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CASE REPORT

Intradural extramedullary spinal metastasis of renal cell carcinoma: illustrative case report and comprehensive review of the literature

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Abstract

Study design Literature review.

Objectives Intradural metastasis of renal cell carcinoma (RCC) has rarely been reported. We describe a case of an intradural extramedullary spinal metastasis to the cervical spine in a 68-year-old male treated for RCC 22 years prior. Additionally, we review the known reports of both intradural extramedullary and intramedullary of RCC.

Methods Case report and literature review.

Results A 68-year-old male with a history of right-sided nephrectomy for RCC preformed 22 years prior now presents with a MRI of the cervical spine showing a 1.5 cm contrast enhancing intradural extramedullary lesion at the level of C3–C4. Surgical resection of the lesion was performed. The tumor's histological and immunohistochemical profile was consistent with metastatic RCC. There are 18 reported cases of intradural extramedullary metastases of sporadic RCC. The average age at diagnosis was 61.6 ± 14.3 years. The interval from diagnosis of primary RCC to diagnosis metastasis ranged from 0 to 264 months (mean 46.8 ± 74.0 months). Sixteen cases of intramedullary renal cell carcinoma metastasis are reported. The average age at time of diagnosis was 53.6 ± 10.2 years. The interval from diagnosis of primary RCC to diagnosis of metastasis ranged from 0 to 180 months (mean 20.9 ± 53.4 months).

Conclusion The 22-year interval from diagnosis of primary RCC to intradural metastasis is the longest latency reported in the literature. Intramedullary metastases tend to have a younger age at diagnosis and shorter interval from diagnosis of primary RCC compared to extramedullary lesions.

Keywords Renal cell metastasis · Intradural metastasis · Intradural extramedullary spinal metastasis

Introduction

Renal cell carcinoma (RCC) is a highly malignant form of cancer. Approximately 30% of patients diagnosed with RCC will present in advanced stages with diffuse metastases [1, 2]. Additionally, 20–40% of patients treated for a primary RCC will go on to develop metastatic disease [1, 2]. The most common sites for metastasis include lung, bone, lymph nodes, and liver [3]. Brain metastases account for approximately 8% reported locations [4]. Intradural metastasis of renal cell carcinoma has rarely been reported. We describe a case of an intradural extramedullary spinal metastasis to the cervical spine in a 68-year-old male treated for RCC 22 years prior. Additionally, we review the known cases of intradural RCC metastases reported in the literature.

Methods

Case report and literature review of 34 known reports of sporadic intradural renal cell metastases.

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Case presentation

Clinical presentation

The patient is a 68-year-old male with a history of right-sided nephrectomy for renal cell carcinoma performed 22 years prior and now presents with bilateral upper extremity pain. Pain began approximately 2 months prior to presentation and has become progressively worse. Patient was neurologically intact on examination. MRI of the cervical spine was performed, which showed a 1.5 cm contrast enhancing intradural extramedullary lesion at the level of C3–C4 on T1-weighted imaging with gadolinium contrast (Fig. 1). Given the size of the tumor and degree of spinal cord compression, patient was offered surgical resection.

Operative procedure

In brief, patient was positioned prone on a Wilson frame, head fixation in a Mayfield head clamp. C3 and C4 laminectomy was performed in standard fashion. The thecal sac was exposed and dura opened sharply. Upon gross observation, a reddish appearing mass was evident along the left lateral aspect of the spinal cord. The tumor appeared to be attached to the lateral aspect of the dura as well. Biopsy of the lesion was sent to pathology, and the frozen section demonstrated features of a high-grade neoplasm. Given these findings, a more aggressive surgical removal was undertaken. The tumor was debulked internally which allowed a plane to develop between the tumor and spinal cord medially. The tumor was gently dissected away from the cord. Additionally, there was some tumor adhesion to the exiting C4 nerve root. A plain was developed between the tumor and nerve root, and the nerve was dissected free. Ultimately, a near gross total resection was achieved. A small amount of tumor capsule adherent to the spinal cord was left behind, to prevent possible injury to the cord with further dissection.

Pathology

On microscopic examination, tumor cells demonstrated pleomorphic epithelioid cells in a papillary pattern. Tumor cells contained pleomorphic nuclei with occasional pseudonuclear inclusions. On immunohistochemical staining, the tumor stained positive for vimentin, EMA, CAM5 and PAX8. Ki67 index was approximately 50%. The tumor's histological and immunohistochemical profile was consistent with metastatic papillary renal cell carcinoma (Fig. 2).

Postoperative course

Postoperatively, the patient did well. He remained neurologically intact and had complete resolution of his preoperative symptoms. MRI with contrast demonstrated excellent resection of the lesion (Fig. 3). He was discharged from the hospital on post-op day 3. A PET/CT scan was performed indicated multiple areas of metastatic disease including the right mediastinum, bilateral pulmonary nodules, and liver lesions. MRI of the brain showed several metastatic lesions. He was started on systemic chemotherapy with temsirolimus. Additionally, the patient received focused proton therapy to the cervical spine. MRI of the cervical spine with contrast performed at 3 months and 6 months postoperatively demonstrated no recurrent disease (Fig. 3).

Literature review

Intradural extramedullary metastasis

To date, there have been 18 reported cases of intradural extramedullary metastases of sporadic renal cell carcinoma [5–19]. The summary of case reports is found in Table 1. Lesions occurred throughout the spine, but had a propensity to metastasize to the cauda equina. The most common locations of intradural extramedullary metastases were the lumbar (59%), thoracolumbar (18%), thoracic

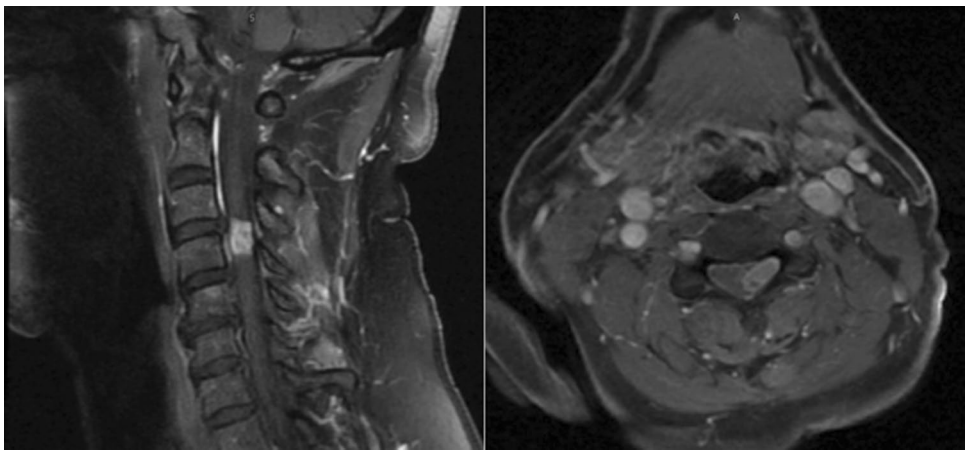

Fig. 1 Preoperative MRI of the cervical spine with contrast. Imaging shows a 1.5 cm contrast enhancing intradural extramedullary lesion at the level of C3–C4

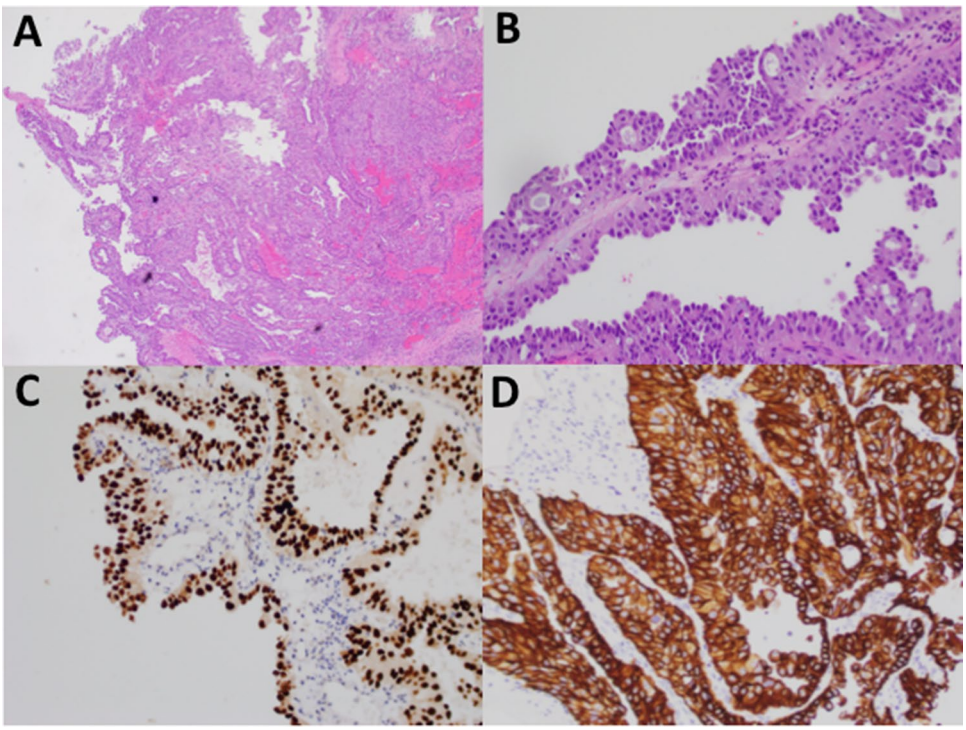

Fig. 2 Convention H&E staining at low (**a**) and high (**b**) power demonstrating pleomorphic tumors cells in a papillary pattern. Immunohistochemical staining demonstrating positive expression of PAX8 (**c**) and CAM 5.2 (**d**)

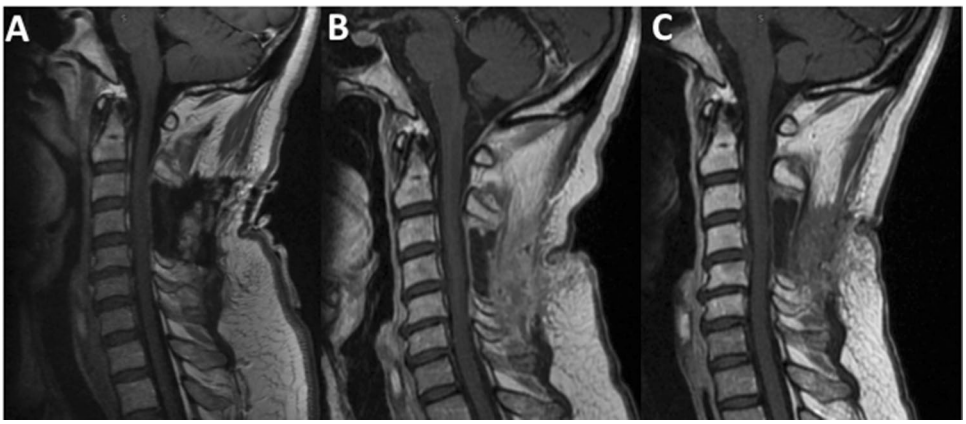

Fig. 3 T1-weighted MRI of the cervical spine with contrast at initial (**a**), 3 months (**b**) and 6 months (**c**) postoperatively showing no residual tumor

(12%) and cervical (12%) spine. The average patient age at time of diagnosis was 61.6 ± 14.3 years. The interval from diagnosis of primary RCC to diagnosis of an intradural extramedullary metastasis ranged from 0 to 264 months (mean 46.8 ± 74 months). In 4 patients (22.2%), the diagnosis of intradural extramedullary metastasis was the first clinical presentation of a primary renal cell carcinoma. Three patients (17.6%) were found to have synchronous brain metastases. Nine patients (50%) were treated with surgery alone, 5 (27.8%) patients received radiation alone, and 4 (22.2%) patients were treated with a combination of surgery and radiation. Average survival was 23.8 ± 25.5 months, with 16 of 18 patients alive at the last known follow-up.

Intradural intramedullary metastasis

Additional review of the literature found 16 known cases of intramedullary renal cell carcinoma metastasis [20–31]. The summary of case reports is found in Table 2. The most common location for intramedullary metastases was cervical (44%), thoracic (44%), and lumbar (12%) spine. The average patient age at time of diagnosis was 53.6 ± 10.2 years. The interval from diagnosis of primary RCC to diagnosis of intradural intramedullary metastasis ranged from 0 to 180 months (mean 20.9 ± 53.4 months). In 8 patients (44.4%), the diagnosis of intradural intramedullary metastasis was the first clinical presentation of a primary renal cell carcinoma. Seven patients (38.8%) were found to have

Table 1 Summary of intradural extramedullary metastases

Author	Year	Age	Sex	Time interval (months)	Location	Brain metastasis	Other metastases	Survival	Treatment
Takashi	1990	51	M	n/a	n/a	n/a	n/a	1*	RT
Maxwell	1999	84	M	60	L2–3	(−)	(−)	n/a	N, S
Mak	2001	59	M	48	L2	(−)	Bone	20	N, S
Takada	2003	61	M	60	L3	(−)	Lung	12	N, S, INF
Kubota	2003	68	M	84	L3	(−)	Lung	24	N, S
Gaetani	2004	36	F	4	L3–4	(+)	(−)	12	N, S, RT
Alfieri	2004	67	F	36	L3–5	(−)	(−)	n/a	N, S
Kim	2004	41	M	12	L2	(−)	(−)	12	N, S
Dobson	2009	81	F	0	L2	(−)	(−)	36	N, S
Jost	2009	82	M	6	C6–7	(+)	(−)	12	N, S, RT
Lin	2011	68	M	6	T12–L1	(−)	(−)	36	N, S, INF, RT
Ji	2013	68	M	192	T12–L1	(−)	Bone	24	N, C, S
Strong	2013	49	F	8	L4	(−)	(−)	24	N, RT
Strong	2013	72	M	0	L2	(−)	(−)	24	RT
Srinivasan	2014	40	M	0	L4–S1	(−)	(−)	n/a	R, C, RT
Heary	2014	54	M	0	T2–T4	(−)	(−)	6*	RT
Capek	2016	61	F	16	T12	(−)	(−)	108	N, S
This case	2017	68	M	264	C3–4	(+)	Lymph, liver, lungs	6	N, S, C, RT

RT radiation therapy, *N* nephrectomy, *S* surgical resection, *INF* interferon therapy, *C* chemo therapy, * deceased, *n/a* not available

Table 2 Summary of intradural intramedullary metastases

Author	Year	Age	Sex	Time interval (months)	Location	Brain metastasis	Other metastasis	Survival	Treatment
Ateaque	2000	52	M	132	C2–3	(−)	(−)	1*	N, S
Schijins	2000	70	F	0	C7	(−)	Liver	12	S
Fakih	2001	56	M	0	C4	(+)	Lung	6*	RT
Fakih	2001	60	M	180	T1–T2	(+)	Lung	5*	N, C, S
Fakih	2001	68	F	2	T8–L2	(−)	(−)	16*	N, RT
Fakih	2001	57	F	0	C7	(+)	Lung	6*	RT
Fakih	2001	46	M	2	T5	(+)	Lung lymph nodes	3*	RT, INF
Poggi	2001	37	M	2	T12	(+)	Bone	n/a	N, INF, RT
Kaya	2003	43	M	0	L1	(−)	n/a	6*	N, S
Gomez	2005	69	M	0	L1	(−)	Lung	16	S
Donovan	2006	41	F	0	C4	(−)	Lung, bone	2	N, S, RT
Asadi	2009	51	F	0	T12	(+)	Bone	n/a	N,S
Parikh	2009	50	M	4	C5	(+)	Lymph nodes	26	N, RT
Komura	2011	57	M	60	C4	(−)	(−)	22	N, S
Zakaria	2012	62	M	0	C7	(−)	Lung, lymph nodes	3*	N, C, S
Park	2013	44	M	6	T12	(−)	(−)	6	C, RT
Gao	2016	51	M	72	T4–5	(−)	(−)	n/a	N, S

RT radiation therapy, *N* nephrectomy, *S* surgical resection, *INF* interferon therapy, *C* chemotherapy, * deceased, *n/a* not available

synchronous brain metastases. Nine patients (52.8%) were treated with surgery alone, 7 (41.2%) patients received radiation alone, and 1 (5.9%) patient was treated with a combination of surgery and radiation. Average survival was

14 ± 9.2 months, with 9 of 17 patients alive at the last known follow-up.

Discussion

Renal cell carcinoma is a highly metastatic disease. The most common locations for RCC metastasis include spread to the lungs (50%), bone (49%), lymph nodes (6–32%), liver (8%), and brain (3%) [32]. In autopsy studies, brain metastases have been more commonly reported in up to 9.6% of cases [33]. Of RCCs which spread to the brain, 50% of lesions are found in the cerebral cortex, 10% in the cerebellum, and 2% in the meninges [34]. Dissemination to the intradural spine is rare, with less than 35 cases reported in the literature. Sporadic intradural metastases of renal cell carcinoma can present as intradural extramedullary lesions or purely intramedullary lesions [5–8].

Here, we reported a case of an intradural extramedullary spinal metastasis to the cervical spine in a 68-year-old male treated for RCC 22 years prior. To our knowledge, this is the longest reported interval from diagnosis of primary RCC to development of an intradural metastasis. The previous longest interval to occurrence reported was 16 years in two individual patients [5, 6]. Ji et al. reported a 68-year-old male who presented with an intradural extramedullary mass in the cauda equine at T12–L1. Similarly, Capek et al. reported a 61-year-old female who presented with an intradural extramedullary lesion at T12. In both cases, patients developed intradural metastases 16 years after nephrectomy for their primary RCC. However, unlike our patient, these two previously reported cases did not have simultaneous systemic metastases at diagnosis. Interestingly, in our patient, his intradural metastasis was the first presentation of advanced disease despite the long latency from primary diagnosis.

Intradural metastases can present early or late in the disease course of renal cell carcinoma. Our review of the literature found intramedullary metastases were more likely to present as the first manifestation of RCC compared to extramedullary lesion, 44.4% versus 22.2%, respectively. Extramedullary metastases tended to have a longer latency of development compared to intramedullary metastases, mean 46.8 ± 74 months versus 20.9 ± 53.4 months, respectively. Patients with intramedullary RCC tended to have a more aggressive disease course. The most common site for metastasis among the two groups was to the lung. Approximately 65% of patients with intramedullary lesions developed metastases to other parts of the body compared to only 28% of patients with extramedullary lesions. In patients with an intradural lesion presenting as the first manifestation of RCC, 88% of intramedullary patients had metastatic lesions at other locations, while no patients in the extramedullary group had lesions at other locations. Overall prognosis is poorer for patients with intramedullary RCC compared to extramedullary RCC. Average survival was 14 ± 9.2 months, with 9 of 17 patients alive at the last known follow-up for intramedullary lesions compared to an average survival of 23.8 ± 25.5 months, with 16 of 18 patients alive at the last known follow-up for extramedullary lesions.

Mechanistic pathways for tumors to metastasize to the intradural spine include (1) hematogenous dissemination (arterial circulation), (2) venous dissemination (Batson plexus), (3) spread through perineural lymphatics, (4) CSF dissemination through the subarachnoid space, and (5) direct spread from adjacent structures [10, 14]. A majority of intradural spinal metastases present with concomitant brain metastases. Intracranial-spinal spread of tumor occurs through dissemination of tumor cells from brain lesions into the CSF and seeding of the spinal cord through gravity directed flow of fluid [35]. Forty-one percent of patients with intramedullary RCC developed brain metastases compared to only 17% of patients with extramedullary RCC. Therefore, brain imaging should be recommended once a diagnosis of metastatic RRC to the intradural spine is made.

Capek et al. suggested possible spread of RCC to the intradural space via propagation along the peripheral nervous system [5]. They presented a case of a T12 intradural extramedullary RCC metastasis which demonstrated marked contrast enhancement and enlargement of the T12 nerve root and dorsal root ganglion on the ipsilateral side of the primary RCC. They hypothesize that tumor cells disseminate along the thoracic and lumbar splanchnic nerves to reach the spinal nerves and intradural space, evident by nerve root involvement of the tumor only on the ipsilateral side as the primary RCC. Similarly, Strong et al. reported a cases of L4 extramedullary metastasis from a left sided RCC with evidence of tumor infiltration of the L4 nerve root [8]. Additionally, RCC metastases can seed the surgical cavities of previously resected tumors. Heary et al. reported a case of a renal cell metastasis to the operative bed of an intradural extramedullary meningioma of the thoracic spine [12]. In patients with VHL, RCC tends to metastasize to sites of CNS hemangioblastoma [7].

Clinical symptoms of intradural metastases include motor weakness, pain and paresthesias, and bladder and bowel dysfunction. The most common clinical symptoms for patients with intradural metastases included lower limb weakness, followed by urinary incontinence [20]. The presence of intradural metastases represents advanced disease with poor prognosis. The goal of treatment is often palliative. Jost et al. reported a series of patients with intradural RCC who underwent surgical resection of their lesion and showed the greatest improvements in motor strength and pain relief compared to relief of paresthesisas and return of normal bladder function [7]. In patients with RCC metastasis to the

cauda equina, prompt surgical resection results in improved symptomatic relief in the majority of patients [10].

Treatment options for intradural metastases include surgical resection, radiation therapy, or a combination of both. In well-experienced hands, surgical resection can be performed safely and effectively [36]. Early surgical resection is associated with improved survival and prognosis in patients with intramedullary lesions [37]. In patients with extramedullary lesions with nerve root involvement, demarcation between tumor and nerve root may be obscured. In these cases, nerve root transection must be considered [8]. Outcomes of surgical resection may be limited by the potential morbidities associated with resection and failure of gross total resection leading to recurrence. Therefore, patients' overall functional status and life expectancy must be taken into account when planning a surgical intervention. Radiation therapy is an option for patients with advanced disease or deemed poor surgical candidates. However, in general renal cell carcinoma is considered relatively radioresistant [38, 39]. Standard radiation therapy may be effective in improving local control and symptomatic relief, but fails to increase overall survival [40, 41]. Alternatively, fractioned stereotactic radiosurgery can be considered. Parikh et al. treated a C5 intramedullary RCC lesion in three fractionated sessions at a dose of 15 Gy [24]. There were no complications, and the patient remained alive at 26 months follow-up. The role of adjunctive radiation therapy following surgical resection is still unclear in the literature. Ultimately, treatment strategies should focus on providing successful palliation and improved quality of life for patients with intradural renal cell carcinoma metastases.

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Compliance with ethical standards

Conflict of interest None of the authors have any potential conflict of interest.

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