CASE REPORT

Solitary cystic cerebellar metastasis in a patient with invasive transitional cell carcinoma of the bladder

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SUMMARY

Transitional cell carcinoma of the bladder (TCC) represents nearly 90% of genitourinary malignancies and typically presents with locally invasive symptoms. Metastasis to the central nervous system (CNS) is uncommon occurring in <5% of patients. When present, metastatic lesions are typically solid, isolated and located in the cerebrum. We report a case of a patient with a history of TCC who presented with lethargy and ataxia and was found to have a solitary cystic cerebellar lesion consistent with metastatic disease. Unfortunately, the prognosis for patients with TCC and CNS metastases is poor. Treatment options include debulking surgery, whole brain radiation, stereotactic radiosurgery and chemotherapy. Unfortunately, treatment may not appreciably extend survival and care is often supportive in previously reported cases. Though uncommon, TCC can metastasise to the CNS and should be considered in the differential diagnosis of patients, particularly those who were treated with aggressive surgery or combination chemotherapy previously.

BACKGROUND

Transitional cell carcinoma (TCC) of the bladder is a common, usually treatment-resistant neoplasm that represents approximately 5% of all cancers. Lower urinary tract TCC comprises 90% of all urothelial cancers with only 10% situated in the upper urinary tract including the renal pelvis. TCC can present with significant local invasive symptoms which include haematuria and obstructive uropathy. Systemic TCC metastases occur both by haematogenous spread into lung, bone, liver and peritoneum and by lymphatic routes locally to regional pelvic lymph nodes, distantly to retroperitoneal and occasionally mediastinal lymph nodes, as well as systemically (commonly to bone, liver and peritoneum).¹ The rate of spread to the brain is low; occurring in only 0–7% of patients with this malignancy.^{2–7} If TCC metastasises to the central nervous system (CNS), it typically presents as an isolated and solid cerebral lesion. CNS metastases have been increasingly reported in patients who have received aggressive surgical resection or combination chemotherapy.⁸ We report a case of a large solitary cystic cerebellar metastasis in a patient with TCC of the bladder and discuss the prognostic and management challenges it presented.

CASE PRESENTATION

A 65-year-old Caucasian man with a significant smoking history presented to our hospital with a 1-week history of unsteadiness, headache, falls and

progressive lethargy. Two years prior, the patient was diagnosed with G3cT3N0M0 transitional cell carcinoma of the bladder with local extension into the muscular wall and perivesicular soft tissues. He underwent neoadjuvant gemcitabine and cisplatin therapy with poor response, followed by cystectomy, neobladder construction and lymph node dissection. Seven months later he suffered recurrence of a urethral mass and repeat studies revealed extension of the tumour into the neobladder. Given disease extent the patient underwent penectomy, total urethrectomy, neobladder takedown and creation of ileal conduit at an outside hospital. He was restaged 10 months later and a CT of the chest/abdomen/pelvis performed showed no evidence of recurrent disease. He was in his usual state of health for approximately 3 months prior to presenting to his local clinic with weakness and pelvic pain and was found to have partially necrotic masses in the pelvis. This was followed by unsteadiness and progressive lethargy, and urgent CT of the brain revealed a single large circumscribed cerebellar mass and referral to our institution was initiated. On presentation to our hospital the patient was cachectic, dysarthric, ataxic and dysmetric. He had noxious odoriferous urine which prompted concern for urinary tract infection and hope for a reversible component to his altered mental status.

INVESTIGATIONS

Admission labs were notable for normocytic anaemia (haemoglobin 10.6 g/dL (13.5–17.5 g/dL)),

Figure 1 MRI of the brain, sagittal T1 image with hyperintense cystic lesion noted in posterior fossa.

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leucocytosis (leucocyte count $16.1 \times 10^9/L$ ($3.5\text{--}10.5 \times 10^9/L$ and creatinine of 1.6 mg/dL ($0.8\text{--}1.3$ mg/dL). Urine culture was positive for *Escherichia coli* but blood cultures were negative.

Initial CT of the head confirmed a 3.9×3.4 cm lesion within the posterior right cerebellar hemisphere with adjacent vasogenic oedema and mass effect on the fourth ventricle. CT of the chest, abdomen and pelvis revealed a 6.8×9.5 cm heterogeneous mass involving the symphysis pubis and right inferior pubic ramus with associated bony destruction and mass effect. There were multiple fluid collections seen in the right hemipelvis and right lower quadrant. There were no lesions or masses noted in the lungs, liver, spleen or pancreas.

MRI of the brain confirmed an ill-defined clear fluid-filled cystic mass in the cerebellum with slight ventricular enlargement, significant displacement of the fourth ventricle anteriorly and laterally, and slight downward displacement of the right cerebellar tonsil (figures 1–3).

DIFFERENTIAL DIAGNOSIS

Differential diagnosis for a solitary cystic intracerebral lesion includes infection (ie, neurocysticercosis), haemorrhage or malignancy (primary or metastatic). The most common malignancy to present as a solitary cystic lesion in the brain is non-small cell lung cancer. Although this patient was a smoker and metastatic lung cancer is high on the differential diagnosis, there were no radiographic findings such as lung or mediastinal lesions to suggest this alternative origin. In the absence of pathological confirmation the most likely explanation for the brain lesion is metastatic TCC.

TREATMENT

Given urinary tract infection the patient was started on broad spectrum antibiotics with minimal improvement in mentation.

For the vasogenic brain oedema the patient was started on dexamethasone with no improvement in symptoms or gross motor function. Owing to the large nature of the cystic mass and involvement of the ventricular system, drainage of the mass or surgical resection was considered. Alternatively, biopsy of the lesion in the pubic ramus for histopathological confirmation of metastatic TCC

was considered. However, given the extent of intracranial disease, the patient's rapid decline and overall poor prognosis and his overall goals of care, this was not pursued and was not felt to alter the patient's treatment choice. Palliative radiotherapy was offered, but declined by the patient due to the equivocal benefit for improving quality of life or survival in this setting. As the patient's main goal of care was to be at home, supportive care only with aggressive symptom management was pursued.

OUTCOME AND FOLLOW-UP

The patient was discharged home with hospice care and died peacefully without significant pain or symptom burden.

DISCUSSION

TCC, the most common type of bladder cancer, metastasises to the CNS in approximately 1% of patients. A review of the literature reports only 290 cases of TCC that have metastasised to the CNS, with the most typical lesions being solitary and tending to appear in the frontal, temporal or parietal lobe.⁹ The incidence of intracranial spread of TCC appears to have increased with more aggressive surgical interventions or more effective combination chemotherapy regimens.⁸

Metastatic spread of TCC of the bladder to the cerebellum is observed less frequently than metastasis to the cerebral cortex. To our knowledge, only seven such case series have been reported in the literature and involved a total of 18 patients. We have reviewed and summarised these seven case series publications, and the characteristics of the 18 patients in those series, all of whom had cerebellar metastasis from TCC (table 1). Patients who present with cerebellar metastases typically have a high grade, high stage primary bladder cancer. They have usually progressed through or had partial response to treatment of TCC with systemic chemotherapy and have widespread systemic metastases. However, a few case reports have described an isolated cerebellar metastasis as the presenting feature of TCC, with no evidence of other distant metastases^{10–12} (table 1). These observations indicate that metastatic TCC should remain on the differential diagnosis for patients presenting with a new isolated cerebellar lesion.

Figure 2 MRI of the brain, axial/oblique T2 fast spin echo image, postgadolinium enhancement.

Figure 3 MRI of the brain, coronal T1 fast spin echo image, postgadolinium enhancement.

Table 1 Previous reports of metastatic transitional cell carcinoma of the bladder to the cerebellum

Author, year published	Patients presented	Presenting symptom with brain metastases	Brain radiographic findings	Disease status prior to development of cerebellar metastases	Evaluation for other metastatic lesions	Treatment, follow up, other findings
McKay, 1930 ¹⁵	1 patient	–	No imaging, isolated cerebellar metastasis	–	–	First reported case, underwent subtotal tumour resection
Kabalin <i>et al</i> , 1988 ¹²	Four patients with solitary lesions noted	Varied 3 of 4 presented with brain mets as primary finding	Varied	3 of 4 presented with brain lesions as evidence of recurrence	–	All patients died. 3 of 4 received aggressive radiation, 2 resected
Shamdas <i>et al</i> , 1992 ¹⁰	1 patient	–	–	pT2 (had intravesicular chemotherapy at that time)	No other distant metastases identified at time of cerebellar lesion	–
Anderson <i>et al</i> , 1992 ²	9 of 293 patients between April 1977–December 1987 had bladder cancer and brain mets	Varied. 7 of 9 had solitary intracranial lesions	Varied	Varied	4 of 9 had no evidence of other disease	Five patients received whole brain irradiation (WBI). Average survival 7 weeks with WBI; 1 solitary mass treated with steroids only survived 4 weeks; 3 combined surgery and chemo therapy average survival 29 months
Davies <i>et al</i> , 2003 ¹¹	56, M	Fall, severe headache ataxia	MRI—R cerebellar tumour 2.5×1.4×0.4 cm plus small occipital lesion	None, presenting feature was related to neurological findings (pT1)	No other distant metastases identified at time of cerebellar lesion	Craniectomy with excision, stereotactic radiotherapy, plan for systemic chemotherapy
Perlmutter <i>et al</i> , 2006 ¹⁶	1 patient, a 71-year-old man	Headaches, ataxia, visual field loss	Isolated cerebellar metastases	pT2 disease at time of radical cystectomy 16 months prior to neurological presentation	No other distant metastases identified at time of cerebellar lesion	Shunt, debulking surgery, WBI. Systemic disease and recurrent brain lesion 7 months later, death 2 months after that on hospice
D'Souza <i>et al</i> , 2011 ⁹	1 patient, a 69-year-old woman	Slurred speech, facial droop, ataxia	CT: 4.8 cm right cerebellar mass	Had prior TURBT for G3pT1 with resection and intravesicular BCG 12 months prior to neurological presentation	No other distant metastases identified at time of cerebellar lesion	Surgical debulking followed by WBI, no recurrence at 21 months

Table excludes reports of isolated or multiple metastases to the cerebrum alone, which number an estimated 10–15 separate reports as the prognosis of cerebral metastases appears to differ from cerebellar metastases.

Prognosis for patients with TCC and CNS metastases is poor, with median survival anywhere from days to 4 months in the absence of aggressive treatment.^{8 13 14} Treatment options for intracranial lesions include surgery, systemic chemotherapy, whole brain radiation or stereotactic radiosurgery. Unfortunately, treatment typically only extends median survival by 1–2 months and may be associated with toxicity or morbidity.^{9 14} Longer range survival has been reported in isolated cases, but more often cerebral lesions over cerebellar lesions.^{2 13}

Learning points

- ▶ Transitional cell carcinoma (TCC) of the genitourinary tract can metastasise to lung, bone, liver, peritoneum and less commonly to the brain and rarely to the cerebellum.
- ▶ Metastatic lesions to the central nervous system (CNS) associated with TCC are typically solitary, solid and located in the frontal, temporal or parietal lobes, but less frequently present as a cystic lesion affecting the cerebellum.
- ▶ Occasionally, a CNS lesion is the presenting feature of an undiagnosed TCC of the bladder. Therefore, it is important to consider underlying TCC when discovering a solitary intracerebral lesion. In a patient with a history of smoking it is more common to expect such a lesion to be associated with a lung malignancy (however, this was not radiographically identified in our patient).

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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