ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 20476-review.doc).

Title: Case of intramedullary spinal cord metastasis of renal cell carcinoma

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Name of Journal: *World Journal of Clinical Urology*

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We improved the manuscript according to the suggestions of the reviewers:

Reviewed by 00503196
The paper with the title << A case of intramedullary spinal cord metastasis of renal cell carcinoma >> describes an unusual metastasis in renal carcinoma and also provides information concerning the frequency of this rare spinal cord metastasis by other neoplasm. Despite the fatal event for the patient the information is valuable for the medical community.

Thank you very much for your comments. As the reviewer commented, intramedullary spinal cord metastasis is an unusual metastasis in RCC. Although the prognosis is poor, recently, surgical treatment is adopted in some cases of ISCM. Early and accurate diagnosis may lead us to optical treatment in each case to improve the patient's quality of life.

Reviewed by 00505633
This case describes a patient with multiple metastases in several organ systems from renal cell cancer. The case is not so unusual that it warrants publication.

Thank you very much for your comments. As the reviewer commented, the case of intramedullary spinal cord metastasis (ISCM) is increasing with prolongation of survival in patients with cancer by effective treatments. But it is still rare in renal cancer.

Rylkken et al. demonstrated that the primary malignancy has not always been diagnosed at the time of ISCM symptom onset or reference MR imaging. Furthermore, they suggested that knowledge of these relevant clinical and imaging features of ISCM and their significance was important for radiologists and the referring clinicians. In this case report, neither the unique nor the effective treatment for ISCM was shown, however, we believed that it was important to inform ISCM more.

We added the sentences concerning the increase in cases of ISCM in "Introduction" and "Discussion."

INTRODUCTION
Intramedullary spinal cord tumors are rare. The improved survival resulting from more effective treatments for many cancers has led to an increased number of publications concerning

intramedullary spinal cord metastasis (ISCM), including case reports and literature reviews; however, it is still extremely rare in renal cancer. Lung cancer and breast cancer are the most common primary tumors associated with ISCM [1,2]. In the present case, a 69 year-old man with a medical history of renal cell carcinoma (RCC) presented with urinary retention and bilateral paralysis of lower extremities. Magnetic resonance imaging (MRI) revealed an ISCM of RCC.

DISCUSSION

In a study of 1096 autopsy cases with neoplasms, 200 cases (18%) were found to harbor central nerves system metastases, and ISCMs were found in 10 cases (0.9%) of those cases. In that report, 199 of the 200 metastatic cases had lung tumors. ISCM might result from venous dissemination via the Batson's plexus or direct nerve root invasion [6]. Most cases of ISCM might have additional metastases with various clinical features that cause unique symptoms such as gait disturbance or leg weakness; however, Rykken et al. reported that the clinical presentation of the ISCM preceded the primary tumor diagnosis in 20% of patients. Those authors suggested that the lack of a known primary malignancy should not dissuade clinicians from considering an ISCM when faced with a spinal cord mass [1].

The mean survival durations were eight months with surgical treatment, four months with irradiation, and two months with palliative treatment. Recently, some authors reported the efficacy of surgical ISCM removal [2,8]. Despite the poor prognosis of most cases, surgical treatment could potentially yield improvements in the nervous symptoms or survival duration one of more than one year after treatment [8].

1 **Rykken JB**, Diehn FE, Hunt CH, Schwartz KM, Eckel LJ, Wood CP, Kaufmann TJ, Lingineni RK, Carter RE, Wald JT. Intramedullary spinal cord metastases: MRI and relevant clinical features from a 13-year institutional case series. AJNR Am J Neuroradiol 2013; 2043-2049
2 **Payer S**, Mende KC, Pract M, Westphal M, Eicker SO. Intramedullary spinal cord metastases: an increasingly common diagnosis. Neurosurg Focus 2015; 39: E15

Reviewed by 00505635

The wide field of molecular pathogenetics of renal cancer could be mentioned in the Discussion section by adding the following reference: Molecular pathogenetics of renal cancer. Am J Nephrol. 2006;26(3):218-31

Thank you very much for your comments. As the reviewer commented, the molecular targeting therapy is the most important strategy for metastatic renal cell carcinoma. We added the sentences concerning the molecular targeting therapy using the article “Molecular pathogenetics of renal cancer” for reference in “2nd paragraph in Discussion.”

Based on an understanding of the mechanism underlying RCC initiation and progression, several clinical trials evaluated the molecular targeting of RCC and observed efficacy against metastatic RCC [7]. However, no reports described the efficacy of the molecular targeting therapies against ISCM, possibly because some metastases already existed at the time of ISCM diagnosis. Several therapies, such as laminectomy, tumor reduction surgery, irradiation therapy, or steroid therapy, are used for ISCM treatment.

7 **Skolarikos AA**, Papatsoris AG, Alivizatos G, Deliveliotis C. Molecular pathogenetics of renal cancer. Am J Nephrol 2006; 26: 218-231