

Peer Review File

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Reviewer A

This is a case report of primary primitive neuroectodermal tumor of urinary bladder.

First, English language of the manuscript needs further editing after revisions.

Reply 1: All the authors have revised and edited the manuscript again carefully.

Second, the abstract is not informative. Please use one sentence to indicate the clinical significance of this case in addition to its rare phenomenon. Please provide more details of this case in the case presentation including the treatment strategies and detailed disease course. Clinicopathological features are also necessary. In the final parts of the abstract, please use several sentences to summarize lessons learned from the case and literature, including early diagnosis, differential diagnosis, treatment, and prognosis.

Reply 2: We have added some more details in the abstract part as follows:

(1)The clinical significance of this case is that we noticed the elevated neuron-specific enolase (NSE) when relapse and metastasis occurred other than the rarity and highly aggressive of bladder PNET.

Changes in the text: see Page 2, line 19-22

(2)We provide more details of this case in the case presentation including the treatment strategies, detailed disease course and clinicopathological features.

Changes in the text: see Page 2, line 25-28, 31-32

(3)We summarized some lessons learned from the case and literature, which shows the factors influence the prognosis.

Changes in the text: see Page 2-3, line 34-45

Third, in the introduction, please have some review on the clinicopathological features, treatment, and prognosis of PNET in sites other than urinary bladder. Please also briefly indicate the clinical significance of this case report.

Reply 3: Due to the rarity of PNETs, we reviewed some literature on PNETs arising in urogenital organs (mainly in kidney), and briefly provided the clinicopathological features, treatment and prognosis in these organs. And we emphasize the clinical significance of this case report in the accumulation of evidence and data analysis.

Changes in the text: see Page 4, line 58-64

Fourth, the authors may consider to use a timeline figure to indicate the onset,

diagnosis, progression, treatment, and death of the case. This is helpful for understanding the case.

Reply 4: We illustrated a timeline figure (Figure 2) to show the detail disease course and treatment strategies at the end of case presentation part. Correspondingly, we attached the figure legend on the manuscript page after the references.
Changes in the text: see Page 7, line 119 and Page 22, line 323-324

Finally, in the discussion part please use a separated paragraph to summarize the clinical characteristics, treatment, progression, and prognosis of the patients. Lessons learned from the case and literature including early diagnosis, differential diagnosis, treatment experiences, and prognosis should be extensively discussed.

Reply 5: We summarized the clinical characteristics, treatment, progression, and prognosis of the patients. And we discussed the lessons learned from the case and literature including early diagnosis, differential diagnosis, treatment experiences, and prognosis.
Changes in the text: see Page 10 line 196-198, 201 and Page 11 line 202-203, 205-209

Reviewer B

Was there a clear plane between the bladder and pelvic bone? Could this lesion have originated from the pelvic bone and invaded the bladder?

Reply 1: The plane between the bladder and pelvic bone was clear. During partial cystectomy, we detected no adhesion of bladder with surrounding tissues. CTU showed a intraluminal tumor. Pathology received from partial cystectomy revealed the lesion didn't infiltrated the full thickness of the bladder wall. Besides, the MRI of pelvic didn't show any metastasis sign 4 months after partial cystectomy on February 7, 2017; So evidences are sufficient to support this lesion was a primary bladder PNET.

What are your thoughts regarding radical versus partial cystectomy? From your case, I suspect early cystectomy after neoadjuvant chemotherapy should be the preferred management option for these patients. The authors should comment on this in the discussion.

Reply 2: Radical cystectomy and (neo)adjuvant chemotherapy were indicated when small round blue malignant cells were detected from the specimen received from cystourethroscopy. But the patient in our case denied radical cystectomy and demanded bladder-preserving surgery.
Changes in the text: Page 9 line176-177

Please comment on the patient's age. I'm surprised a neuroectodermal tumor could

present so late in life.

Reply 3: We reviewed all the 17 literature and included the patient information of this case. We found the median age of bladder PNET was 47.5 yrs (10-81 yrs). Obviously, this finding contrast with patients' age of other sites.