are often associated with other systemic metastatic disease (particularly as a result of hematogenous spread from the lung or liver).²⁶ As such, these patients often have poor performance status at presentation. In patients with a low KPS, it has been suggested that SRS may be indicated if the low KPS is due to the cerebral metastasis and not extracranial disease.²⁷ With regard to cavernous sinus lesions, while some studies have reported positive outcomes of SRS for benign tumours,^{28–30} limited evidence exists for SRS in the context of cavernous sinus metastasis. Mori et al. report at least partial improvement of cranial nerve deficits in 4 of 9 patients with either cavernous sinus or both cavernous sinus and sella turcica metastasis.^{31,32} In the case of our patient, given his poor performance status and comorbidity with lung metastasis, palliative measures were opted for.

In addition, our patient was also found to demonstrate perineural tumor spread along V3 extending into Meckel's cave with associated trigeminal neuralgia. Malignant trigeminal neuralgia is more commonly associated with neoplasms of the head and neck region and has only been reported in colorectal carcinoma in 3 patients.^{33–35} No previous report of concomitant cavernous sinus syndrome and malignant trigeminal neuralgia exists. The presence of perineural invasion is known to be a poor prognostic factor in stage II and III colorectal carcinomas and may represent more aggressive tumor phenotypes.³⁶ However, its relevance in metastatic disease has yet to be elucidated.

Conclusions

Cavernous sinus syndrome may result from colorectal cancer metastasis and is exceedingly rare. We report the second case in the literature with histopathologic confirmation, as well as the first case presenting with concurrent perineural invasion resulting in malignant trigeminal neuralgia. Clinicians managing colorectal cancer should be aware of the rare, but significant, risk of metastasis to the cavernous sinus when managing those patients.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Conflicts of interest

None of the authors have any financial disclosure or conflicts of interest.

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