CASE REPORT

Case Report: Good responsiveness of metastatic sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation to immune checkpoint inhibitor after radical surgery and adjuvant chemotherapy [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: Sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation (SUCCD) in the ureter has a poor prognosis and is a rare histological variant of ureteral cancer. The majority of ureteral cancers are urothelial carcinomas.

Clinical case: We present a case of well-controlled metastatic SUCCD treated with an immune checkpoint inhibitor after radical surgery and failed adjuvant chemotherapy. The patient was a 68-year-old male with previous cure history of cT1 staged esophageal squamous cell carcinoma referred to the urology department for a right hydronephroureterosis complicating an intraureteral enhancing mass. After ureteroscopic biopsy and intraureteral urine cytology, atypical pleomorphic cell nests and chondroid tissue consistent with sarcomatoid urothelial carcinoma were observed. The patient underwent a successful radical right nephroureterectomy with bladder cuffing. The final diagnosis was a pT3N0 sarcomatoid urothelial carcinoma (heterologous component: chondrosarcoma > 95%) located at the right distal ureter and right renal calyx with infiltration of the periureteric fat and renal parenchyma of the renal capsule. On the postoperative one-month follow-up computed tomography scan, multiple enlarged lymph nodes and metastatic lung nodules were detected. The initiated adjuvant three cycles of gemcitabine-carboplatin therapy was marked by disease progression;

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2. **Katsuhiro Ito** , Kyoto University, Ishida Fushimi-ku, Japan

Any reports and responses or comments on the article can be found at the end of the article.

thus, second-line therapy with atezolizumab was used for treatment. After five cycles of atezolizumab, the tumors showed a partial response without any grade 3 complications.

Conclusion: The recurrent metastatic SUCCD showed good response to the immune checkpoint inhibitor after unsuccessful therapy with radical surgery and first line chemotherapy despite the unfavorable outcome of the pathology.

Keywords

urothelial carcinoma, sarcoma, chondrosarcoma, immune checkpoint inhibitor, atezolizumab

This article is included in the **Oncology** gateway.

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Author roles: Lee HH: Conceptualization, Formal Analysis, Writing – Original Draft Preparation; Kang HJ: Data Curation, Methodology, Supervision; Park WS: Formal Analysis, Resources, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; Choi W: Conceptualization, Formal Analysis, Investigation, Resources, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; Seo HK: Conceptualization, Resources, Supervision, Writing – Review & Editing; Kim SH: Conceptualization, Formal Analysis, Funding Acquisition, Investigation, Methodology, Resources, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

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Introduction

Ureteral cancer is rare, with a prevalence of less than 10% of all urinary tract urothelial carcinomas. Most (>90%) urothelial carcinomas occurring in the ureter are transitional cell carcinomas, while the others (<10%) include sarcomatoid urothelial carcinoma, squamous cell carcinoma, adenocarcinoma, and small cell carcinoma¹. Among the rare histology types, urothelial carcinoma with chondrosarcomatous differentiation is the most rare². A recent review by Lu *et al.* showed a poor survival outcome in 25 sarcomatoid ureter cancer cases with chondrosarcomatous differentiation². In this case study, we present a 68-year-old patient recently diagnosed with sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation of the right ureter discovered during esophageal cancer treatment. We thereby report a case of good response to the immune checkpoint inhibitor with an overall review of the histopathological characteristics of sarcomatoid ureteral cancer with some genetic background.

Case description

A 68-year-old male patient was referred to the urology department for right hydronephrosis complicating an incidental distal ureter stricture, which was found during an abdominal computed tomography (CT) scan for distal esophageal cancer. The patient was recently diagnosed with a 1.2 cm round-shaped distal esophageal squamous cell carcinoma, clinically stage T1, and was receiving a two-week 6600 cGy proton therapy in 33 fractions. The patient had a past medical history of restrictive lung disease, alcoholic liver cirrhosis (Child A), and was a heavy ex-smoker.

The CT treatment-planning scan showed right hydronephroureterosis due to distal ureteral stricture and ureter kinking. A CT urography was further performed at the urology department showing an abnormal ureteral kinking lesion with a distal intraureteral enhancing mass, just above the ureterovesical junction of the bladder (Figure 1A). Ureteral cancer was suspected given the findings in the right distal ureter: irregular wall thickening, and hydronephrosis with multiple small stones. Cystoscopy and microscopic urine analysis using the Nuclear

Matrix Protein 22 test showed negative findings, except for benign hyperplasia of the prostate and a moderate trabeculated bladder without any voiding symptoms. Further, ureteroscopic biopsy with intraureteral urine cytology under general anesthesia found atypical cells, atypical pleomorphic cell nests, and chondroid tissue, consistent with sarcomatoid urothelial carcinoma (Figure 1B).

After the first two-week proton therapy, the patient underwent a successful right open radical nephroureterectomy from the 11th intercostal incision and pelvic Gibson incision for bladder cuffing without a positive resection margin and intratumoral positive lymph nodes. Macroscopically, the pelvocalyx was enlarged, and the cut surface revealed multiple whitish solid tumors measuring up to $2.1 \times 1.7 \times 1.3$ cm in the pelvis and extending to the cortex. The tumor also involved the distal ureter (Figure 2A). Microscopically, the tumor had a biphasic appearance of a high-grade urothelial carcinoma and a sarcomatous component with chondrosarcomatous differentiation (Figure 2B). Immunohistochemical analysis indicated that the sarcomatous areas were positive for vimentin, and the areas of malignant urothelial cells were diffusely positive for pan-cytokeratin and p63 (Figure 2C). Based on the histological and immunohistochemical findings, a pT3N0 sarcomatoid urothelial carcinoma (heterologous component of chondrosarcoma >95% positive for vimentin, p63, and pan-cytokeratin) located at the right distal ureter and a separate small tumor in the right renal calyx were diagnosed. The tumor in the renal calyx infiltrated the periureteric fat and renal parenchyma of the renal capsule.

The patient was discharged within 10 days without any complication including azotemia and resumed the two-week proton therapy for esophageal cancer. On the postoperative one-month follow-up CT scan, an increased size and necrosis of aortocaval lymph nodes and multiple metastatic lung nodules were detected. Three cycles of adjuvant gemcitabine and carboplatin (gemcitabine 1000mg/m² D1, 8, and carboplatin AUC 5 D1, every 3 weeks) chemotherapy was administered due to the decreased renal function because of an underlying chronic kidney disease.

Figure 1. (A) Preoperative CT urography and (B) ureteroscopy findings.

Figure 2. (A) Gross specimen of a right distal ureter mass and of a satellite renal pelvis tumor, (B) microscopic findings, and (C) immunohistochemical findings. (A) The cut surface of the resected kidney shows multiple whitish solid homogenous masses in the pelvic region extending to the renal parenchyma. The tumor in the distal ureter shows an irregular nodularity on the surface, a thickened wall, and periureteric fat invasion. (B) The tumor shows an area of urothelial carcinoma forming an epithelial component and sarcomatous area with abundant chondroid production, and the two components are fused together. (C) Immunohistochemical staining shows strong cytokeratin positivity in the urothelial carcinoma component and vimentin positivity in the cartilaginous sarcoma component.

The follow-up imaging after 3 cycles (9 weeks) of the initial treatment regimen indicated disease progression; thus, a second-line systemic therapy was initiated using an immune checkpoint inhibitor, atezolizumab (1200mg, every 3 weeks). After three cycles of atezolizumab, the multiple enlarged lymph nodes and lung nodules were no longer enlarged, and after five cycles of atezolizumab the overall size of multiple metastatic lesions decreased (Figure 3), indicating a partial response to atezolizumab. The patient has undergone seven cycles of atezolizumab without any grade 3 adverse event, and will continue to be treated.

Discussion

Chondrosarcoma is one of the most common malignant bone tumors in adults³. Chondrosarcomas are further stratified into conventional, mesenchymal, dedifferentiated, and clear cell subtypes. The conventional chondrosarcoma represents about 85% of all chondrosarcomas and is notoriously difficult to treat with chemotherapy³. According to the 4th edition of the World Health Organization Classification of Tumors, the International Agency for Research on Cancer defined the sarcomatoid variants of urothelial carcinoma as being histologically indistinguishable from those of sarcomas with a prevalence of 0.6% of all bladder tumors⁴. The most common symptom of SUCCD is gross hematuria with male predominance (ratio 3:1). The aggressive pathologic feature results in mostly nodal and visceral metastases at the time of diagnosis, like in our case. Our patient had an underlying alcoholic liver cirrhosis, a chronic pulmonary disease, and a distal esophageal cancer being treated with radiation therapy. He was diagnosed with pT3NxM0 chondrosarcoma with multiple sites at the distal (pT2) and the proximal ureter (pT3). Our case was similar to a surgical case of an 81-year-old Japanese female with a multifocal, synchronous pT2 sarcomatoid ureteral cancer and pT3 renal pelvic urothelial carcinoma with multiple visceral metastases diagnosed on postoperative month 11⁵. Our patient had no nodal enlargement or

metastases at the time of preoperative workups; however, the lung metastases and multiple nodal enlargement observed on postoperative month one strongly support the speculation that micrometastases were already present at the time of diagnosis of the right hydronephroureterosis and surgery. It is also worth noting that our patient presented with multiple gross hematurias during the esophageal cancer workups, and the right atrophic kidney with cystic changes and hydronephrosis were suggestive of a long-existent tumor.

The prognosis of SUCCD is dismal (3–24 months survival time)² because the majority of urothelial carcinoma cases with sarcomatoid differentiation are known to be high grade, with an increased risk of micrometastases at the time of diagnosis due to late diagnosis, and have challenges associated with diagnosing a rare multifocal ureteral cancer^{6–9}. Therefore, surgical resection is the primary treatment choice especially for chemoradiation-resistant tumors despite diagnosis at advanced stages. However, several retrospective case series and clinical trials have proposed the use of either anti-angiogenic inhibitors or immune therapy in the current genetic era.

Immunotherapy has had enormous success in treating multiple cancer subtypes. Success has been particularly seen with immune checkpoint inhibitors, which are now approved as standard therapy in melanoma, lung cancer, and genitourinary cancers. Immunotherapy agents are increasingly demonstrating success in many cancer subtypes, and there have been preclinical suggestions that they may do the same in chondrosarcoma. The PI3K-Akt-mTOR, SRC, and Hedgehog pathways are the potential oncogenic targets for chondrosarcoma with VEGF2 inhibitors^{10,11}. Other identified targets with next-generation sequencing are recurrent alterations in TP53, ACVR2A, COL2A1, YEATS2, and IDH¹². These play a role in chondrosarcoma; therefore, they could be potential targets for immunomodulatory agents. In addition, immune checkpoint inhibitors have been

Figure 3. Comparison of metastatic tumors between baseline CT at the start of the immune checkpoint inhibitor and follow-up CT after five cycles of the immune checkpoint inhibitor.

successful treatments for sarcomas. Atezolizumab, an immune checkpoint inhibitor, has been approved for second-line therapy in ureteral cancer in Korea and in our case we observed a good response. A previous 67-year-old male patient treated with four cycles of nivolumab resulted in a near-complete response in metastatic pulmonary nodules¹³. Immune checkpoint inhibitors have been suggested to provide tumor-specific immune responses against cancer-specific antigens such as NY-ESO-1 or LAGE-1 in sarcoma patients with dedifferentiated chondrosarcoma, as well as chondrosarcoma cell lines^{13–15}. The expected favorable outcome with the use of a single agent PD1 inhibitor with/without immunomodulatory agents in chondrosarcoma needs to be further investigated.

In conclusion, this recurrent metastatic case of carcinoma is a rare variant of multifocal synchronous ureteral cancers which responded well to atezolizumab. Our findings will help in early diagnosis, treatment planning, and better management with immune checkpoint inhibitors in case the current chemotherapy fails; thus, ensuring improved prognoses. In future, a series

of case reports and studies would highlight the clinical benefit of checkpoint inhibitors with/without immunomodulatory agents in this disease clearly.

Ethical considerations and consent

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient and the caregiver of the patient.

This retrospective study was approved by the Institutional Review Board (IRB) of the National Cancer Center (IRB No. NCC 2020- 0313-0001). This case report was proceeded in accordance with the tenets of the ethical guidelines and regulations of the World Medical Association Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

References

- Soria F, Shariat SF, Lerner SP, *et al.*: **Epidemiology, diagnosis, preoperative evaluation and prognostic assessment of upper-tract urothelial carcinoma (UTUC).** *World J Urol.* 2017; **35**(3): 379–87.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Lu W, Wang Y, Li Y, *et al.*: **Sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation of the ureter: A case report and review of the literature.** *Oncol Lett.* 2017; **13**(3): 1331–7.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Wagner MJ, Livingston JA, Patel SR, *et al.*: **Chemotherapy for Bone Sarcoma in Adults.** *J Oncol Pract.* 2016; **12**(3): 208–16.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Montironi R, Lopez-Beltran A: **The 2004 WHO classification of bladder tumors: a summary and commentary.** *Int J Surg Pathol.* 2005; **13**(2): 143–53.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Takemura K, Motoi T, Tonooka A, *et al.*: **Multifocal Synchronous Upper Urinary Tract Carcinosarcoma (Sarcomatoid Carcinoma) With Rhabdomyoblastic Differentiation.** *Int J Surg Pathol.* 2019; **27**(5): 547–52.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Nicolas MM, Nazarullah A, Guo CC: **Sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation of the ureter: a case report.** *Anal Quant Cytopathol Histopathol.* 2014; **36**(2): 111–6.
[PubMed Abstract](#)
- Johnin K, Kadowaki T, Kushima M, *et al.*: **Primary heterologous carcinosarcoma of the ureter with necrotic malignant polyps. Report of a**

- case and review of the literature. *Urol Int.* 2003; **70**(3): 232–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
8. Fleming S: **Carcinosarcoma (mixed mesodermal tumor) of the ureter.** *J Urol.* 1987; **138**(5): 1234–5.
[PubMed Abstract](#) | [Publisher Full Text](#)
 9. Perimenis P, Athanasopoulos A, Geraghty J, *et al.*: **Carcinosarcoma of the ureter: a rare, pleomorphic, aggressive malignancy.** *Int Urol Nephrol.* 2003; **35**(4): 491–3.
[PubMed Abstract](#) | [Publisher Full Text](#)
 10. Polychronidou G, Karavasilis V, Pollack SM, *et al.*: **Novel therapeutic approaches in chondrosarcoma.** *Future Oncol.* 2017; **13**(7): 637–48.
[PubMed Abstract](#) | [Publisher Full Text](#)
 11. Jones RL, Katz D, Loggers ET, *et al.*: **Clinical benefit of antiangiogenic therapy in advanced and metastatic chondrosarcoma.** *Med Oncol.* 2017; **34**(10): 167.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 12. Totoki Y, Yoshida A, Hosoda F, *et al.*: **Unique mutation portraits and frequent *COL2A1* gene alteration in chondrosarcoma.** *Genome Res.* 2014; **24**(9): 1411–20.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 13. Wagner MJ, Ricciotti RW, Mantilla J, *et al.*: **Response to PD1 inhibition in conventional chondrosarcoma.** *J Immunother Cancer.* 2018; **6**(1): 94.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 14. Hiraki A, Ikeda K, Yoshino T, *et al.*: **Tumor-specific cytotoxic T lymphocyte responses against chondrosarcoma with HLA haplotype loss restricted by the remaining HLA class I allele.** *Biochem Biophys Res Commun.* 2001; **286**(4): 786–91.
[PubMed Abstract](#) | [Publisher Full Text](#)
 15. Pollack SM, Li Y, Blaisdell MJ, *et al.*: **NYSEO-1/LAGE-1s and PRAME are targets for antigen specific T cells in chondrosarcoma following treatment with 5-Aza-2-deoxycytidine.** *PLoS One.* 2012; **7**(2): e32165.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

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Reviewer Report 29 November 2021

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Katsuhiro Ito

Department of Urology, Kyoto University, Ishida Fushimi-ku, Kyoto, Japan

In this study, the authors reported the case of sarcomatoid urothelial carcinoma with chondrosarcomatous component and the favorable response to the immune checkpoint inhibitor. Although sarcomatoid urothelial carcinoma of the ureter accounts for <10% of ureteral cancer, I think chondrosarcomatous lesion is relatively common among sarcomatoid variants. Nonetheless, it is an important report to share the outcomes of the immune checkpoint inhibitor for this rare disease.

Specific comments:

1. In the introduction, the authors said that the chondrosarcomatous differentiation is the rarest subtype and cited the study from Lu *et al.*, however, in the study from Lu *et al.* the majority of the sarcomatoid UC is accompanied by the chondrosarcomatous component. Please correct the sentence.
2. Lu *et al.* reported sarcomatoid UC of the ureter, and not all were sarcomatoid ureter cancer cases with chondrosarcomatous differentiation. Please correct it.
3. Case presentation is OK, but I recommend the authors show not only LN but also lung CT scan before/after atezolizumab.
4. "Adjuvant gemcitabine and...": Adjuvant chemotherapy generally means chemotherapy to avoid recurrence. As the patient had already experienced lung mets, the term "adjuvant" should be avoided.
5. "(heterologous component of chondrosarcoma >95% positive for vimentin, p63, and pan-cytokeratin)": This sentence seems unclear. Was more than 95% of the area positive for both vimentin and pan CK?
6. Are there any findings that the metastatic lesion includes a chondrosarcomatous component?

7. The discussion was not straightforward. Since the patient was diagnosed as sarcomatoid UC, not chondrosarcoma, the first paragraph of the discussion seems irrelevant.
8. The authors discussed the genetic alteration of chondrosarcoma. Is there any evidence that these genetic mutations are present in sarcomatoid UC?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Urology, cancer immunotherapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Mar 2022

Sung Han KIM

We thank the editors and the reviewer (Prof Katsuhiko Ito) for his thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions.

The manuscript has been rechecked and the necessary changes have been made in accordance with the reviewers' suggestions. The responses to all comments have been prepared and attached herewith.

Responses to Reviewer's Comments

1. In the introduction, the authors said that the chondrosarcomatous differentiation is the rarest subtype and cited the study from Lu et al., however, in the study from Lu et al. the majority of the sarcomatoid UC is accompanied by the chondrosarcomatous component. Please correct the sentence.

Response: We corrected the sentence according to the reviewer's remark as follows (page 2 lines 60-62):

"Among the rare histology types, urothelial carcinoma with chondrosarcomatous differentiation is relatively common among sarcomatoid variants."

2. Lu et al. reported sarcomatoid UC of the ureter, and not all were sarcomatoid ureter cancer cases with chondrosarcomatous differentiation. Please correct it.

Response: We corrected the sentences as follows (page 2 lines 63-64):

"A recent review by Lu et al. showed a poor survival outcome in sarcomatoid ureter cancer cases with chondrosarcomatous differentiation among their 25 sarcomatoid ureter cancer cases²."

3. Case presentation is OK, but I recommend the authors show not only LN but also lung CT scan before/after atezolizumab.

Response: Due to the limited images according to the guidelines, we selected those targeted LN lesions better to show the therapeutic responses to the immune checkpoint inhibitors in this case report.

4. "Adjuvant gemcitabine and...": Adjuvant chemotherapy generally means chemotherapy to avoid recurrence. As the patient had already experienced lung mets, the term "adjuvant" should be avoided.

Response: Thank you for the remark. We deleted the "adjuvant" in the abstract section and in the case presentation section of the manuscript (page 2, lines 46-48 and page 3, lines 106-107).

5. "(heterologous component of chondrosarcoma >95% positive for vimentin, p63, and pan-cytokeratin)": This sentence seems unclear. Was more than 95% of the area positive for both vimentin and pan CK?

Response: We changed the phrase as follows:

"heterologous component of chondrosarcoma positive for vimentin, p63, and pan-cytokeratin"(page 3, lines 100-101).

6. Are there any findings that the metastatic lesion includes a chondrosarcomatous component?

Response: Unfortunately, we did not do target biopsy on the metastatic lesions.

7. The discussion was not straightforward. Since the patient was diagnosed as sarcomatoid UC, not chondrosarcoma, the first paragraph of the discussion seems irrelevant.

Response: We deleted the first paragraph of the chondrosarcoma explanation section to better clarify the sarcomatoid variant of urothelial carcinoma (page 4, lines 117)

8. The authors discussed the genetic alteration of chondrosarcoma. Is there any evidence that these genetic mutations are present in sarcomatoid UC?

Response: There exist several papers elucidating the importance of genetic profiling in sarcomatoid urothelial carcinoma. One article from Cell Press (Cell Rep. 2019 May 7;27(6):1781-1793.e4. doi: 10.1016/j.celrep.2019.04.048.) is where Bogdan Czerniak and his research team introduced research about a comprehensive genomic analysis of 28 cases of SARC and 84 cases of conventional urothelial carcinoma (UC), with the TCGA cohort of 408 muscle-invasive bladder cancers serving as the reference. They found out that sarcomatoid urothelial carcinoma shows a distinct mutational landscape, with enrichment of TP53, RB1, and PIK3CA mutations which might give important implications for the development of more effective therapies, such as immune check-point inhibitors. We added this reference and their research articles to show whether it is possible that genetic profiling might be an important implication for future effective therapies using immune therapy in sarcomatoid urothelial carcinoma. We added some of the sentences to show the genetic profiling research in sarcomatoid urothelial carcinoma in the manuscript (page 4, lines 150-154). We also added a new reference (#12) as follows in the reference section (page 6 lines 211-212).

Competing Interests: I and other coauthors have no competing interests.

Reviewer Report 18 March 2021

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Wan Song

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In this study, they presented a case of sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation in the ureter treated with an immune checkpoint inhibitor after radical surgery and failed adjuvant chemotherapy. They showed that immune checkpoint inhibitor might be a successful option in case the current chemotherapy failed. Congratulations on good and inspiring work. It is pleasure to review high quality cases.

References

1. Lu W, Wang Y, Li Y, Cao Y, et al.: Sarcomatoid urothelial carcinoma with chondrosarcomatous differentiation of the ureter: A case report and review of the literature. *Oncol Lett.* 2017; **13** (3): 1331-1337 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Urologic oncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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