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. 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.

The patient subsequently underwent partial cystectomy with right pelvic lymph node dissection. Pathology of the bladder mass revealed a 4.1 × 2.9 × 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
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. Less common sites of recurrence include the pelvis, orbit, soft tissue, mediastinum, eyelid, skin, colon, contralateral kidney, and bone marrow. It also rarely presents in the vena cava with extension into the right atrium. 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. The median time interval to relapse is about 24 months, with a range of 5 months to 8 years after completion of treatment. Previous treatment regimens included cyclophosphamide, ifosfamide, and etoposide; however, recent utilization of additional chemotherapy agents has resulted in very few late relapses. For example, in the National Wilms Tumor Study-5 trial, only 1 of 21 relapses occurred beyond 3 years. 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. 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


