

Leptomeningeal Carcinomatosis as an Initial and Sole Manifestation of Papillary Renal Cell Carcinoma

Shazia Bashir¹, G.M. Wani¹, Asim Rather¹, Naseer A. Choh²

ABSTRACT

Introduction: Leptomeningeal carcinomatosis (LMC) is an infrequent and devastating complication of systemic malignancy. Although it occurs in 5 – 20% of patients with metastatic cancer, its association with papillary renal cell carcinoma (RCC) is extremely rare. To the best of our knowledge, there are only 3 published case reports of leptomeningeal metastasis occurring in patients with papillary RCC.

Case report: Herein, we describe a case of a 45 year old man presenting for the first time with a clinical picture of cauda equina syndrome. MRI spine was suggestive of leptomeningeal carcinomatosis and the diagnosis was confirmed with CSF cytology. Contrast enhanced CT abdomen, revealed a heterogeneous mass arising from the mid pole of left kidney. CT guided biopsy and histopathological examination confirmed the diagnosis of papillary RCC. There was no evidence of any other systemic metastasis.

Conclusion: This case illustrates a rare occurrence of LMC as an initial and isolated metastatic manifestation of papillary RCC. Early diagnosis of this condition requires high index of clinical suspicion and an integrated approach using multiple diagnostic modalities.

Keywords: Leptomeningeal carcinomatosis, Renal cell carcinoma, Papillary renal cell carcinoma

INTRODUCTION

Leptomeningeal carcinomatosis (LMC), also known as carcinomatous meningitis (CM) or neoplastic meningitis (NM), is a term used to describe the infiltration of the leptomeninges by malignant cells with or without parenchymal CNS involvement. LMC was first reported by Eberth in 1870 as a rare complication of systemic malignancy.¹ In the recent times, it has become an increasingly frequent complication of various solid tumors (especially cancers of breast, lung and malignant melanoma), and hematological malignancies like leukemia and lymphoma.^{2,3} This increase in the incidence has partly been attributed to improved survival of cancer patients and partly to the advancement in imaging modalities, which permit early diagnosis of this condition.⁴ Although it occurs in 5 – 20% of patients with metastatic cancer, its association with renal cell carcinoma (RCC) is rare, even more so with papillary RCC.^{1,2,4} To date, we are only aware of 3 published case reports of LMC occurring in association with papillary RCC.⁴ Herein, we describe a rare case of LMC presenting as a sole manifestation of occult papillary RCC.

CASE REPORT

A 45 year old male patient was admitted in our hospital with history of lower back pain, weakness of lower limbs, bowel and bladder disturbances since 1 month. He also complained of occasional paraesthesia in the buttocks and feet. Due to

progressive weakness, he was unable to stand or walk since 1 week. There was no significant past or family history. His personal history was significant of smoking. On examination, he had lower motor neuron type of weakness of bilateral lower limbs (Power- Grade 3/5 in both limbs), hyporeflexia and saddle hypoaesthesia. Anal sphincter tone was decreased. Babinski sign was negative. Higher mental functions were intact. There were no signs of meningismus and cranial nerve examination was normal. There was no abnormality detected on other systems' examination. A clinical impression of cauda equina syndrome was made. Hemogram revealed mild microcytic-hypochromic anemia (Hb-10.2 gm/dl), while TLC, DLC and platelet count were normal. Urine examination was positive for microscopic hematuria (12-15 RBCs/HPF). Serum biochemistry was within normal limits. X-ray chest and lumbosacral spine were unremarkable. He was further evaluated with MRI lumbosacral spine. On contrast T1 weighted images, there was patchy nodular leptomeningeal enhancement from L1 to L5 (Figure 1). These findings were suggestive of leptomeningeal deposits and the patient was advised to undergo lumbar puncture for CSF examination and further evaluation. CSF analysis showed high protein (10 g/L) and low glucose levels (0.15 mmol/L). CSF viral, bacterial and fungal cultures were negative. CSF cytology was positive for atypical malignant cells. Ultrasound abdomen/pelvis was performed and it revealed an exophytic, hypoechoic mass lesion measuring 3.9 x 3.6cm arising from the mid-pole of right kidney. Further, a CECT abdomen/pelvis was done which confirmed the same findings and demonstrated that the lesion was heterogeneously enhancing and extending into perirenal space (Figure 2). HRCT chest, MRI brain and upper spine were unremarkable. A CT guided biopsy of the lesion was performed and tissue was sent for histopathological examination which revealed papillary cell carcinoma (Figure 3). A bone scan was also performed and was normal.

DISCUSSION

RCC is the most common type of primary renal tumors and accounts for about 7% of all cancers in men.⁴ The most common histological type is clear cell carcinoma, also called

¹Senior Residents, ²Associate Professor, Department of Radiodiagnosis and Imaging, SKIMS, Srinagar, Jammu and Kashmir, India

Corresponding author: Dr. Shazia Bashir, Senior Resident, Department of Radiodiagnosis, SKIMS, Srinagar, Jammu and Kashmir, India. 190020

How to cite this article: Shazia Bashir, G.M. Wani, Asim Rather, Naseer A. Choh. Leptomeningeal carcinomatosis as an initial and sole manifestation of papillary renal cell carcinoma. International Journal of Contemporary Medical Research 2016;3(4):1058-1060.



Figure-1: MRI spine (contrast T1 weighted image): Arrows showing patchy nodular leptomeningeal enhancement from L1 to L5.

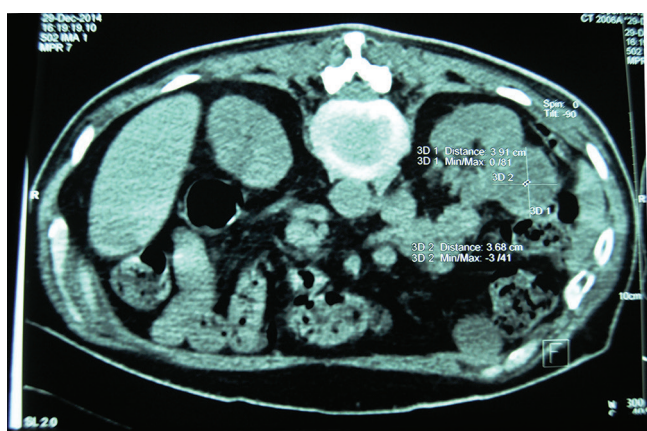


Figure-2: Contrast enhanced CT abdomen demonstrating 3.91 × 3.68 cm heterogeneously enhancing exophytic mass lesion arising from mid-pole of right kidney.

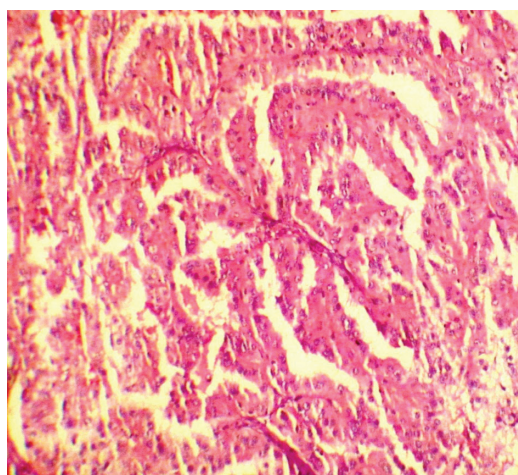


Figure-3: Histopathological examination (Hematoxylin and Eosin staining) of the biopsy specimen demonstrating papillary renal cell carcinoma.

conventional RCC, which represents 75–80% of RCC. Papillary (10–15%), chromophobe (5%) and other more rare forms such as collecting duct carcinoma (<1%) comprise the remainder.⁴ Although majority of the patients present with localized resectable disease, up to one-third have locally advanced or metastatic disease by the time of diagnosis.⁵ The

most common sites of metastases are lung, bone, liver and CNS in decreasing order of frequency. CNS metastasis occurs in approximately 5% of patients with RCC.⁶ Most of these CNS metastases occur in the brain parenchyma, while involvement of the leptomeninges is a distinctly rare phenomenon, with only a few documented cases reported in literature.^{4,6} On studying these cases, we made a few interesting observations. First, barring a few, nearly all of these patients had clear cell variant of RCC.⁴ Second, in all of these cases, RCC was clinically manifest either at the time of diagnosis of LMC or well before it. Third, in most of these cases, patients had evidence of distant metastases elsewhere in the body, including brain parenchyma, lungs or bone. Considering these facts, our case was unique, as the patient presented, for the first time, with cauda equina syndrome consequent to LMC, as an initial and sole manifestation of an occult papillary RCC. Mechanisms of leptomeningeal seeding include haematogenous spread, direct extension from dural or parenchymal metastasis, and/or spread from the venous plexus (from leptomeningeal veins). Haematogenous spread is the most common route. Perineural extension along the epineurium or perineurium of cranial or spinal nerves can occur from paravertebral metastases. Once tumour cells enter the CSF, they can spread along the meningeal surface to distant areas of the central nervous system. Proliferation of malignant cells can lead to formation of bulky masses. Even in the absence of gross evidence of disease, there can be microscopic evidence of disseminated tumour involvement of the leptomeninges throughout the central nervous system.⁴ In our case, macroscopic involvement was limited to L1 to L5 level and the patient did not have any other evidence of systemic metastasis, which was rather unexpected. Clinically, multifocal neurologic signs and symptoms are the hallmark of LMC. Manifestations may be consequent to meningeal irritation, raised intracranial tension, cranial nerve or spinal/radicular infiltration and/or associated parenchymal CNS involvement.^{2,4} In our patient, the clinical picture was that of isolated cauda equina syndrome. Diagnosis of LMC is a challenging task. CSF cytology and MRI brain/spine are the cornerstones of diagnosing this condition, but neither of them have an adequately high sensitivity. A lumbar puncture may reveal high CSF opening pressure, elevated proteins with reduced glucose in the CSF. The presence of atypical cells in CSF cytology is highly specific for LMC, however false negative rates approaching 40% have been reported. Multiple lumbar punctures may help in achieving sensitivity of upto 90 %.⁷ A variety of CSF tumor markers have also been studied in patients with LMC but are of limited value due to poor sensitivity and specificity. Among these are CEA (breast, lung, colon and bladder cancer), PSA (prostate cancer), CA-15-3 (breast cancer), CA-125 (ovarian cancer), CA 19-9 (lung cancer), MART-1 and MAGE-3 (melanoma), and β -HCG (choriocarcinoma, embryonal carcinoma, germ cell tumors).⁸ Newer techniques including CSF flow cytometry, polymerase chain reaction (PCR) and fluorescence in situ hybridization (FISH) may increase the diagnostic yield of CSF studies.⁴ Among neuroimaging imaging modalities, gadolinium enhanced MRI is superior to CECT in detecting LMC. The sensitivity of MRI is about 60 to 70% while that

of CT scan is around 30%.⁹ Post-gadolinium T1 images may demonstrate linear or nodular enhancement on the surface of the cerebrum or within the cerebellar folia, basal cisterns, cranial or spinal nerves and nerve roots. Other conditions that may mimic LMC include neurosarcoidosis, chronic meningitis or Guillain-Barre syndrome. Fluid-attenuated inversion recovery (FLAIR) sequences are somewhat less sensitive than T1 gadolinium images, but may detect small abnormalities as bright signals within the subarachnoid space often missed with gadolinium. Contrast-enhanced FLAIR may further improve the sensitivity. A comparison of these three techniques suggests that contrast enhanced T1 images remain the most accurate with a sensitivity of 59% and specificity of 93%, compared to unenhanced FLAIR of 12% and 93%, enhanced FLAIR of 41% and 88%, respectively. Using all three sequences the sensitivity is 65%.¹⁰ Once diagnosed, LMC presents a formidable challenge to the oncologists, with limited therapeutic options and dismal prognosis. Without treatment, median survival of patients with LMC is around 4-6 weeks. Various treatment modalities including systemic chemotherapy, immunotherapy, intrathecal chemotherapy and local irradiation are all palliative and primarily aimed at reducing disability and improving quality of life, with only a marginal effect on prolonging survival.⁷

CONCLUSION

Our case illustrates a rare occurrence of LMC as an initial and isolated metastatic manifestation of papillary RCC. Early diagnosis of this condition requires high index of clinical suspicion and an integrated multifaceted approach comprising of various imaging and non-imaging modalities. As of date, there is scarce data available on such association and therapeutic options remain limited. With accumulating experience in future, there is a vast scope of improvement in both diagnostic as well as therapeutic modalities in managing this condition.

REFERENCES:

1. Eberth CJ. Zur Entwicklung des Epitheliomas (Cholesteatomas) der Pia unter der Lungs. Virchow's Arch 1870;49:51-63.
2. Jayson GC, Howell A. Carcinomatous meningitis in solid tumours. Ann Oncol 1996;7:773-786.
3. Grossman SA, Krabak US. Leptomeningeal carcinomatosis. Cancer Treat Rev 1999;25:103-109.
4. Chilkulwar A, Pottimutyapu R, Wu F, Padooru KR, Pingali SR, Kassem M. Leptomeningeal carcinomatosis associated with papillary renal cell carcinoma. eCancer-medicalscience. 2014;8:468.
5. Ruiz-Cerdá JL, Jiménez Cruz F. Surgical treatment for renal cancer metastases. Actas Urológicas Españolas 2009;33:593-602.
6. Crino PR, Sater RA, Sperling M, Katsetos CD. Renal cell carcinomatous meningitis: pathologic and immunohistochemical features. Neurology 1995;45:189-91.
7. Kaplan JG, DeSouza TG, Farkash A et al. Leptomeningeal metastases: comparison of clinical features and laboratory data of solid tumours, lymphomas, and leukemias. J Neurooncol 1990;9:225-229.
8. Chamberlain MC. Cytologically negative carcinomatous meningitis: usefulness of CSF biochemical markers.

Neurology 1998;50:1173-1175.

9. Chamberlain MC, Sandy AD, Press GA. Leptomeningeal metastasis: a comparison of gadolinium enhanced MR and contrast enhanced CT of the brain. Neurology 1990;40:435-438.
10. Singh SK, Leeds, NE, Ginsberg LE. MR imaging of leptomeningeal metastases: Comparison of three sequences. Am J Neuroradiol 2002;23:817-821.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 19-02-2016; **Published online:** 18-03-2016