Bladder Recurrence of Clear Cell Sarcoma of the Kidney Seven Years After Initial Presentation

John Weaver, Tammy Ho, Adam Lang, Joel F. Koenig, Douglas E. Coplen, Louis Dehner, and Erica J. Traxel

Clear cell sarcoma of the kidney (CCSK) is the second most common pediatric renal malignancy after Wilms tumor. CCSK has the potential to metastasize to distant sites and was historically known as the bone metastasizing renal tumor. We report an exceedingly rare case of a bladder recurrence of CCSK. Our patient presented with gross hematuria 7 years after initial complete response. He was found to have a large sessile bladder tumor and underwent a partial cystectomy with right pelvic lymph node dissection. Final pathology was metastatic CCSK. UROLOGY 106: 193–195, 2017. Published by Elsevier Inc.

Clear cell sarcoma of the kidney (CCSK), historically known as the bone metastasizing renal tumor, comprises approximately 5% of all primary renal tumors in children, and is the second most common pediatric renal malignancy after Wilms tumor.[1-3] We report a case of a bladder recurrence of CCSK years after an initial complete response. We performed a PubMed search of all available CCSK literature, and for all articles that specifically discussed recurrences of CCSK we examined their respective reference lists. We were unable to find another reported case of a bladder recurrence of CCSK in the literature (Figs. 1–3).

CASE REPORT

A 4-year-old child with gross hematuria and a renal mass was treated with a right radical nephrectomy. Pathology revealed stage II CCSK. Margins and lymph nodes were negative and he was treated per the AREN0321 trial with vincristine, cyclophosphamide (without mesna), doxorubicin, and etoposide followed by flank radiation.

He had no evidence of recurrence on regular follow-up until presenting with gross hematuria 7 years later. Cross sectional imaging of the abdomen and pelvis showed a 2 cm mass within the anterolateral right bladder wall. Examination under anesthesia and cystoscopy revealed a firm but mobile right pelvic mass and an erythematous sessile-appearing lesion on the right anterolateral wall that was 3 cm removed from the right ureteral orifice. Pathology from multiple superficial and deep biopsies revealed a myxoid pattern similar in appearance to the original CCSK. Stains were positive for vimentin and smooth muscle actin, but were nonreactive for BCL2, which is expressed in CCSK. Differential diagnosis included metastatic CCSK and inflammatory myofibroblastic tumor. Systematic biopsies of the remaining bladder mucosa were normal.

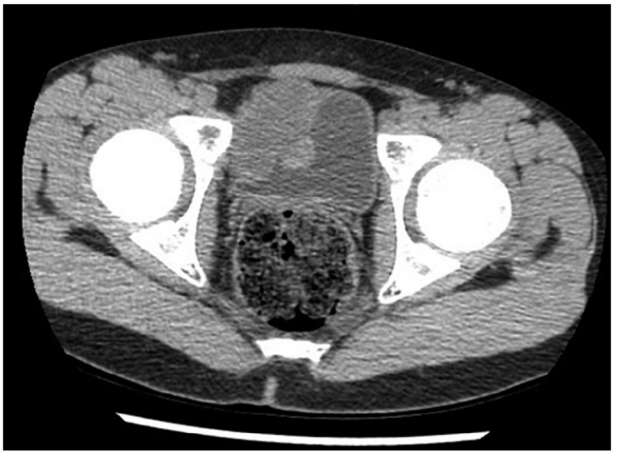

Figure 1. Noncontrast computed tomography axial image demonstrating right anterolateral bladder wall mass.

The patient subsequently underwent partial cystectomy with right pelvic lymph node dissection. Pathology of the bladder mass revealed a $4.1 \times 2.9 \times 2.9$ cm malignant myxoid neoplasm, consistent with metastatic CCSK. Tumor invasion was seen through the muscularis propria with vascular space invasion. All margins and lymph nodes were negative. The ureteral orifice was not involved.

Whole body imaging including brain magnetic resonance imaging (MRI) revealed no evidence of residual

Financial Disclosure: *The authors declare that they have no relevant financial interests.*
Funding Support: *Pediatric Urology Oncology Work Group Session at the 2016 Pediatric Fall Congress, supported by the Society of Pediatric Urology, Dallas, Texas.*

From the Department of Surgery, Division of Urology, St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, MO; the Department of Pathology and Immunology, Washington University School of Medicine, St. Louis, MO; and the Department of Urology, Children's Mercy Hospital, Kansas City, MO

Address correspondence to: Erica J. Traxel, M.D., Division of Urologic Surgery, Washington University School of Medicine, 4960 Children's Place, Campus Box 8242, St. Louis, MO 63110. E-mail: traxele@wudosis.wustl.edu

Submitted: February 7, 2017, accepted (with revisions): April 10, 2017

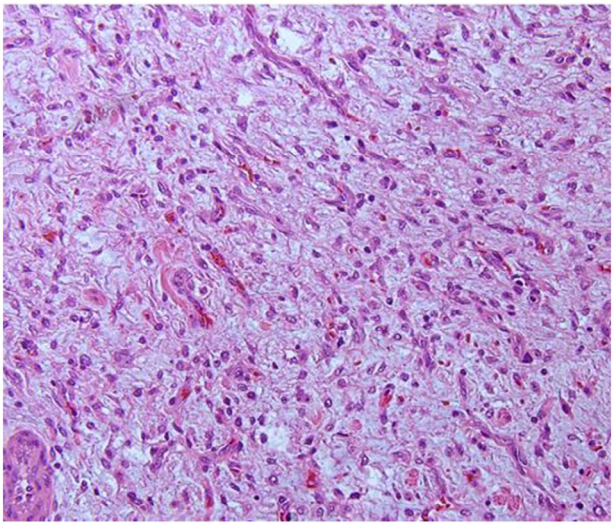

Figure 2. Clear cell sarcoma of the kidney, showing representative from the bladder metastasis. The myxoid neoplasm has modest cellularity and atypia. Networks of delicate blood vessels percolate the tumor. Rare mitoses are identified (hematoxylin and eosin, original magnification ×200). (Color version available online.)

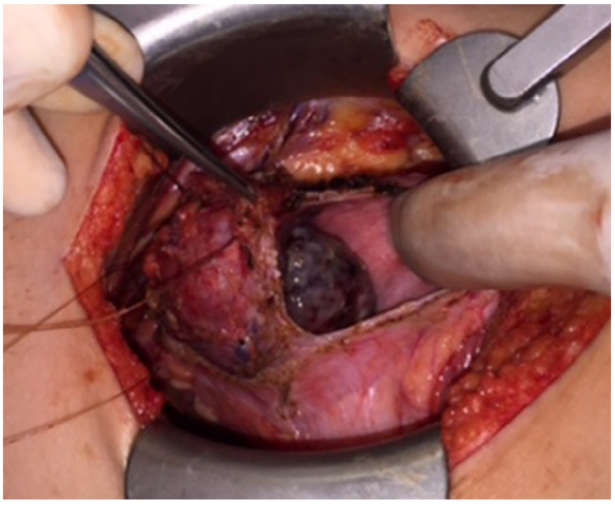

Figure 3. Intraoperative view through cystotomy. (Color version available online.)

disease. Hematology-oncology recommended autologous bone marrow transplant and high-dose chemotherapy with carboplatin, thiotepa, and etoposide. MRI of the abdomen and pelvis showed no evidence of recurrent disease at 7-month follow-up.

DISCUSSION

CCSK has the potential to metastasize to distant sites and was historically known as the bone metastasizing renal tumor. However, recent reports have indicated that the brain has now surpassed the bone as the most common site of CCSK recurrence with other sites including bone, lungs, retroperitoneum, lymph nodes, and liver.[1,3-5] Less common sites of recurrence include the pelvis, orbit, soft tissue, mediastinum, eyelid, skin, colon, contralateral kidney, and bone marrow.[6-9] It also rarely presents in the vena cava with extension into the right atrium.[10-12] We present a case of a bladder recurrence of CCSK. This was discrete from the ureteral orifice so was presumably hematogenous spread as opposed to shedding of tumor cells down the right ureter.

Approximately 20%-40% (range 14%-78%) of CCSK patients experience a relapse.[13] The median time interval to relapse is about 24 months, with a range of 5 months to 8 years after completion of treatment.[3,13,14] Previous treatment regimens included cyclophosphamide, ifosfamide, and etoposide; however, recent utilization of additional chemotherapy agents has resulted in very few late relapses.[13] For example, in the National Wilms Tumor Study-5 trial, only 1 of 21 relapses occurred beyond 3 years.[6] This is at odds with our case in which our patient received vincristine, cyclophosphamide, doxorubicin, and etoposide followed by flank radiation, but still had a recurrence 7 years after his initial complete response.

A recent large combined report described 37 relapses in 237 patients with an initial complete response.[15] Median time from initial diagnosis to relapse was 17 months (5.5 months to 6.6 years). Only brain metastases occurred beyond 38 months from initial treatment, and there were no bladder recurrences. Treatments after recurrence consisted of chemotherapy (n = 30), surgery (n = 19), and radiotherapy (n = 18), followed by high-dose chemotherapy and autologous bone marrow transplantation in 14 patients. Secondary complete response was achieved in 59%, of whom 68% developed a second relapse. Five-year event-free and overall survival after relapse was 18% and 26%, respectively.

CONCLUSION

Our case of a bladder recurrence of CCSK presenting years after an initial complete response is exceedingly rare and we were unable to find another reported case in the literature. Our patient relapsed despite having been treated with combined surgical resection, flank radiation, and the latest chemotherapy options. In the future, gross hematuria in the setting of a prior CCSK should alert physicians to the possibility of a bladder recurrence.

References

1. Sotelo-Avila C, Gonzalez-Crussi F, Sadowinski S, Gooch WM, Pena R. Clear cell sarcoma of the kidney: a clinicopathologic study of 21 patients with long-term follow-up evaluation. *Hum Pathol.* 1986;16:1219-1230.
2. Huang CC, Cutcliffe C, Coffin C. Classification of malignant pediatric tumors by gene expression. *Pediatr Blood Cancer.* 2006;46:728-738.
3. Argani P, Perlman EJ, Breslow NE, et al. Clear cell sarcoma of the kidney: a review of 351 cases from the National Wilms Tumor Study Group Pathology Center. *Am J Surg Pathol.* 2000;24:4-18.
4. Marsden HB, Lawler W, Kumar PM. Bone metastasizing renal tumour of childhood. Morphological and clinical features and differences from Wilms' tumor. *Cancer.* 1978;42:1922-1928.

5. Furtwangler R, Reignhard H, Beier R. Clear-cell sarcoma (CCSK) of the kidney-results of the SIOP 93-01/GHOP trial. *Pediatr Blood Cancer*. 2005;45:423.
6. Seibel NL, Sun J, Anderson R, et al. Outcome of clear cell sarcoma of the kidney treated on the National Wilms Tumor Study-5 (NWTS). *J Clin Onc*. 2006;24(18 suppl):9000-9000.
7. Oda H, Shiga J, Machinami R. Clear cell sarcoma of the kidney: two cases in adults. *Cancer*. 1993;71:2286-2291.
8. Parikh SH, Chintagumpala M, Hicks J, et al. Clear cell sarcoma of the kidney: an unusual presentation and review of the literature. *J Pediatr Hematol Oncol*. 1998;20:165-168.
9. Kababri ME, Khattab M, Khorassani ME, et al. Clear cell sarcoma of the kidney: a study of 13 cases. *Arch Pediatr*. 2004;11:794-799.
10. Toyoda Y, Yamashiota C, Sugimoto T, Yoshida M, Okada M. Clear cell sarcoma of the kidney with tumor extension into the right atrium. *J Cardiovasc Surg (Torino)*. 1998;39:489-491.
11. Zigman A, Shen I. Clear cell sarcoma of the kidney with cavoatrial tumor thrombus: complete resection in a child. *J Pediatr Surg*. 2006;41:1464-1466.
12. Sugandhi N, Munghate G, Malankar DP, et al. Pediatric clear cell sarcoma of the kidney with cavoatrial thrombus. *J Pediatr Surg*. 2011;46:2387-2390.
13. Gooskens SLM, Furtwangler R, Vujanic GM, Dome JS, Graf N, van den Heuvel-Eibrink MM. Clear cell sarcoma of the kidney: a review. *Eur J Cancer*. 2012;48:2219-2226.
14. Kusumakumary P, Chellam VG, Rojymon J, Hariharan S, Krishnan NM. Late recurrence of clear cell sarcoma of the kidney. *Med Pediatr Oncol*. 1997;28:355-357.
15. Gooskens SL, Furtwangler R, Spreafico F, et al. Treatment and outcome of patients with relapsed clear cell sarcoma of the kidney: a combined SIOP and AIEOP study. *Br J Cancer*. 2014;111:227-233.