Case Report

Primary Ewing's sarcoma/primitive neuroectodermal tumor of the kidney and its clinical features

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Abbreviations & Acronyms
CT = computed tomography
ESFT = Ewing sarcoma family tumor
RCC = renal cell carcinoma

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Introduction: Ewing sarcoma family tumor is a malignant tumor that is primarily of bone origin; it rarely occurs in the kidney.
Case presentation: A 22-year-old woman presented with hematuria. Computed tomography revealed a 6 × 6-cm mass in the lower pole of the right kidney with invasion into the right renal vein. A right laparoscopic radical nephrectomy was performed. The tumor was completely encapsulated. Based on the small-round-cell histology, diffusely CD99-positive tumor cells, and *EWS* (ex7)–*FLi1* (ex6) fusion gene break point transcript, we diagnosed Ewing sarcoma/primitive neuroectodermal tumor of the kidney. After surgery, eight cycles of adjuvant chemotherapy including vincristine, doxorubicin (Adriamycin®), cyclophosphamide, ifosfamide, and etoposide were given. No evidence of recurrence has been observed 13 months from diagnosis.
Conclusion: This was a rare Ewing sarcoma family tumor in the kidney of a young female with no remarkable family medical history.

Key words: Ewing sarcoma, primary renal ESFT, secondary cancer.

Keynote message

A rare Ewing sarcoma family tumor (ESFT) in the kidney of a young adult female is described. The ESFT was a 6 × 6-cm mass in the right kidney's lower pole with invasion into the right renal vein. A laparoscopic radical nephrectomy was performed, and eight cycles of adjuvant chemotherapy were administered. No recurrence has been observed at 13 months post-diagnosis.

Introduction

The ESFT are primary tumors that affects bones or soft tissue, and they are highly cellular-malignant small round-cell tumors. Although it has been thought that ESFTs rarely occur in the retroperitoneum, there are a few reports of this.[1] In clinical practice, <1% of retroperitoneum tumors are observed as a renal mass.[2] ESFT of the kidney has aggressive clinical behavior and a poor prognosis, and its preoperative discrimination from RCC is very difficult. Since an ESFT may be cured with early treatment, it is important to establish its precise clinical features and develop treatment strategies in accord with those features.

Case report

The patient was a 22-year-old Japanese woman with gross hematuria who had undergone treatment for acute lymphocytic leukemia 14 years earlier. At her presentation, an ultrasound examination revealed a right renal solid mass. We scheduled a CT examination, but she came to us again the day before the CT exam due to severe gross hematuria and lower back pain. Cystoscopy showed bleeding from the right ureteral orifice. She was hospitalized.

There were no remarkable physical and laboratory findings. The CT exam showed a 6 × 6-cm mass with low contrast enhancement in the lower pole of the right kidney, with

invasion into right renal vein. There was no metastasis (Fig. 1a,b). From the above inspection, we diagnosed as right RCC and performed a laparoscopic radical nephrectomy. We confirmed the complete resection of the thrombus. The macroscopic specimen was well-circumscribed and solid with necrosis and hemorrhage (Fig. 1c,d). The microscopic examination of the hematoxylin and eosin-stained sample showed small round cells (Fig. 2a,b). There was film formation among the renal parenchyma around the tumor. Immunohistochemistry indicated that the tumor was positive for CD99 (Fig. 2c).

The fluorescence in situ hybridization analysis was positive for the EWSR1 gene, which was conforming to ESFT (Fig. 2d). We administered adjuvant chemotherapy consisting of the combination of vincristine, doxorubicin, and ifosfamide alternating with the cisplatin-etoposide regimen. The patient has remained without recurrence for more than 1 year.

Discussion

A primary renal ESFT can be clinically indistinguishable from RCC. RCC is the most numerous types of renal carcinoma, accounting for approx. 80% of all cases.[2] RCCs originate in the renal cortex. Although other malignant renal tumors such as collecting duct carcinoma and transitional cell carcinoma of the renal pelvis are known for certain, ESFTs have a specific translocated gene that results in a chimeric fusion protein, and their origins are not clear. It has been hypothesized that ESFTs can be derived from the neural crest cells.[3]

Based on the present patient's CT results, we suspected chromophobe or papillary nodular carcinoma and other types of RCC. During the course of the disease, the patient was maintained with bladder tamponade and was able to undergo surgery. The review by Rowe *et al*. noted that the reported neoadjuvant chemotherapy was seldom done (the current standard of care for ESFT), often because the patients with ESFT had undergone early total tumor resection without diagnostic biopsy.[4] Patients with distant metastases and young patients were more likely to undergo a diagnostic biopsy as the initial management, allowing for the use of neoadjuvant chemotherapy.[4]

The advantages of having a confirmed diagnosis preoperatively are that (i) preoperative chemotherapy can be administered while the patient still has preserved renal function, and (ii) the explanation of this can be given to the patient and his/her family members preoperatively. The concerns about disease local recurrence in the biopsy needle tract have been dampened by the clinical experiences at several sarcoma specialist units; pooled data from four institutions demonstrated that there were only two cases of presumed needle tract seeding among 547 patients who underwent a percutaneous biopsy of what proved to be retroperitoneal sarcoma (0.37%).[5]

Primary renal ESFTs have no specific findings on imaging and may be less likely to benefit from imaging. The clinical features include pain (due to rapid extension of the capsule) and hematuria (due to disruption of the urinary tract), which occur relatively early in the course of the disease. The enlarged tumor can extend to a renal vein and the inferior vena cava. A biopsy may be an option for renal masses with these characteristics, considering the special cases of tumors for which preoperative chemotherapy is considered.

However, Tarek *et al*. reported that lesions confined to the kidney was treated with a nephrectomy and adjuvant chemotherapy had favorable outcomes,[6] and that in cases with a rapidly growing tumor, immediate surgery before a biopsy may provide a better outcome. We believe that this is beneficial to patients' quality of life because it reduces the time with pain and hematuria and the anxiety of having a tumor.

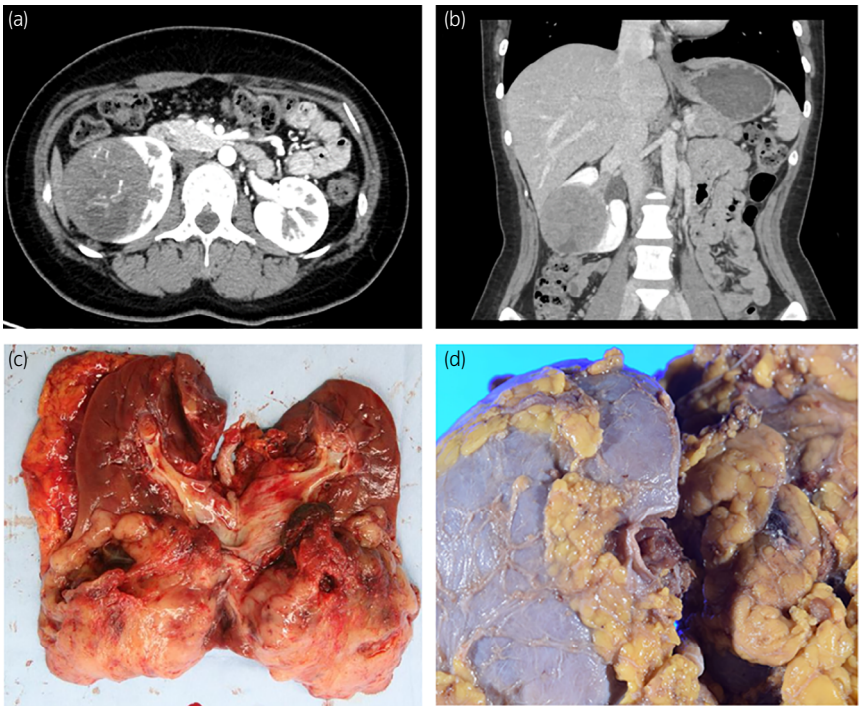

Fig. 1 CT images and specimens. CT scan in the arterial phase shows a slowly contrasted mass with necrosis components. (a) A coronal-reformatted image shows the extension of the thrombosis in the right renal vein. (b) Gross appearance of the nephrectomy specimen. It measures 6 × 6 × 6 cm and replaces half of the kidney. It is well circumscribed, solid, and gray in tone with areas of necrosis and hemorrhage. (c) After fixing, we confirmed the complete excision of the thrombus (d).

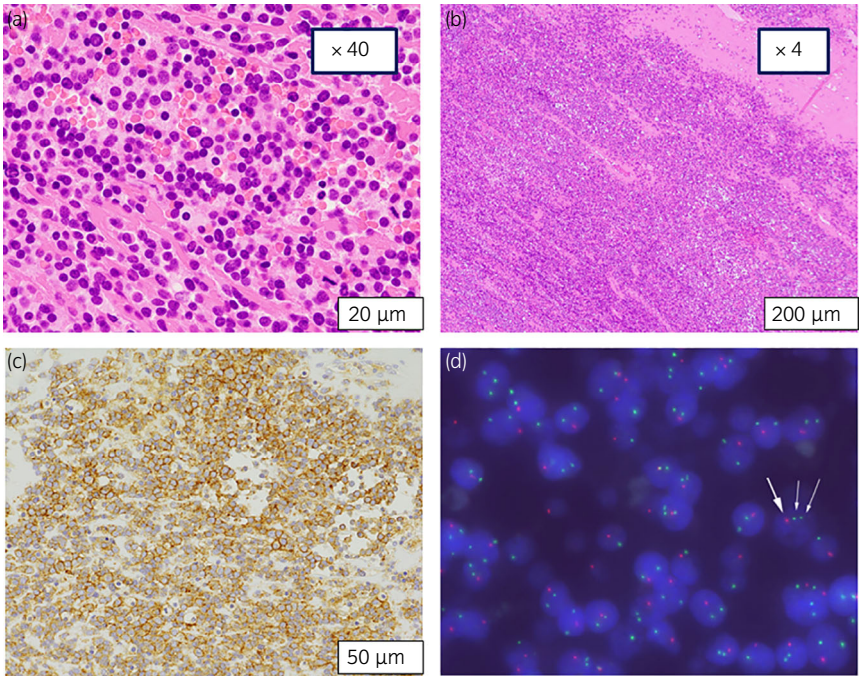

Fig. 2 H&E stained and immunostained specimens. Diffusely small round cells tumor on H&E (a, b). The cells were arranged in sheets with a high N/C ratio, speckled chromatin, and inconspicuous nucleoli. Immunostaining for CD99 (c). A split signal was observed via FISH using an EWSR1 dual-color break-apart probe. In normal cells, the red and green signals are close to or appear yellow (*yellow arrowhead*). In gene-translocated cells, two signals are split (*green and red arrows*) (d).

The present patient developed it ESFT after overcoming leukemia in her childhood. With the recent advances in chemotherapy, secondary cancers in cancer survivors have become a problem. More than 80% of pediatric cancer patients are expected to survive for a long time.[7] Secondary cancers have a direct impact on their outcomes and greatly affect their quality of life. Although pediatric chemotherapy and radiotherapy have improved to reduce toxicity while enhancing efficacy, the risk of secondary cancers remain. These malignancies are often induced by radiotherapy or chemotherapy, and the patients are then resistant to those treatments. In addition, survivors of childhood cancers are more likely develop second cancers due to genetic factors and side effects of treatment. According to the ESFT summary and treatment policy in past reports,[1,3,4,6,7] the most common chemo regimen is known as VD(or A)C/IE (vincristine, doxorubicin (or Adriamycin), and cyclophosphamide). It alternates between 2 combinations of drugs, given every 2 to 3 weeks at least 9 weeks before surgery or radiation, and then will get more chemo afterward as well. Usually a total of about 14 to 15 cycles of chemo are given.[7]

In 2169 Acute lymphocytic leukemia survivors data,[8] the most common malignancies were 46 myeloid malignancies, 3 lymphomas, 16 carcinomas excluding basal cell carcinoma, 6 sarcomas (not sure if ESFTs were included), and 22 brain tumors. In a cohort study of long-term outcomes childhood cancer survivors without limiting the type,[9]conclusion the results strongly suggest that doxorubicin exposure in them increases the risk of subsequent solid cancers and breast cancer, whereas cyclophosphamide exposure increases the risk of subsequent sarcomas. However, ESFT is excluded from this analysis data, and the specific value is uncertain. ESFT from the kidney as a secondary cancer in ALL survivor has not been reported within the scope of our research. According to other studies,[10] more than half of them has developed secondary cancer more than 20 years ago.[9] Careful monitoring is important so that another cancer can be caught early for life.

Author contributions

Shiori Saikawa: Writing – original draft; writing – review and editing. Minekatsu Taga: Supervision. Yasushi Matsuda: Supervision. Koji Suzuki: Supervision. Aina Yamaguchi: Investigation. Mana Fukushima: Investigation. Yoshiaki Imamura: Supervision. Hideaki Ito: Supervision. Osamu Yokoyama: Supervision.

Conflict of interest

The authors declare no conflict of interest.

Approval of the research protocol by an Institutional Reviewer Board

N/A.

Informed consent

Informed consent was obtained from the patient.

Registry and the Registration No. of the study/trial

N/A.

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