Rapid-developed primary malignant myoepithelioma in cavernous sinus: case report and review of the literature

Qun Wu, MD,a Song-Xue Guo, MS,b Jian-Min Zhang, MD,a Yuan Hong, MDa*

a Department of Neurosurgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, 88# Jiefang Road, Hangzhou, Zhejiang, China, 310009(Qun Wu: wuqun30639@sina.cn; Jianmin Zhang: zjm135vip@sina.com)

b Department of Neurosurgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, 3# East Qingchun Road, Hangzhou, Zhejiang, China, 310016(Songxue Guo: hy0904cjr@qq.com)

*Corresponding author

Yuan Hong, MD, Department of Neurosurgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, 88# Jiefang Road, Hangzhou, Zhejiang, China, 310009. Tel & Fax: +86-571-87784715. (E-mail address: hy0904@live.cn)

Financial Disclosure: None reported.
Rapid-developed primary malignant myoepithelioma in cavernous sinus: case report and review of the literature

Qun Wu, MD, Song-Xue Guo, MS, Jian-Min Zhang, MD, Yuan Hong, MD

ABSTRACT

Background: Myoepithelial carcinoma, also called malignant myoepithelioma, is a relatively rare malignant tumor that occurs most frequently in the salivary glands. A few isolated cases have been described in other locations, including the lung, bronchus, oral cavity, nasopharynx and larynx. The region of cavernous sinus is an uncommon condition of involvement in myoepithelial carcinoma. To the best of our knowledge, this is the first report of myoepithelial carcinoma arising from cavernous sinus.

Case presentation: Herein, we report a case of 48-year-old woman who presented with a 1-month history of diplopia and blepharoptosis and radiological evidence of a rapid developing cavernous sinus tumor. The patient underwent trans-sphenoidal biopsy and histological diagnosis showed a myoepithelial carcinoma. After diagnosis, the tumor grew rapidly and the clinical symptom deteriorated progressively, and therefore she received a pterional craniotomy with partial tumor removal. The patient eventually showed a worse prognosis, and was died two month after the initial operation. Because no organ of origin of the myoepithelial carcinoma, other than the cavernous sinus, was detected, this case was diagnosed as a primary intracranial myoepithelial carcinoma.

Conclusion: The purpose of presenting this case report is to raise awareness among clinicians to consider myoepithelial carcinoma as a differential diagnosis when a cavernous sinus mass is identified. Furthermore, ideal management strategy for myoepithelial carcinoma is not known and the prognosis of myoepithelial carcinoma seems to be unfavorable; therefore, more cases are needed to enhance our knowledge of the diagnosis, treatment, and prognosis of this rare intracranial lesion.

Keywords: Myoepithelial carcinoma, Cavernous sinus, Treatment, Pathology
**Background**

Myoepithelial carcinoma, is a malignant tumor usually happened in the salivary glands and there is a marked proliferation of myoepithelial cells, which normally present in the salivary, mammary and sweat glands [1, 2]. Less commonly, these tumors have been found in lung [3], bronchus [4], oral cavity [5, 6], nasopharynx [7], and larynx [8]. However, primary intracranial myoepithelioma is extremely rare and only two cases have been described according to our literature search. Neither of these reported cases involved the cavernous sinus. Here we report a rare case of myoepithelial carcinoma in cavernous sinus and discuss its clinical, histopathological, and immunohistochemical features, as well as the prognosis.

**Case presentation**

A 48-year-old woman was admitted to our hospital with symptoms of diplopia and blepharoptosis for one month. Before being to our hospital, the patient had visited the department of neurology in other hospital with symptoms aforementioned, and had not obtained abnormal result from performed Magnetic Resonance Imaging (MRI) (Figure 1A) and endocrine assessment. Although, having taken a corticosteroid therapy, her symptoms were ameliorated, these symptoms reappeared after drug withdrawal. Repeated MRI one month later demonstrated a mass lesion located in the left cavernous sinus with obscure boundary. The lesion was isointense in T1-weighted MRI sequences and hypointense in T2-weighted sequences. After intravenous contrast agent administration, T1-weighted images showed intense and inhomogenous enhancement of the mass (Figure 1B). She was referred to our hospital for further evaluation and treatment.

At the time of admission, physical examination (PE) of the patient showed left eye abnormal signs as blepharoptosis, a 4mm-diameter pupil with light reflex retardation, limited movement and visual field loss of upside, downside and temporal side, which were considered as results of homo-side oculomotor and abducent neves paralysis caused by mass pressure. Signs of pain and touch sensation reduction on left forehead skin also were observed with PE. No involvement of other cranial nerves was
observed. The pituitary hormones test show nothing abnormal. A general examination did not show any metastatic lesions in other areas. CT angiography revealed no cerebral aneurysms.

The preoperative differential diagnosis included pituitary adenoma invading the cavernous sinus, inflammation, metastatic brain tumor and primary malignant tumor arising in the cavernous sinus. As follows, we adopted the suggestion to use corticosteroid therapy on her for the aim of diagnosis. During the time of corticosteroid therapy, her symptom of blepharoptosis was relieved, while there is no change on other symptoms about sensation and pupil. Furthermore, the patient felt more serious headache, and then take an MRI scan, which result indicate a larger scope of mass than before (Figure 1C). With consideration to malignant tumor, for making an accurate diagnosis, an advisement of endoscopic trans-sphenoidal approach biopsy was presented to the patient and her family, and then they agreed with our suggestion. The biopsy was performed and digital pathological specimens of this rubbery mass were sent to Department of Pathology and Laboratory Medicine of UCLA Medical Center. A surgical pathology consult report returned and made a final diagnosis as myoepithelial carcinoma. Histological investigation of specimens revealed that a tumor composed of hyper-cellular, moderately pleomorphic round to polygonal tumor cells with moderate to marked nuclear atypia, and eosinophilic cytoplasm is noted. Metachromatic background substance and mitotic figures are present. There are areas of hemorrhage or necrosis (Figure 2). Immunohistochemistry (IHC) demonstrated that the tumor cells were positive for smooth muscle actin (SMA), glial fibrillary acidic protein (GFAP), S-100, and vimentin (Figure 3). The MIB-1 (Ki-67) proliferation index of rhabdoid and spindle-shaped cells were 60%. Staining for Desmin, EMA, CK5/6, CD138, myosin, HMB45, CD79a, and CD45 was negative. The histological findings of the tumor were compatible with myoepithelial carcinoma. The patient was then recommended for postoperative radiotherapy and chemotherapy. Due to the economic reasons, they refused the adjuvant treatment. After biopsy, her left pupil was progressively enlarging to the state of mydriasis, while the diameter of right pupil also gradually increased to 5mm with a reduction of light reflex. The signs
caused by effected facial and hypoglossal nerves were found by usual PE. The general condition of the patient was progressively deteriorated. A repeated MRI showed a more severe progressive development of tumor, which filling the left cavernous sinus and extending into the ipsilateral middle fossa (Figure 1D). Given the lesion’s expansion and the patient’s clinical deterioration, a pterional craniotomy for resection of progressed tumor to relieve intracranial pressure of the patient was performed. Only incomplete surgical resection was accomplished because the tumor extended to the hypothalamus and enclosed the left cavernous carotid artery. Postoperative MRI presented a large residue and successive growth of tumor (Figure 1E, F). This pathological finding was compatible with the initial biopsy findings. The final pathological diagnosis of the disease was spindle cell tumor, especially consider myoepithelial carcinoma of cavernous sinus. The patient died two weeks after the second operation due to rapid clinical deterioration, approximately four months from the onset of the initial symptoms. Autopsy was not performed.

**Discussion**

Myoepithelial carcinoma, also known as malignant myepithelioma, is rare tumor arising from salivary glands, which includes parotid glands, submandibular glands etc, and is accounting for less than 1% of the tumors of this region [9]. It is defined as a malignant neoplasm composed exclusively of tumor cells with myoepithelial differentiation. Myoepithelial carcinoma is usually found in the major salivary glands and breasts [2, 10]. Additionally, minor salivary glands which are distributed throughout lung, bronchus, oral cavity, nasopharynx and larynx, are also possible sites for occurrence of myoepithelial carcinoma. Date suggests that patients of almost any age may be affected, averaging 55 years, and the sex incidence is nearly equal [11]. The tumour arises either as a carcinoma arising from a preexisting benign tumour (pleomorphic adenoma or benign myoepithelioma) or de novo. It is characterized by markedly invasive growth and poor prognosis. Preoperative diagnosis may be difficult or impossible for myoepithelial carcinoma due to nonspecific clinical manifestation and imaging characteristics. Histological
examination supplemented with IHC staining studies is the most reliable and conclusive method of diagnose. From a pathological point of view, myoepithelial carcinoma commonly contains a marked proliferation myoepithelial cell, and morphologically, neoplastic myoepithelial cells present variously, including spindle, plasmacytoid, clear, epithelioid and stellate types [11, 12]. The presence of significant atypia, atypic mitotic figure, hemorrhage, and necrosis has been considered features of malignancy. An immunohistochemical study using a panel of epithelial and myogenic markers is essential to diagnosing this tumor. In common, as immunohistochemical characteristics, the neoplasm exhibits positive of vimentin, ctokeratin, myoepithelial special stain (such as SMA or S-100) and GFAP, all of which are considered as designated labels for myoepithelial carcinoma [2, 13, 14].

In this case, the tumor commonly consists of epithelioid cells and spindle cells with moderate to marked nuclear atypia (Figure 2A, B). The malignancy of the tumor is supported by cellular pleomorphism, nuclear atypia, hemorrhage, necrotic areas, a high mitotic activity and a high proliferative MIB-1 index in the neoplasm under light microscope. There are some tumors which also show similar spindle cell composition, such as pleomorphic adenoma, germ cell neoplasm, parachordoma, craniopharyngiomas, epithelioid sarcoma. Distinguishing myoepithelial carcinoma from other tumors is as difficult radiographically as clinically. Therefore, to make a final diagnosis of the present case, immunohistochemical studies are necessary. The expression patterns of the epithelial and myogenic markers are somewhat varied in each case, and may reflect the degree of myoepithelial cell differentiation. The combination of SMA, GFAP, S-100, and vimentin positive (Figure 3) in these lesions aids in the diagnosis of myoepithelial carcinoma. Finally, combined HE staining with immunohistochemical expression, we considered the tumor as myoepithelial carcinoma.

Intracranial primary myoepithelial carcinoma is extremely rare and has never been noted within the cavernous sinus. In view of this rare site for myoepithelial carcinoma, we only find two case reported intracranial primary myoepithelial carcinoma by help of medline and pubmed. Although there are some differences among three cases, we can
still explore possible explanation of occurrence of this salivary gland tumor. Carsten Nieder et al [15] had reported a similar case with a primary myoepithelial carcinoma in sellar region. The tumor in this case showed a longer progression of development, and there was no invasion to cavernous sinus. In addition, Sibel Erdogan et al [16] described a case of myoepithelial carcinoma arising in intracranial dura outside sellar region. In comparison to two cases, our case showed a rapid development (it only lasts four month from initial to dead) and a rare invasion to cavernous sinus. No occurrence within the cavernous sinus has been described previously.

The origin of myoepithelial carcinoma remains obscure. At first, we try to find some proofs of extracranial source with salivary gland distribution to explain as a metastatic tumor. However, with regard to the negative findings of the chest CT scan and nasal endoscopic check, we excluded possible primary sources, such as bronchus, nasopharynx, etc. Therefore, the primary determination of this case in cavernous sinus has been taken an understand of occurrence of salivary gland heterotopia into consideration. Histologically, sellar region is a neighboring site for oral cavity, nasopharynx and larynx, where there is salivary gland existing. And known reports had presented some sellar region salivary gland tumors may be related to salivary gland rests in sellar region or pituitary [17, 18]. In addition, a possible origin of multipotential stem cell also needs to be contained in consideration.

Since intracranial myoepithelial carcinomas are such a rare entity, effective management strategies have not been established. Treatment options include surgical resection, chemotherapy, radiotherapy, or a combination of these approaches. Surgical resection is the mainstay of therapy for myoepithelial carcinoma, but in some circumstances it may not be technically feasible due to rich vascularity and involvement of the cavernous sinus and carotid arteries. Radiation therapy and chemotherapy can also be used for myoepithelial carcinoma. But there is no consensus whether postoperative adjuvant therapy is even required, as the prognosis of this condition is unclear. Moreover, the sensitivity of the tumor cells to radiotherapy or chemotherapy has also not been established. Some authors reported that radiotherapy or concurrent chemoradiotherapy is effective for local recurrence and distant metastase [19, 20]. But
other reports confirmed the lack of effectiveness of this adjuvant treatment for both local and distant recurrences [15, 21]. The overall prognosis of myoepithelial carcinoma is poor. Several studies reported aggressive clinical behaviors for myoepithelial carcinoma, and the average metastatic rate was 47% and the mortality rate was 29% after a mean of 32 months[20]. Some factors have been evaluated as potential prognostic indicators, including clinical stage, site and size of the tumour, high proliferative activity, extensive invasion into the surrounding tissue, perineural permeation, the abnormal presence of nuclear DNA content, and marked cellular pleomorphism [22]. In our case, the course of the disease was very unfavorable, due to some factors including complete resection could not be achieved, radiotherapy or chemotherapy has not been used, and high proliferative activity (Ki-67 is 60%).

**Conclusion**

In conclusion, intracranial myoepithelial carcinoma is extremely rare or often misdiagnosed lesion. This is the first reported case of a myoepithelial carcinoma arising within the cavernous sinus. Preoperative diagnosis may be difficult or impossible due to nonspecific clinical manifestation and imaging characteristics, so diagnosis can only be made postoperatively based on histopathological and immunohistochemical data. The purpose of presenting this case report is to raise awareness among clinicians to consider this clinical entity as a differential diagnosis when a cavernous sinus mass is identified. Furthermore, ideal management strategy for myoepithelial carcinoma is not known. Surgical resection has been the accepted treatment for myoepithelial carcinoma. But the role of chemotherapy or radiotherapy is controversial. The prognosis of myoepithelial carcinoma seems to be unfavorable; therefore, more cases are needed to enhance our knowledge of the diagnosis, treatment, and prognosis of this rare intracranial lesion.

**Consent**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.
List of abbreviations:
MRI; Magnetic Resonance Imaging
PE; physical examination
IHC; Immunohistochemistry
SMA; Smooth muscle actin
GFAP; Glial fibrillary acidic protein

Competing interests
All authors declare no competing interest.

Authors' Contributions
Wu drafted the first manuscript and made a contribution to acquisition and interpretation of data. Guo and Zhang performed the clinical work-up and literature search. Hong revised the manuscript that led to the final approval of the current submission. All authors read and approved the final manuscript.

Authors' information
a Department of Neurosurgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, 88# Jiefang Road, Hangzhou, Zhejiang, China, 310009(Qun Wu: wuqun30639@sina.cn; Jianmin Zhang: zjm135vip@sina.com; Yuan Hong: hy0904@live.cn)
b Department of Neurosurgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, 3# East Qingchun Road, Hangzhou, Zhejiang, China, 310016(Songxue Guo: hy0904cxr@qq.com)

REFERENCES


Figure legends

Figure1. Continuous neuroimaging development of myoepithelial carcinoma in the case. Coronal T1-weighted postcontrast images showed normal (A). Follow-up images 1 month later showed a new left cavernous sinus mass with heterogeneous signal intensity (B). Preoperative images showed a larger scope of mass than before (C). Post-biopsy images showed a more serve progressive development of tumor, which filling the left cavernous sinus and extending into the ipsilateral middle fossa (D). Postoperative images showed large residue and successive growth of tumor (E, F).

Figure2. Histological photomicrographs. Hematoxylin and eosin stain (×100) shows an epithelioid neoplasm composed of hyper-cellular, moderately pleomorphic round to polygonal tumor cells embedded in a myxoid stroma. There are areas of hemorrhage or necrosis (A). Hematoxylin and eosin stain (× 400) Higher power magnification demonstrates the cells have round to ovoid nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm. Metachromatic background substance and mitotic figures are present (B).

Figure3. Immunohistochemical stains. The tumor cells demonstrated immunoreactivity for SMA (A), GFAP (B), S-100 (C), vimentin (D). Original magnification × 400.