

# Ewing Sarcoma Family of Tumors (ESFTs) of Renal Origin Presenting With Bone Metastases: A Case Report

Review began 03/26/2025

Review ended 04/22/2025

Published 04/23/2025

© Copyright 2025

Jakowczuk et al. This is an open access article distributed under the terms of the Creative Commons Attribution License CC-BY 4.0., which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

DOI: 10.7759/cureus.82829

Tiffany E. Jakowczuk<sup>1</sup>, Gord G. Zhu<sup>2</sup>, Jeffrey J. Tomaszewski<sup>3</sup>, Tae Won Kim<sup>4</sup>, Marc Zeffren<sup>5</sup>, Daisy C. Obiora<sup>5</sup>, Veniamin Barshay<sup>5</sup>, Tina B. Edmonston<sup>2</sup>, Hadi Shojaei<sup>2</sup>, Ruth Birbe<sup>2</sup>

1. Cooper Medical School, Rowan University, Camden, USA 2. Pathology, Cooper University Hospital, Camden, USA 3. Urology, Cooper University Hospital, Camden, USA 4. Orthopedics, Cooper University Hospital, Camden, USA 5. Radiology, Cooper University Hospital, Camden, USA

Corresponding author: Ruth Birbe, birbe-ruth@cooperhealth.edu

## Abstract

We report a unique case of a female patient in her fifth decade of life who presented with groin pain and was found to have a right kidney mass measuring approximately 8 cm, in addition to multiple bone metastases. Both the nephrectomy specimen and the bone biopsy were found to belong to the Ewing sarcoma family of tumors (ESFTs). This was confirmed by immunohistochemical studies and fluorescence in situ hybridization (FISH) showing *EWSR1* gene rearrangement. Molecular analysis with next-generation sequencing (NGS) showed a type II *EWSR1:FLI1* gene fusion. The patient's disease progressed rapidly, and she passed away approximately three months after admission. Although extremely rare in the kidney, ESFT should be considered in patients who present with clinically aggressive kidney tumors.

**Categories:** Urology, Pathology, Orthopedics

**Keywords:** ewing sarcoma (es), ewing sarcoma family of tumors(esft), ewing sarcoma of the kidney, extra-skeletal ewing sarcoma, fluorescence in situ hybridization (fish), metastatic renal cancer, next generation sequencing (ngs), res: renal ewing sarcoma, urologic neoplasms

## Introduction

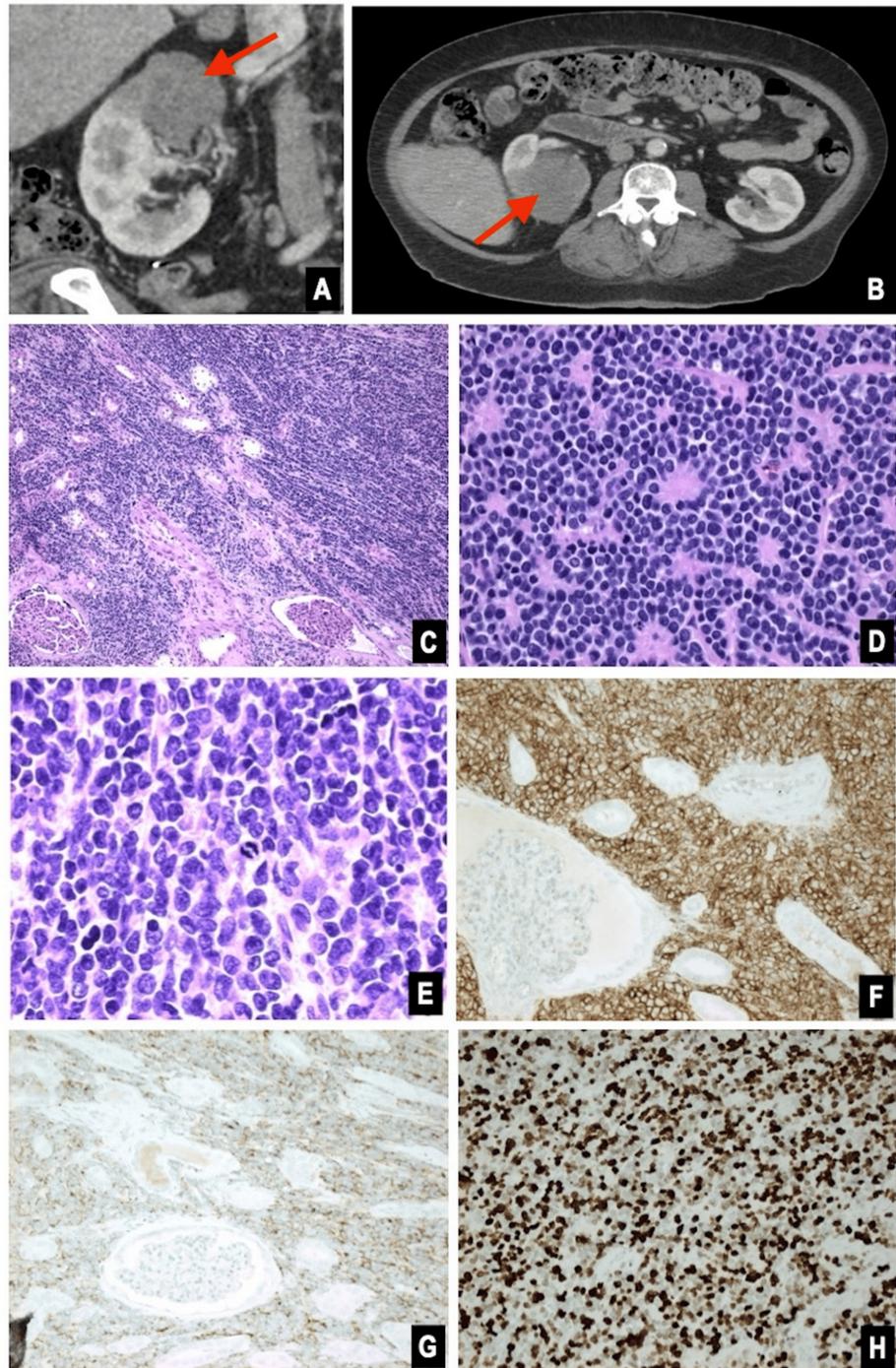
Ewing sarcoma family of tumors (ESFTs), which includes Ewing sarcoma and primitive neuroectodermal tumors (PNETs), is a group of aggressive malignant neoplasms characterized by small round blue cells and fusion of the *EWSR1* gene with other genes such as *FLI1* and *ERG* [1]. ESFT of renal origin behaves more aggressively than those arising in other sites, including bone [2-6]. Up to 50% of patients present with metastasis, and only 50% of those survive after five years [2-3].

## Case Presentation

A woman in her fifth decade of life with a history of diabetes and nephrolithiasis presented with groin pain. Computed tomography (CT) imaging of the pelvis revealed a 7.8 cm centrally necrotic, hypovascular right renal mass (Figure 1). Magnetic resonance imaging (MRI) and a nuclear bone scan showed multiple bone lesions involving the right femur, ribs, iliac bone, and clavicle. MRI of the femur lesion is shown in Figure 2. Biopsy of the involved femur revealed a small round blue cell tumor with crush artifact (Figure 2). Immunohistochemical studies demonstrated positive CD99, synaptophysin, and NKX2.2. The Ki-67 proliferation index was 80%, and fluorescence in situ hybridization (FISH) analysis showed *EWSR1* gene rearrangement. A robotic-assisted laparoscopic radical nephrectomy produced an 8.5 cm lobulated, solid, tan tumor that extended into the pelvic mucosa and perinephric fat. Histologically, the tumor comprised monomorphic small round blue cells with rosettes, necrosis, and a high mitotic count (20 mitoses per 10 high-power fields). The immunoprofile of the renal tumor resembled that of the bone biopsy (Figure 1). Thus, the pathologic stage was pT2, pNx, pM1 (bone), with a histologic grade of 3 (French Federation of Cancer Centers Sarcoma Group). Based on these findings, a diagnosis of renal ESFT was made. Next-generation sequencing (NGS) molecular analysis of the kidney tumor showed a type II *EWSR1:FLI1* gene fusion between exon 7 of *EWSR1* and exon 5 of *FLI1* (Figure 3). The patient experienced a complicated postoperative course and rapid disease progression, including pathologic fractures, sepsis, additional bone metastases, and retroperitoneal lymphadenopathy. After electing hospice care, she expired approximately three months after admission.

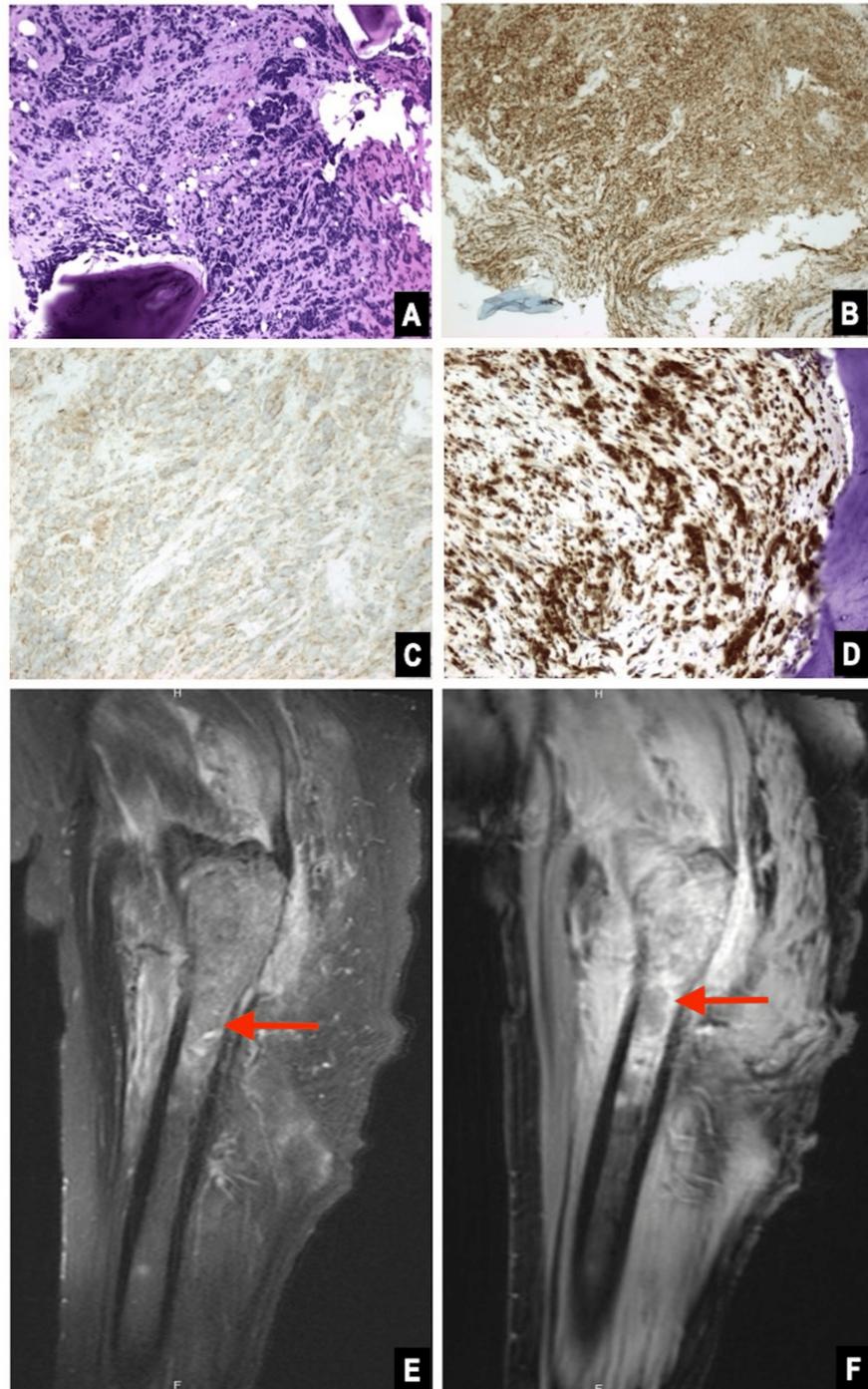
### How to cite this article

Jakowczuk T E, Zhu G G, Tomaszewski J J, et al. (April 23, 2025) Ewing Sarcoma Family of Tumors (ESFTs) of Renal Origin Presenting With Bone Metastases: A Case Report. Cureus 17(4): e82829. DOI 10.7759/cureus.82829



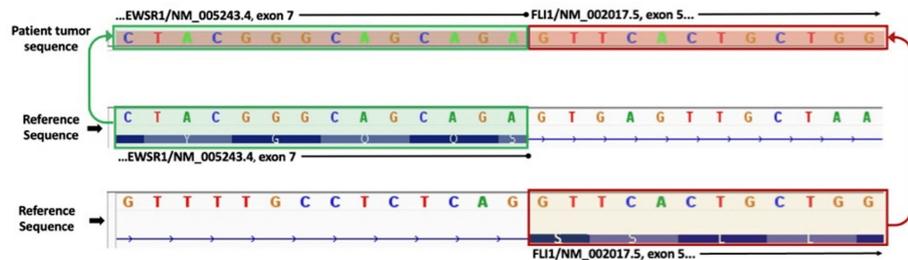
**FIGURE 1: Right renal mass.**

Computed tomography (CT): coronal (A) and axial (B), with area of interest identified by arrows. Pathology of nephrectomy: hematoxylin and eosin (H&E) stain at 100x (C), 400x (D), and 600x (E). Immunohistochemical stains positive for CD99 (F), synaptophysin (G), and Ki-67 with a high proliferation index between 80% and 90% (H).



**FIGURE 2: Right femur lesion.**

Pathology of bone biopsy: hematoxylin and eosin (H&E) at 200x (A). Immunohistochemical stains positive for CD99 (B), synaptophysin (C), and Ki67 with a high proliferation index (D). Magnetic resonance imaging (MRI): T1 fat-saturated before (E) and after (F) contrast, sagittal view, with area of interest identified by arrows.



**FIGURE 3: Next-generation sequencing (NGS) of the kidney tumor demonstrating a type II fusion of exon 7 of EWSR1 with exon 5 of FLI1.**

Review of the patient's electronic medical record revealed numerous prior CT scans of the abdomen and pelvis as early as eight years before presentation. Most appeared to be without contrast, presumably for evaluation of her known history of nephrolithiasis. Approximately four years before presentation, she underwent renal ultrasound (RUS), during which a questionable 4.8 cm right lateral midpole mass versus prominent renal tissue was noted, with no further workup per chart review. A chest radiograph in the month before presentation was unremarkable, and a hip radiograph in the days leading up to presentation showed only an 8 mm intertrochanteric cyst in the right femur.

## Discussion

Extraskeletal ESFTs, which represent up to 30% of all cases of ESFT [7], were first described in 1975 by Angervall and Enzinger [8]. In contrast to skeletal ESFT, which most commonly affects males in the second decade of life [9], patients with extraskeletal ESFT are more often female and tend to be older [7,10]. However, current literature suggests that the demographics of patients with renal ESFT seem to match more closely with those of skeletal ESFT [2-5], making this case presentation even rarer. Overall survival of patients with extraskeletal ESFT can be worse in the first two years compared to patients with skeletal ESFT. After two years, patients with skeletal ESFT exhibit lower overall survival [7].

Mor et al. were the first to describe ESFT of renal origin in 1994, at which time peripheral PNETs were already regarded as aggressive neoplasms with early metastasis to other sites such as bone [6]. More recent studies found that nearly half of all patients with renal ESFT had distant metastasis at presentation [2-5]. Bone metastases occur in up to 15% of patients with advanced-stage renal tumors within the first year of diagnosis [11], whereas primary malignant Ewing sarcoma accounts for fewer than 0.2% of all cancers diagnosed in the United States [12].

Symptoms of renal ESFT are nonspecific, initially leading clinicians to consider more common neoplasms [2-4]. Due to the rarity of primary renal ESFT, there is currently no standardized protocol for treating this entity [2-4]. The association between nephrolithiasis and renal ESFT has not yet been elucidated. A 2015 meta-analysis demonstrated an increased risk of other renal cancers in patients with kidney stones, but only in male patients [13].

## Conclusions

While ESFTs are most commonly known to affect the bones, extraskeletal ESFTs have been reported and are often more aggressive. Along with evidence from existing literature, the presence of a sizable renal lesion four years before presentation supports the diagnosis of primary renal ESFT in our patient. This case adds to the body of knowledge on renal ESFTs and confirms their aggressive behavior.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

**Concept and design:** Tiffany E. Jakowczuk, Ruth Birbe

**Drafting of the manuscript:** Tiffany E. Jakowczuk, Ruth Birbe

**Acquisition, analysis, or interpretation of data:** Gord G. Zhu, Jeffrey J. Tomaszewski, Tae Won Kim, Marc Zeffren, Daisy C. Obiora, Veniamin Barshay, Tina B. Edmonston, Hadi Shojaei, Ruth Birbe

**Critical review of the manuscript for important intellectual content:** Gord G. Zhu, Jeffrey J. Tomaszewski, Tae Won Kim, Marc Zeffren, Daisy C. Obiora, Veniamin Barshay, Tina B. Edmonston, Hadi Shojaei, Ruth Birbe

**Supervision:** Ruth Birbe

## Disclosures

**Human subjects:** Consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

## References

1. Ishiguro M, Yuki M, Fukushige T, Mizoguchi M, Kaneko Y, Morishige T, Iwasaki H: Molecular cytogenetic characterization of two established ESFT cell lines. *Hum Cell*. 2017, 30:41-8. [10.1007/s13577-016-0145-7](https://doi.org/10.1007/s13577-016-0145-7)
2. Li J, Nie F, Li Y: Extraosseous Ewing's sarcoma/peripheral primitive neuroectodermal tumour of the kidney: a case report and literature review. *BMC Urol*. 2022, 22:197. [10.1186/s12894-022-01146-w](https://doi.org/10.1186/s12894-022-01146-w)
3. Liang L, Song H, Ma B, et al.: Renal Ewing's sarcoma/primitive neuroectodermal tumor (PNET): a case series of 7 patients and literature review. *Transl Androl Urol*. 2021, 10:548-54. [10.21037/tau-20-1122](https://doi.org/10.21037/tau-20-1122)
4. Rowe RG, Thomas DG, Schuetze SM, Hafez KS, Lawlor ER, Chugh R: Ewing sarcoma of the kidney: case series and literature review of an often overlooked entity in the diagnosis of primary renal tumors. *Urology*. 2013, 81:347-53. [10.1016/j.urology.2012.10.016](https://doi.org/10.1016/j.urology.2012.10.016)
5. Tarek N, Said R, Andersen CR, et al.: Primary Ewing sarcoma/primitive neuroectodermal tumor of the kidney: the MD Anderson Cancer Center experience. *Cancers (Basel)*. 2020, 12: [10.3390/cancers12102927](https://doi.org/10.3390/cancers12102927)
6. Mor Y, Nass D, Raviv G, Neumann Y, Nativ O, Goldwasser B: Malignant peripheral primitive neuroectodermal tumor (PNET) of the kidney. *Med Pediatr Oncol*. 1994, 23:437-40. [10.1002/mpo.2950230508](https://doi.org/10.1002/mpo.2950230508)
7. Applebaum MA, Worch J, Matthay KK, Goldsby R, Neuhaus J, West DC, Dubois SG: Clinical features and outcomes in patients with extraskeletal Ewing sarcoma. *Cancer*. 2011, 117:3027-32. [10.1002/cncr.25840](https://doi.org/10.1002/cncr.25840)
8. Angervall L, Enzinger F: Extraskeletal neoplasm resembling Ewing's sarcoma. *Cancer*. 1975, 36:240-51. [10.1002/1097-0142\(197507\)36:1<240::aid-cncr2820360127>3.0.co;2-h](https://doi.org/10.1002/1097-0142(197507)36:1<240::aid-cncr2820360127>3.0.co;2-h)
9. Choi EY, Gardner JM, Lucas DR, McHugh JB, Patel RM: Ewing sarcoma. *Semin Diagn Pathol*. 2014, 31:39-47. [10.1053/j.semdp.2014.01.002](https://doi.org/10.1053/j.semdp.2014.01.002)
10. Lynch AD, Gani F, Meyer CF, Morris CD, Ahuja N, Johnston FM: Extraskeletal versus skeletal Ewing sarcoma in the adult population: controversies in care. *Surg Oncol*. 2018, 27:373-9. [10.1016/j.suronc.2018.05.016](https://doi.org/10.1016/j.suronc.2018.05.016)
11. Hernandez RK, Wade SW, Reich A, Pirolli M, Liede A, Lyman GH: Incidence of bone metastases in patients with solid tumors: analysis of oncology electronic medical records in the United States. *BMC Cancer*. 2018, 18:44. [10.1186/s12885-017-3922-0](https://doi.org/10.1186/s12885-017-3922-0)
12. Hameed M, Dorfman H: Primary malignant bone tumors--recent developments. *Semin Diagn Pathol*. 2011, 28:86-101. [10.1053/j.semdp.2011.02.002](https://doi.org/10.1053/j.semdp.2011.02.002)
13. Cheungpasitporn W, Thongprayoon C, O'Corragain OA, Edmonds PJ, Ungprasert P, Kittanamongkolchai W, Erickson SB: The risk of kidney cancer in patients with kidney stones: a systematic review and meta-analysis. *QJM*. 2015, 108:205-12. [10.1093/qjmed/hcu195](https://doi.org/10.1093/qjmed/hcu195)