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Clinical Study

Carcinomatous meningitis from urachal carcinoma: the first reported case

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Summary

Carcinomatous meningitis (CM) occurs in less than 10% of cancer patients. Although patients frequently present with a focal complaint, multifocal signs are often found following careful neurological examination. The gold standard for diagnosis remains the demonstration of neoplastic cells in the cerebrospinal fluid. Despite the discouraging prognosis, palliative treatment may improve quality of life and lengthen lifespan. We report a patient with known primary carcinoma of the urachus who presented with headaches, nausea, vomiting and ataxia 1 week following resection of a nodular arachnoidal metastasis (indenting the cerebellum). Lumbar cerebrospinal fluid subsequently confirmed carcinomatous meningitis. This is the first reported case of carcinomatous meningitis resulting from metastatic urachal carcinoma.

Introduction

First described by Eberth in 1870, carcinomatous meningitis (CM) (also known as leptomeningeal carcinomatosis) occurs when neoplastic cells gain access to the cerebrospinal fluid [1]. Although recognized clinically in 4–7% of all cancer patients, the incidence of asymptomatic CM is much higher, due in part to increased clinical suspicion and the advances in treatment allowing many patients to live long enough to develop leptomeningeal disease [2,3]. Many primary cancers have been reported to cause CM, most commonly breast cancer, lung cancer, and melanoma [2,3]. However, there have been no reports of urachal carcinoma manifesting as CM. We present the first reported case of a patient with metastatic cancer of the urachus who developed symptomatic leptomeningeal disease. Detailed are her symptoms, signs, management, pathology, and therapy.

Case report

A 33-year-old woman presented with headache and skew diplopia. Three years earlier, she was diagnosed with a 5 cm urachal cyst revealed by biopsy to contain an invasive and *in-situ* non-transitional cell adenocarcinoma. Subsequent cyst resection revealed well-differentiated *in-situ* adenocarcinoma and infiltrating adenocarcinoma in the adjacent wall of the cyst. Laparotomy and partial cystectomy involving the umbilicus, urachal ligament, and bladder revealed five negative lymph nodes with no residual tumor. The patient was monitored with computerized tomography (CT) scans and chest X-rays every 3 months. Six months prior to admission she was found to have a 4 cm diameter right lower lobe lung mass extending from the right hilum posteriorly and caudally, revealed by endoscopic biopsy to be metastatic adenocarcinoma, associated with two positive lymph nodes (one in the right lower lung, and one paratracheal) post-lobectomy. Magnetic resonance imaging (MRI) of the brain with and without contrast at this time was negative for metastatic brain disease. One month following resection, the patient discovered a palpable 4 mm lesion in the subcutaneous fat of her left abdomen, revealed by biopsy to be metastatic adenocarcinoma. She was subsequently started on weekly chemotherapy (3 months prior to admission) with Irinotecan 125 mg/m^2, Leucovorin 20 mg/m^2 and 5-fluorouracil (5-FU) 500 mg/m^2, with bevicizimab 14 mg/kg every 2 weeks. This regimen was maintained until presentation.

Three months after the initiation of chemotherapy, the patient had a CT scan of the chest, abdomen and pelvis demonstrating no evidence of recurrent disease. However, she complained of lower back pain, headaches, nausea and vomiting at the time of this evaluation. MRI of the brain revealed abnormal enhancement in the area of the superior cerebellum bilaterally with a 1.6 cm diameter nodule in the superior right cerebellum, prompting admission (Figure 1). Subsequent administration of dexamethasone resulted in temporary symptom relief and normalization of her neurological exam. MRI of the cervical spine (obtained because of a possible enhancing cervical lesion seen on the brain MRI) revealed possible small superficial intradural enhancing foci at C5 and T1, suggestive for leptomeningeal metastases (Figure 2). Whole-body radioisotope bone and joint scan was negative for osseous metastatic disease. Three days later, she underwent suboccipital

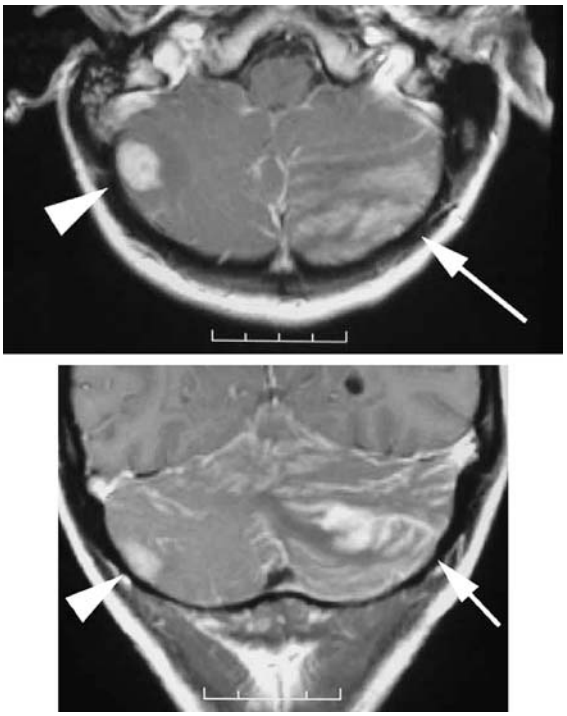

Figure 1. Axial and coronal brain MRI with gadolinium enhancement at time of presentation. Axial image: Wide arrow indicates homogenously enhancing right superficial lateral cerebellar hemisphere lesion (1.6 cm in diameter) without apparent adjacent edema. Skinny arrow indicates irregularly shaped superior left cerebellar hemisphere enhancing lesion (1.4 cm in diameter) with associated edema. Coronal image: Arrows indicate leptomeningeal enhancement on the surface of both superior hemispheres.

craniectomy for excision of the superficial right cerebellar lesion. Pathology confirmed the lesion to be metastatic adenocarcinoma, consistent with her prior disease (Figure 3). She was discharged home neurologically intact on postoperative day 6. Consultations were pursued for whole-brain external beam radiation therapy (whole-brain versus craniospinal) and possible intrathecal chemotherapy.

On postoperative day 7, she returned and was readmitted with increased headache, nausea, vomiting, and difficulty ambulating. Lumbar puncture (LP) was performed the next day because of the suspicion of carcinomatous meningitis. The opening pressure was markedly elevated. Cytologic examination of the cerebrospinal fluid revealed the presence of malignant cells, establishing the diagnosis of carcinomatous meningitis (Figure 4).

An intraventricular catheter and subgaleal (Ommaya) reservoir was implanted the next day and treatment with radiation therapy and dexamethasone was initiated. Nine days following implantation, she developed severe headaches, depressed mental status, and focal neurological deficits. Elevated intracranial pressures were documented by LP. Head CT revealed increased ventricular size compared to prior head CT, and a right ventriculoperitoneal (VP) shunt was completed by connecting a valve and distal catheter to the existing Ommaya reservoir and ventricular catheter system. Following VP shunt completion, her symptoms markedly improved. After extensive consultations and

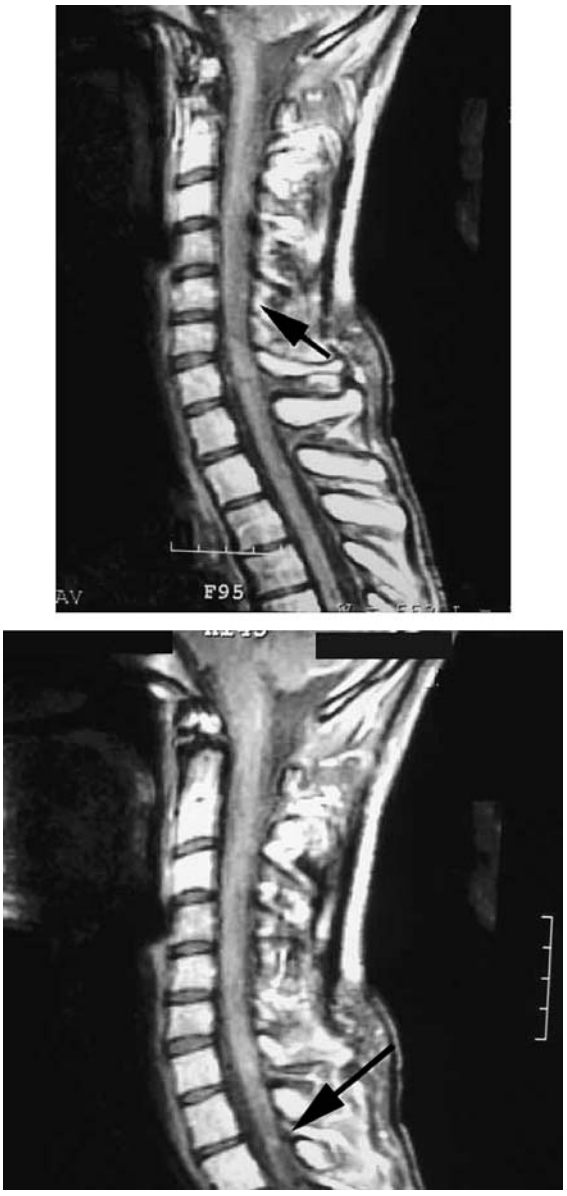

Figure 2. Sagittal cervical spine MRI (T1 with contrast) demonstrating possible small superficial intradural enhancing foci at C5 (superior image) and T1 (inferior image) suggestive of leptomeningeal metastases. These were not visible on axial imaging.

discussion with the patient, the patient decided not to have intrathecal treatment. She was started on daily oral temozolomide (115 mg). Unfortunately, her disease progression was quite rapid, resulting in death 2 months after initial neurologic presentation.

Discussion

The urachus is the anatomic remnant of the intraembryonic portion of the allantois, typically having closed at birth and identifiable only as the median umbilical ligament. Persistence beyond birth predisposes to a number of congenital and acquired disorders [4]. Urachal carcinoma is an extremely rare neoplasm, accounting for only 0.01% of all malignancies in adults, and 0.34% of bladder carcinomas [5]. Most commonly seen in patients between ages 40 and 70, it has a male

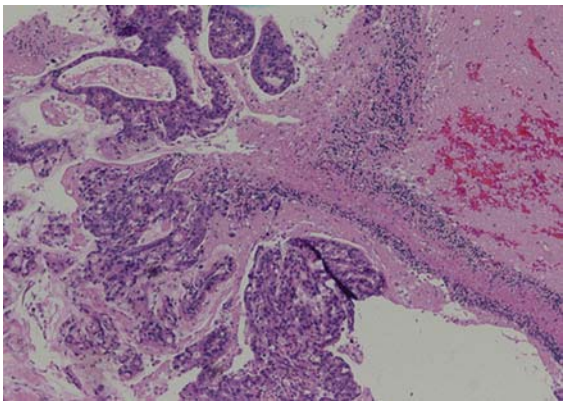

Figure 3. Photomicrograph of the cerebellum (hematoxylin and eosin stain, original magnification 100×): well-differentiated adenocarinoma infiltrating the cerebellum.

predilection and involves the bladder by infiltration [6]. Because it spreads locally in the space of Retzius, abdominal wall and peritoneum, it is usually associated with few symptoms until late in the disease course [6,7]. Urachal carcinoma is associated with a poor prognosis because nearly 95% of patients present with muscle invasion or metastases at the time of diagnosis [7]. Moreover, it is highly resistant to chemotherapy and radiation therapy, and does not respond to regimens that are used for metastatic transitional cell carcinoma of the bladder [5,6]. Adenocarcinoma is by far the most common type of urachal carcinoma, occurring in 90% of cases [5]. With adequate surgical intervention, the overall 5-year survival rate is approximately 40% [6,8].

The most common sites of metastatic disease in urachal carcinoma are the regional lymph nodes, omentum, liver, lung, and bone [6,9]. The central nervous system involvement our patient experienced is very uncommon, with fewer than 10 reported cases of brain metastases and no previous reports of leptomeningeal involvement [10,11]. Radiographic imaging, particularly MRI with gadolinium enhancement, is often helpful in establishing the diagnosis of CM [12] (Figure 2). However, because false negatives do occur, the gold standard for diagnosing CM remains the demonstration of malignant cells in the CSF, as in our patient (Figure 4).

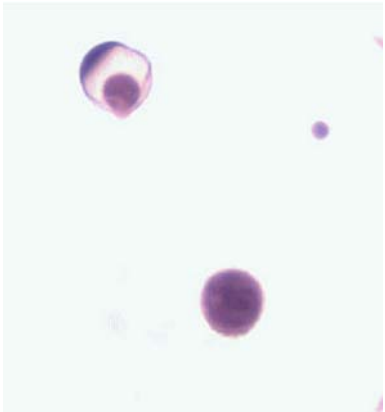

Figure 4. Photomicrograph of the cerebrospinal fluid cytology (hematoxylin and eosin stain, original magnification 400×): large cells with enlarged, hyperchromatic nuclei within the cerebrospinal fluid.

Because the treatment of CM is not curative, the primary goals are: local control, palliation, improvement/stabilization of neurological symptoms, and prolonged survival [13]. The standard of care in treatment involves intrathecal chemotherapy (via a ventricular catheter and an Ommaya reservoir), radiation therapy, and/or systemic chemotherapy. Eight percent of Ommaya reservoir patients develop hydrocephalus necessitating conversion to a VP shunt, as our patient did [14]. Of the intrathecal chemotherapeutic options, temozolomide has emerged as the newest, and potentially least toxic option [15]. Systemic chemotherapy, when possible, should be considered, since it obviates the risk of surgery, allows patients with CSF obstruction to be treated without correction of the flow abnormality, allows a wider array of cytotoxic agents to be administered orally or intravenously, decreases the risk of early and delayed neurotoxicity, and may provide a more uniform distribution of drug [14–16]. Because of these advantages, and due to the complications our patient experienced following Ommaya reservoir placement, she was placed on systemic temozolomide.

In patients who are untreated/unresponsive to treatment, median survival is 4–6 weeks, with death usually resulting from progressive neurologic dysfunction [3]. However, in treatment-responsive patients, median survival has been reported as long as 9 months, with isolated cases of survival as long as 29 months [17]. Favorable prognostic factors include: excellent performance status, minimal/absent fixed neurologic deficits, normal CSF flow scans, minimal systemic disease, and responsive systemic tumor [18,19].

In summary, this case represents the first report of urachal carcinoma resulting in carcinomatous meningitis. This case underscores the need to recognize carcinomatous meningitis as part of the differential diagnosis in patients with known primary tumor who present with unexplained neurological symptoms. Although the prognosis for this patient population is disappointing, early diagnosis and treatment may improve quality of life and prolong survival by many months.

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