CASE REPORT

Metastasis of malignant myoepithelial carcinoma to the brain

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Accepted 22 June 2018

SUMMARY

Myoepithelial tumours are a rare form of salivary gland neoplasm and intracranial metastases have rarely been described. The authors present the case of a 61-year-old patient with a history of primary myoepithelial carcinoma of the right foot. Metastases were found in the third ventricle, left temporal lobe and right frontal lobe. The third ventricular and left temporal lobe tumours were resected in a two-stage operation. Pathology of the third ventricular lesion was most consistent with metastasis. MRI of the spine 2 weeks after his operation revealed an intradural mass with several lesions in the lumbar thecal space suggesting further metastases. The patient succumbed to his disease 2 months after his two-stage operation and 5 years after his initial diagnosis. This appears to be the first case in the literature of multiple primary myoepithelial carcinoma metastases to the brain. Further information is needed to provide diagnostic and therapeutic recommendations.

BACKGROUND

Myoepithelial tumours are a rare form of salivary gland neoplasm and can be classified as either benign myoepitheliomas or malignant myoepithelial carcinomas. Benign myoepithelioma has an excellent prognosis with complete resection; however, it may recur with subtotal resection.^{1,2} Myoepithelial carcinoma frequently demonstrates more aggressive behaviour and may metastasise to distant sites in up to 32%–52% of patients.^{1–3} There have only been four reports of metastatic intracranial myoepithelial carcinoma reported in the literature. The purpose of this paper is to describe the first case of myoepithelial carcinoma to present with multiple central nervous system (CNS) metastases, including third ventricular and spinal cord metastases.

CASE PRESENTATION

A 61-year-old man presented with a 3-year history of a persistent right foot mass and chronic right foot pain. Palpable inguinal lymph nodes were present on examination. Lymph node dissection was consistent with myoepithelial carcinoma of the right foot with metastatic lymph node involvement. The patient opted for conservative surveillance at that time. Three years after this diagnosis, pulmonary and hepatic lesions were found and he elected for left wedge pneumonectomy and initiation of chemotherapy. However, despite multiple chemotherapeutic regimens over the next 2 years, there

was further pulmonary and liver progression, as well as the discovery of new omental metastases. Five years after his initial diagnosis, he experienced acute confusion, worsening balance and ataxia. An MRI of the brain was ordered to evaluate the possibility of cerebral metastases.

INVESTIGATIONS

Neuroimaging findings

MRI of the brain revealed three intracranial masses. The first was a heterogeneously enhancing lobulated mass located within the third ventricle at the level of the foramen of Monro with mild dilatation of the third and lateral ventricles (figure 1A, B). A second cystic mass was located within the inferior temporal gyrus of the left temporal lobe (figure 1C, D) and a third contrast-enhancing dural-based lesion was located in the right lateral frontal lobe. The patient was referred to neurosurgery for further evaluation.

TREATMENT

A two-staged operation was performed. First, the third ventricular mass was resected, followed by resection of the cystic, left temporal lobe mass 6 days later. This was complicated only by transient aphasia and left upper extremity weakness, which resolved by the second postoperative day.

OUTCOME AND FOLLOW-UP

Approximately 2 weeks after the second-stage operation, the patient described worsening neck and upper back pain and new-onset bilateral leg weakness. MRI of the lumbar spine was ordered and showed three enhancing lesions within the thecal space (figure 2). The largest lesion (16 mm) was present at the level of the L1 vertebral body, with other nodules seen along the distal cauda equina, suggestive of further metastases. Therefore, a decision was made to urgently initiate palliative radiation therapy to the whole brain and to T12–L2. Unfortunately, the patient succumbed to his disease 2 months after his two-staged operation, 5 years after his initial diagnosis.

Pathology

Pathology of the third ventricular mass showed a malignant, cellular, spindle cell proliferation with high nuclear to cytoplasmic ratio, moderate nuclear atypia, mitotic activity and apoptosis. The tumour was negative for several epithelial, meningotheelial, glioneuronal, melanocytic, lymphoid and

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To cite: Ellens NR, Camelo-Piragua S, Ellens SM, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224285

Figure 1 Radiographic imaging. Sagittal (A) and axial (B) T1 MRI of third ventricular mass. Sagittal (C) and axial (D) T1 MRI of left temporal lobe stage 2.

mesenchymal markers (AE1/AE3, MNF116, cytokeratin cocktail, CK7, CK20, TTF1, P63, EMA, progesterone receptor, GFAP, synaptophysin, Melan A, tyrosinase, CD43, CD45, CD10, SMM),

Figure 2 MRI of lumbar spine demonstrating intradural lesions.

Figure 3 Histopathology of third ventricular tumour. (A) H&E staining shows a well-circumscribed, malignant, hypercellular, spindle cell tumour with prominent mitotic activity. The tumour is diffusely positive for S100 (B) and SOX10 (C). Proliferation index (Ki-67) is about 30% (D). The tumour was negative for other myoepithelial markers such as p63, EMA, cytokeratin, actin and GFAP.

with positivity only to S100 and SOX10 (figure 3). Neurofilament highlighted the absence of axons within the tumour indicating the relative well-defined nature with the surrounding parenchyma, highly suggestive of a metastatic lesion.

Left temporal lobe tumour pathology demonstrated nearly identical tumour markers, most importantly demonstrating positivity for S100. However, positivity for SOX10 staining was not evaluated in this specimen.

Although the histology and immunohistochemistry of these specimens are not exactly characteristic of myoepithelial tissue, it was felt that this was due to malignant transformation and changes in expression, rather than a new tumour altogether. Therefore, having considered and largely excluded other possible primary and metastatic lesions, a clinicopathological correlation suggested that this was indeed a metastatic myoepithelial carcinoma.

DISCUSSION

Myoepithelial tumours are a rare form of salivary gland neoplasm, and the spectrum and classification of these tumours is diverse and complex. Tumours of myoepithelial origin typically occur in the salivary glands, scalp, sinuses, nasopharynx, larynx, palate, trunk, limbs and viscera.⁴

Most commonly these present as benign myoepitheliomas, but malignant myoepitheliomas, also known as myoepithelial carcinomas, have been known to metastasise to the lungs, bone, soft tissue, skin, liver and brain.⁵ Often, this classification can be made on the basis of metastasis. When arising *de novo*, rather than differentiating these tumours based on their architectural features, myoepithelial carcinomas can be differentiated by their cytologic atypia, increased nucleus:cytoplasm ratio and identifiable nucleoli.^{2,3,6}

Traditionally, these tumours were thought to contain only plasmacytoid or spindle cell morphologies.² However, recent studies have described myoepithelial tumours with various morphological cellularities including spindle, epithelioid, plasmacytoid, clear and stellate.⁶⁻⁸ Due to the similar histological nature of myoepithelial tumours with mixed tumours (pleomorphic adenomas) and parachordomas, these tumours are often collectively referred to

as 'MMP' tumours.⁹ Immunohistochemistry (IHC) of myoepithelial tumours frequently stains positive for EMA, S100, p63, GFAP, cytokeratin (AE1/AE3), CD10 and myogenic markers including calponin and smooth muscle actin.^{2-4 6 7} Interestingly, our patient had negative staining for many IHC markers typically present in myoepithelial tumours. This is presumably due to the malignant nature of the tumour, demonstrated by its propensity for intracranial metastasis, resulting in malignant transformation and increasing loss of expression of typical IHC markers.

The only markers present in this tumour at this point of malignancy were S100 and SOX10. These markers are often seen in peripheral nerve tumours and melanocytic lesions. However, other markers associated with those entities and clinical evidence of those types of tumours were not identified. A recent study of more than 5000 cases showed that SOX10 can also be seen in a proportion of myoepithelial tumours, suggesting that this is likely one of the few markers retained in this metastatic lesion.¹⁰

There have been very few examples of intracranial myoepithelial tumours described in the literature. The only example of a benign myoepithelioma arising intracranially was described by Vajtai *et al* and presented in the cerebellopontine angle.¹¹ Its benign nature was supported by long-term survival. Hayward *et al* has also described a case of benign myoepithelioma arising from direct extension from the orbital apex into the middle cranial fossa.⁴

Alternatively, there have been eight cases of intracranial malignant myoepithelial carcinoma reported.^{2 3 6 9 12-15} Of these eight, three of them occurred as a primary tumour in the cranial dura, sellar region and cavernous sinus.^{6 14 15} Additionally, another case involved direct extension from the parotid gland to involve, but not penetrate, the dura.¹³

Therefore, there have only been four cases of myoepithelial carcinoma metastasising intracranially.^{2 3 9 12} Of these four cases, two presented in 14-year-old girls.^{3 9} Unfortunately, of the other two cases, only one was described in detail.¹² In this case, Pogrel described a woman diagnosed with a parotid epithelial-myoeplithelial carcinoma of intercalated duct origin. This tumour metastasised to the temporal lobe and was not amenable to surgical resection. The patient died 2 months later, 20 months after her initial diagnosis.

The case presentation outlined in this paper is unique in multiple aspects. Most significantly, all previously reported cases of intracranial myoepithelial tumours, whether benign or malignant, primary or metastatic, have presented as a single, solitary tumour. The reported locations include metastasis to the clivus, temporal lobe, temporal bone, middle cranial fossa, cranial dura, cavernous sinus and sellar region.^{4 6 9 12-15} Interestingly, in our case, the patient developed three intracranial metastases. Additionally, further imaging also showed the presence of multiple metastases to the spinal cord, which has not been previously reported in the literature. It is important to note, however, that imaging of the spine was not performed immediately prior to this patient's two-staged operation. Therefore, it is difficult to determine whether his spinal lesions were present prior to surgery or whether they occurred via cerebrospinal fluid seeding, secondary to piecemeal resection of the tumour. The latter seems unlikely given the size of the spinal cord lesions and their symptomatic presentation only 2 weeks after surgery. However, the lack of data available regarding the metastatic spread of these tumours, particularly to the CNS, makes this determination particularly challenging.

CONCLUSION

Ultimately, metastatic intracranial myoepithelial carcinoma is an extremely rare tumour and may not possess many of the classic

immunohistochemical features present in other myoepithelial tumours. Currently, there is no standard therapy for these patients with metastatic spread of myoepithelial carcinoma to the CNS. However, piecemeal surgical resection may contribute to CNS seeding and further metastatic spread. This possibility should be taken into consideration when determining surgical approach and en bloc resection, if feasible, may minimise this risk. It may also be advisable to order complete imaging of the neuroaxis prior to surgery due to the possibility of subclinical spinal metastases, which may alter therapy.

Learning points

- ▶ Myoepithelial tumours are a rare form of salivary gland neoplasm and can rarely present intracranially.
- ▶ Myoepithelial tumours may metastasise to the brain or spinal canal and, therefore, complete imaging of the neuroaxis should be considered.
- ▶ There is no standard therapy for patients with metastatic spread of myoepithelial carcinoma to the central nervous system (CNS). However, piecemeal surgical resection may contribute to CNS seeding and further metastatic spread.

Contributors NRE contributed to the conception and design, acquisition of case information, drafting, revising and approving the final version of the manuscript. SC-P contributed to the design, acquisition and interpretation of case information, drafting, revising and approving the final version of the manuscript. SME contributed to the design, acquisition of case information, drafting, revising and approving the final version of the manuscript. JES contributed to the conception and design, acquisition of case information, drafting, revising and approving the final version of the manuscript. Dr Justin C Clark contributed to the conception and design, acquisition of case information, drafting, revising and approving the final version of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Next of kin consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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