Merkel cell carcinoma (MCC)

Merkel cell carcinoma (MCC) is a rare cutaneous malignancy of neuroendocrine origin.

Harary et al., from the Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, conducted a systematic review of the literature to identify cases reporting on management of distant MCC brain metastases (BM). A pooled survival analysis was performed on the institutional and literature cases to assess predictors of OS.

Forty cases were included for analysis, describing operative [14] and non-operative [26] management. Median time to central nervous system involvement was 17.0-mos (interquartile range 10.5-26.5), and most patients had a single BM (62.5%). Management of intracranial disease included radiotherapy (82.5%), systemic therapy (59.5%) and surgical resection (35%). Operative management was associated with a lower intracranial disease burden (DB), but similar DB. Both neurosurgery (hazard ratio [HR] 0.18, 95% confidence interval [CI]: 0.06-0.54, p = 0.002), having RT (HR 0.37, 95% CI: 0.14:0.93, p = 0.04) and having a single BM (extensive intracranial DB: HR 2.51, 95% CI: 1.12-5.6, p = 0.03) conferred an OS benefit on risk-unadjusted analysis. Only, neurosurgical resection was an independent predictor of OS (HR 0.12, 95% CI: 0.03-0.49, p = 0.003), controlling for age, DB and radiotherapy.

Resection of MCC BM may confer a survival benefit given appropriate patient selection. Prospective investigation of multimodal management of neurometastatic MCC is warranted, especially given the promise of new immunotherapy agents in treating MCC [1].

Case reports

A 59-year-old woman was admitted with a 4-month history of progressive and severe dorsal back pain, without neurological signs. The patient had been surgically treated for a recidivated MCC in the occipital region in 2007, 2011, and 2013. (In 2013, the surgical treatment also included lateral cervical lymph node dissection). Chemotherapy and radiotherapy had come after the treatments. Magnetic resonance imaging (MRI) of the dorsal spine showed metastatic vertebral involvement with cord impingement of the T7-T8 levels. A total body CT scan revealed lungs and liver metastases, besides vertebral district. After a multidisciplinary consult a palliative surgery was decided and a posterior dorsal approach was employed: Radiofrequency (RF) thermoablation was followed by the injection of cement of T7 and T8 and transpedicle fixation T5-T9. The postoperative course was uneventful and followed by a further adjuvant therapy.

Spinal metastases from MCC are described in literature only exceptionally. The clinical course is presented, along with a review of literature [2].

This case is particularly unusual in that, not only was no established primary lesion identified, but also the patient has survived for 10 years following initial diagnosis and for 9 years following excision of a single brain metastasis [3].

A case of Merkel cell carcinoma of the spine and evaluate the treatment paradigms utilized in the prior reports. Result A 76-year-old man with a history of Merkel cell carcinoma presented with 2-week history of progressive difficulty ambulating and a solitary T5 epidural mass encasing the spinal cord. The patient underwent a T5 corpectomy with cage placement and T3 to T7 posterior fusion with postoperative neurologic improvement and a return to ambulation. Three weeks postoperatively, the patient re-presented with new-onset weakness and widespread metastatic spinal disease with epidural compression at the T8 level. Six weeks postoperatively, he was placed in hospice care. Conclusion Prior reports in the literature demonstrated a poor prognosis for Merkel cell carcinoma metastasis to the spine with survival ranging from 1 to 9 months after diagnosis. Although neurologic decline necessitates a surgical intervention, the assessment of operative benefit should take into account the prognosis associated with the primary tumor subtype [4)].

In this report Jacob et al., propose a novel approach to treat merkel cell carcinoma (MCC) brain metastases and present a review of the literature in an attempt to establish a treatment algorithm and provide prognosis. MCC is a rare neuroendocrine malignancy affecting the aging population. This malignancy has a very aggressive behavior with frequent metastases. We report a 61-year-old man with a prior history of MCC who presented with diplopia. Brain MRI revealed a single right thalamic lesion consistent with metastasis. In the two weeks following GammaKnife stereotactic radiosurgery (Elekta, Stockholm, Sweden) the diplopia improved. A brain MRI demonstrated shrinkage of the tumor. From our literature search we found only six other patients with MCC brain metastases. The majority of these patients were treated with whole brain radiation in conjunction with chemotherapy. We propose that stereotactic radiosurgery can be used as a first line therapy for patients with MCC metastatic brain disease [5)].

A case of Merkel cell carcinoma displaying unique patterns of differentiation in the primary focus and brain metastasis. The skin primary was almost uniformly small cell carcinoma positive for epithelial and neuroendocrine markers, with a few glial fibrillary acidic protein- and cytokeratin 20-positive cells. The neoplasm contained giant cells immunoreactive for neurofilament and negative for epithelial markers. The neck lymph node metastasis was a typical neuroendocrine Merkel cell carcinoma positive for cytokeratin 20. A solitary dural intracranial metastasis displayed features of aggressive ganglioneuroblastoma, expressing many neuronal antigens with no evidence of glial or epithelial differentiation. After total gross resection, the tumor recurred within 3 months, and the patient developed skeletal metastases and died 6 months after craniotomy [6)].

Madden et al., report a rare case of MCC metastatic to the spine in an immunocompromised patient. Methods A 55-year-old male with previously resected MCC, immunocompromised due to cardiac transplant, presented with sharp mid-thoracic back pain radiating around the trunk to the midline. Computed tomography of the thoracic spine showed a dorsal epidural mass from T6 to T8 with compression of the spinal cord. Laminectomy and subtotal tumor resection were performed, and pathology confirmed Merkel cell tumor through immunohistochemistry staining positive for cytokeratin 20 and negative for thyroid transcription factor-1. Results Further treatment with radiation therapy was initiated, and the patient did well for 4 months after surgery, but returned with a lesion in the cervical spine. He then opted for hospice care. Conclusions With an increasing number of immunocompromised patients presenting with back pain, MCC should be considered in the differential diagnosis of spinal metastatic disease [7)].

A case of a 78-year-old male with intracranial extra-axial metastatic MCC involving the left cerebellopontine angle is presented.

A retrosigmoid craniectomy was performed with complete resection of the metastatic focus. Adjuvant treatment included whole-brain radiation therapy followed by etoposide and carboplatin chemotherapy. Seven months postoperatively, the patient was free of metastatic disease.

Surgical resection should be performed when feasible to prevent local recurrence. This may be followed by early adjuvant fractionated whole-brain radiotherapy and systemic chemotherapy; however, no clinical trials have been performed to demonstrate a survival benefit [8].

A unique case of a pituitary metastasis of MCC in a 65-year-old patient with a history of pituitary adenoma. This case is particularly novel due to the fact that the primary site of the MCC is unknown [9].

A rare case of Merkel cell carcinoma with extra-dural spinal metastasis causing paraplegia. There are only four reported cases in literature. A 57-year-old lady presented with a breast lump, multiple truncal skin swellings, low back pain and rapidly progressive paraplegia. MRI showed multiple epidural soft tissue masses causing neural compression. A biopsy from the truncal skin lesion was diagnosed as Merkel cell carcinoma (MCC). Posterior decompression and tumor debulking at all three sites of neural compression was performed. Histopathology of the epidural tumor was consistent with MCC and the diagnosis was confirmed by immuno-histochemistry staining for cytokeratin-20. She was started on chemotherapy and radiotherapy. One month after diagnosis she died due to extensive metastasis. The short term palliative response seen in our patient demonstrates the poor prognosis for patients with spinal metastasis [10].

An unusual case of Merkel cell carcinoma presenting as a frontal scalp mass with apparent invasion into underlying brain parenchyma through grossly intact calvaria. Despite wide local excision, craniectomy, intracranial tumor resection, and postoperative adjuvant irradiation, widespread systemic metastases resistant to chemotherapy developed, and the patient died 9 months after surgery. This case report confirms that Merkel cell carcinoma of the head and neck, already known to be an aggressive tumor, has the capacity for rapid intracranial extension. We propose that in this case, the mechanism of intracranial metastasis was via communicating veins rather than through bone destruction or systemic metastasis. Appropriate preoperative imaging should be carried out to define the extent of this tumor when it is adjacent to the skull. We found contrast-enhanced magnetic resonance imaging to be superior to computed tomography for defining soft tissue extent and marrow space involvement within underlying bone [11].

A 63-year-old man presented with a rare metastatic Merkel cell carcinoma (MCC) involving the lumbosacral spine and causing nerve root compression. Magnetic resonance (MR) imaging revealed an extradural soft tissue mass at the L5-S1 levels. The tumor was subtotally removed and chemotherapy was administered, but he died of multiple metastases from the primary epigastric

tumor. Lumbosacral metastatic epidural tumor can manifest as lumbar disc disease symptoms, but MR imaging can non-invasively and rapidly reveal the presence of spinal epidural tumor and any extension to the spinal canal. Extradural MCC metastasis in the lumbosacral area should be considered in the differential diagnosis of radicular symptoms caused by disc herniation [12].

A 48-year-old woman with MCC of the left elbow and a right cerebellar metastasis. After the right cerebellar mass was totally resected, radiation treatment and chemotherapy were performed. Eight cases of brain metastasis have been reported in the literature, but only 5 have been presented in sufficient detail for analysis. Therapy for brain metastases has always been palliative whole-brain irradiation and chemotherapy except for our patient, who underwent total removal of the tumor and survived for 11 months without neurological deficit. Except in the case of 1 with a particularly radiosensitive MCC, the patients with brain metastases died within 9 months after detection of the brain lesions. If possible, aggressive excision of brain metastases as well as of the primary lesion should be done [13].

A 57-year-old female, who had been complaining of anosmia for 8 years, was admitted to the otolaryngological department because an intranasal tumor was found. Then, removal of the tumor and radiotherapy was carried out. After these procedures, the patient suffered from a high fever and CSF rhinorrhea. At this stage, our neurosurgical department was consulted. CT scan revealed a partially calcified low density mass with a slight enhancement effect at the left frontal base. Under the diagnosis of intracranial invasion by intranasal neuroendocrine carcinoma, the patient was operated on. Through bifrontal craniotomy and a combination of extra- and intradural approach, the tumor was excised. After that, the dura and the skull base were reconstructed. On histological examination, the tumor was found to consist of NSE positive cells forming some glandular structures. Electron microscopic study disclosed neurosecretory granules in the cytoplasmic process. These findings are typical of neuroendocrine carcinoma and compatible to those of the intranasal tumor previously removed. Neuroendocrine carcinoma is rare in itself and there have been reported only two cases of its invasion of the skull base. The clinical features, diagnostic procedures, pathological findings, and treatment of this tumor are discussed in this report [14].

A case arising in the calvarium and involving the bone, dura, and underlying brain is presented. The histopathology and immunohistochemical staining characteristics of tumor were consistent with those of Merkel cell tumor. The natural history and histopathology of this tumor are discussed, along with the possible explanation for the origin of this tumor in the calvarium [15].

Alexander et al., reported a case of Merkel cell carcinoma with proven brain metastases and a solid choroidal tumor. The patient responded well to radiation and chemotherapy and is alive and neurologically intact three years after diagnosis. All previous patients with metastatic Merkel cell carcinoma to the brain died within two months of the diagnosis. They used this case to discuss possible routes of metastatic dissemination and to review the treatment options in patients with distant metastatic disease. This is the first reported case of presumed choroidal metastasis of Merkel cell carcinoma and the longest documented survival in a patient with brain involvement [16].

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