Urology Case Reports 53 (2024) 102657

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

Primary sclerosing epithelioid fibrosarcoma of the kidney: A rare case report

Kuan-Hsien Wu [a,b], Yen-Shuo Huang [c], Ching-Chia Li [a,b,d,*]

[a] Department of Urology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[b] Graduate Institute of Clinical Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan
[c] Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan
[d] Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

ARTICLE INFO

Keywords:
Sclerosingepithelioidfibrosarcoma
Kidney
Immunohistochemistry
MUC4
EWSR1

ABSTRACT

Sclerosing epithelioid fibrosarcoma (SEF) represents a rare variant of fibrosarcoma primarily arising in the deep soft tissue of the extremities and trunk. The author reported a rare case of SEF emerged primarily in the kidney. Clinically, the patient complained of hematuria. The diagnosis was confirmed by histological examination and immunohistochemical staining of MUC4. Subsequent fluorescence in situ hybridization (FISH) analysis detected the presence of EWSR1 gene rearrangement, further confirming the histological diagnosis. The patient has been alive with 12 months follow-ups after nephrectomy. The disease should be considered in the differential diagnosis for primary renal tumors.

1. Introduction

Sclerosing epithelioid fibrosarcoma (SEF) is a rare variant of soft tissue fibrosarcoma, first documented by Meis-Kindblom in 1995.[1] Histologically, it is characterized by infiltrative nests and cords of epithelioid cells with clear cytoplasm, all situated within a backdrop of hyalinized stroma. Patients typically present as young to middle-aged adults, with no significant gender preference. The most common primary sites are the deep soft tissues of the extremities, with the trunk, head, and neck regions following in frequency.[1,2] Although visceral primaries are exceptionally rare, the most reported location is kidney.[3–10] SEF typically exhibits an aggressive clinical course, characterized by frequent local recurrence and metastasis, despite its low incidence rate.[1,2] It poses diagnostic challenges both clinically and pathologically. We present a case of SEF that arose primarily in the kidney, along with discussing the clinical and molecular pathogenetic comprehension.

2. Case report

A 31-year-old man without any underlying disease reported gross hematuria for one week. The patient denied having fever or any other urinary or gastrointestinal symptoms. He has a family history of colorectal cancer but denied any environmental exposures. He visited our hospital's Urology outpatient clinic due to persistent and worsening hematuria. Upon arrival, physical exams showed no signs of flank pain or abdominal pain. Urine cytology revealed a negative result for high-grade urothelial carcinoma. A contrast-enhanced computed tomography (CT) scan of the abdomen depicted a well-circumscribed 8.8 cm heterogeneous enhanced mass at the right kidney with perirenal fat invasion, classified as clinical stage cT3a (American Joint Committee on Cancer 8th edition) (Fig. 1).[11] There was neither regional metastatic lymphadenopathy nor distant metastasis.

The patient asked for right laparoscopic radical nephrectomy and adrenalectomy, and the operation was scheduled (Fig. 2A). He recovered well after the surgery. The surgical margins were free of tumor, and the pathologic stage was pT2.[11] Grossly, it is a well-circumscribed tumor lesion with a multilobulated, tan and fleshy cut surface (Fig. 2B). Microscopically, the tumor showed cords or sheets of epithelioid cells embedded within prominent hyalinized sclerotic collagenous stroma (Fig. 2C and D). Immunohistochemically, the tumor cells are diffusely positive for MUC4 with scattered EMA expression (Fig. 3), while being negative for CD34, STAT6, NKX2.2, SS18-SSX, BCOR, SATB2, ETV4, S100, SOX10, TrkABC, ALK, ROS1 and BRAF. Retained H3K27me3 and SMARCA4 are noted. Rearrangement of EWSR1 is detected by fluorescence in situ hybridization (FISH) with split or isolated and amplified

* Corresponding author. No. 100, Shih-Chuan 1st Road, Sanmin Dist., Kaohsiung, 80708, Taiwan.
E-mail address: u101001063@gap.kmu.edu.tw (C.-C. Li).

https://doi.org/10.1016/j.eucr.2024.102657
Received 14 December 2023; Received in revised form 7 January 2024; Accepted 10 January 2024
Available online 11 January 2024

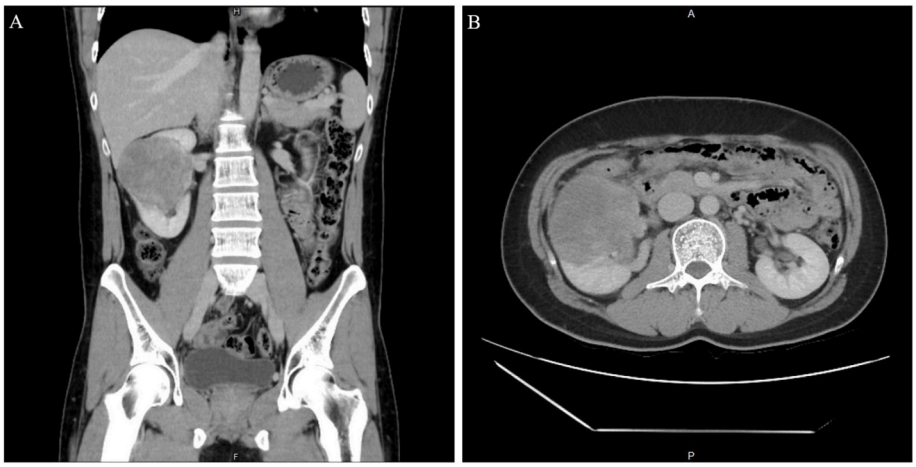

Fig. 1. Abdominal CT (A, coronal view; B, axial view) depicting a well-circumscribed heterogeneous enhanced mass at the right kidney with perirenal fat invasion.

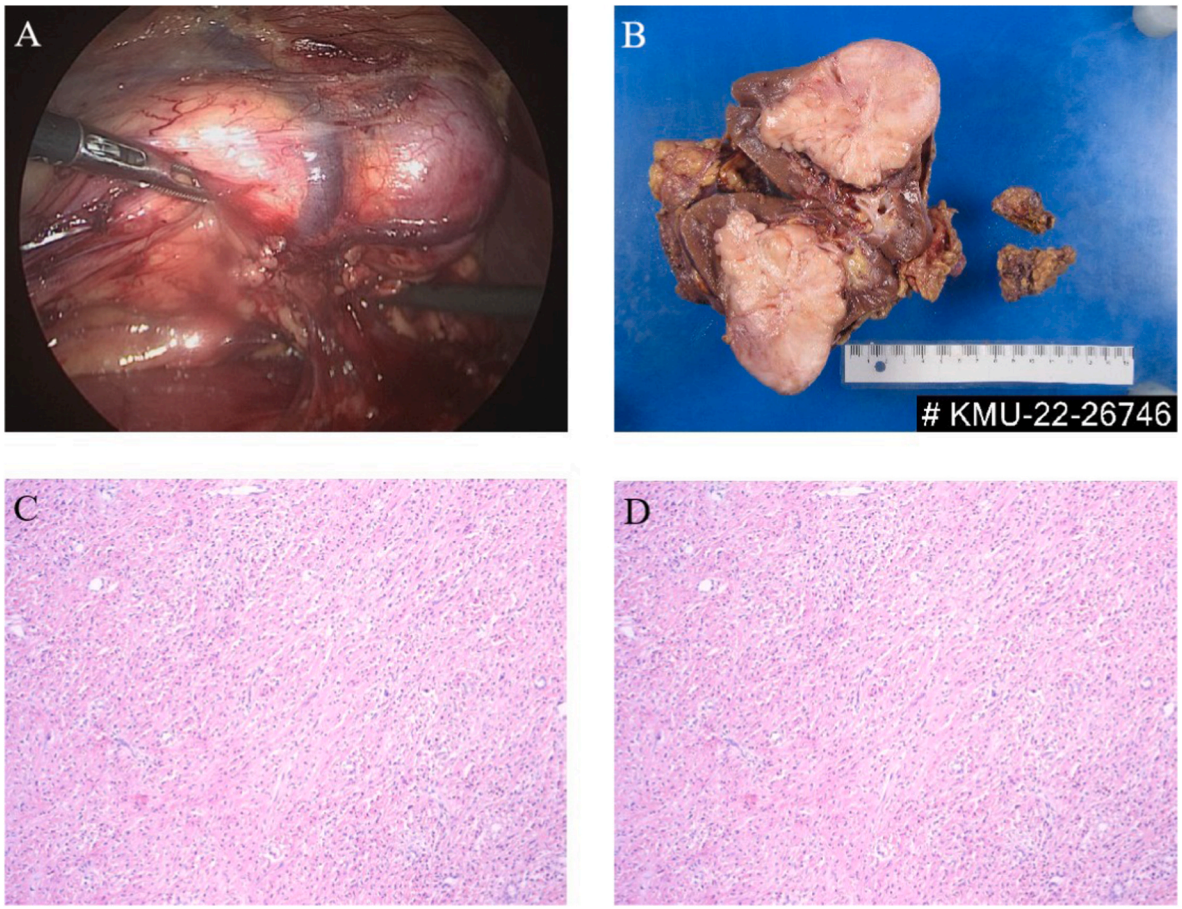

Fig. 2. A, Right renal mass was found under laparoscopy. B, Grossly, a well-circumscribed tumor lesion with a multilobulated, tan and fleshy cut surface. C, Section showing cords or sheets of epithelioid cells embedded within prominent hyalinized sclerotic collagenous stroma (H&E; original magnification, 100 ×). D, Higher magnification showing cords and strands of relatively bland and monomorphic epithelioid cells with round to oval nuclei and pale cytoplasm (H&E; original magnification, 400 ×).

red signals, while the FUS gene is normal. Next generation sequencing (NGS) using Archer pan-solid panel reveals EWSR-CREB3L1 fusion. Repeated CT after one year follow up disclosed no definite evidence of local recurrence or distant metastasis. The patient was alive with no evidence of disease.

3. Discussion

SEF primarily originates in somatic soft tissues, but it is extraordinarily rare when occurring at intraabdominal sites, particularly affecting visceral organs such as the cecum, liver, lung, pancreas, and ovary.[9] The first reported case of primary renal SEF was documented in 2014, emphasizing the importance of molecular studies in understanding SEF.[3]

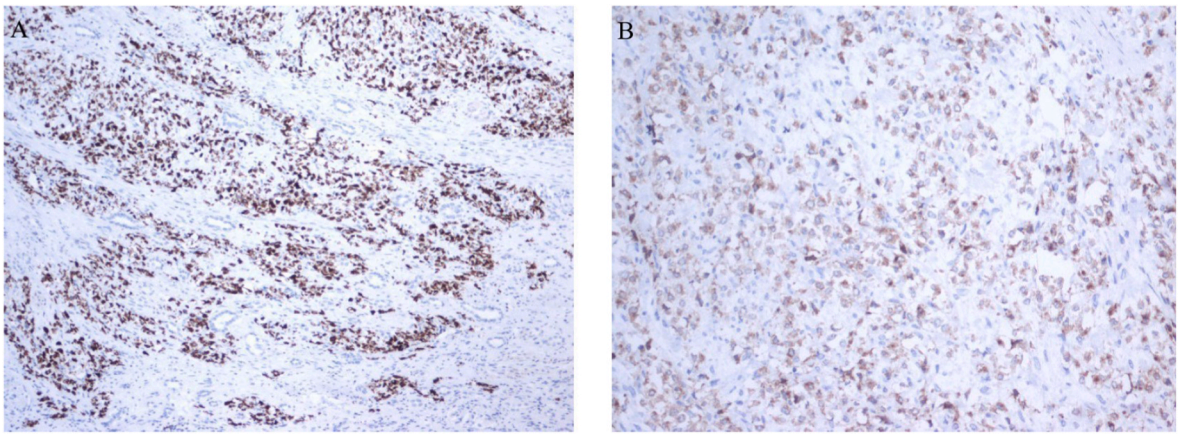

Fig. 3. Immunohistochemically, the neoplastic cells diffuse and strong positive for MUC4 (A) and scattered EMA (B) expression, respectively. (IHC; original magnification, 200 ×).

In total, including our case, there are twelve reported cases in the English scientific literature.[3–10] Patients were 5 males and 7 females, ranging in age from 4 to 61 years (mean, 34; median, 34 years). The tumors varied in size, with measurements spanning from 4.2 to 25 cm in maximum diameter, and a mean size of 10.8 cm.

Patients typically present with clinical symptoms such as flank or abdominal pain. In our case, the chief complaint was hematuria, which required differentiation from other potential causes of hematuria. Given the high prevalence of upper tract urothelial carcinoma in Taiwan,[12,13] this consideration becomes particularly important. Radiological examinations, including ultrasonography and CT scans, often reveal a solid mass with soft tissue density located on either side of the kidney. 5 of 12 (42 %) reported case of primary SEF presented with metastatic disease. The most common sites for metastasis include lung, liver, bone, spinal cord, and lymph nodes.[9] Currently, surgery remains the primary treatment approach for renal SEF. In cases with metastases, an aggressive multimodal treatment strategy, including chemotherapy and radiation therapy, is often considered.[4,5,8,10] However, due to the limited number of cases, the effectiveness of multimodal treatment remains unknown.

On histologic examination, reported cases of renal SEF consistently exhibited a similar morphology. They were uniformly characterized by the presence of cords composed of polygonal or epithelioid cells, featuring angulated nuclei and clear cytoplasm. These cellular structures were set against a backdrop of hyaline sclerosis, often seen entrapping renal tubules, or encircling renal glomeruli.[4,5]

Immunohistochemistry for MUC 4, a highly sensitive and specific marker for SEF, was detected in neoplastic cells of all cases of renal SEF. Variable staining of EMA and CD99, as well as the expression of vimentin and bcl-2 were reported in some SEF cases, but these markers are not diagnostically significant. To distinguish SEF from other potential mimics, it's worth noting that SEF consistently tested negative for pankeratin, PAX8, desmin, α-SMA, CD34, S100 protein, ERG, HMB45, GATA3, and CD117.

At the molecular level, most renal SEF harbored a reciprocal chromosomal translocation resulting in generation of EWSR1-CREB3L1 fusion gene.[4,5,7,10] In our case, the molecular assay consistently confirmed this finding. A minority of SEF showed deletion or splitting of EWSR1 gene.[3,6,9] Therefore, detection of EWSR1 gene rearrangement through molecular assay is considered highly helpful in the diagnosis and differential diagnosis of SEF, especially in cases arising at visceral organs.

The rarity of renal SEF can pose a challenge in making the diagnosis. The differential diagnosis of renal SEF includes clear cell carcinoma, lymphoma, metastases lesion, and rare cases such as neuroectodermal tumor in the kidney.[14] Benign neoplasms should also be considered. In some cases, renal tumors are incidentally discovered during health checks without any associated symptoms. Although the morphological features and immunophenotype of SEF can resemble other neoplasms, it's worth noting that MUC4 immunoreactivity is not observed in these other entities. Therefore, an antibody work-up for differential diagnosis plays a crucial role in accurately identifying SEF.

4. Conclusion

A rare case of primary renal SEF, a neoplasm known for its more aggressive clinical course, was presented in this study. The disease is often marked by frequent synchronous metastatic disease. Surgical removal is typically the preferred treatment for localized renal disease. However, in cases with metastases, multimodal treatment should be considered. Molecular studies and immunohistochemistry serve as powerful diagnostic tools, assisting in achieving an accurate diagnosis of renal SEF.

Ethics approval and consent to participate

Approval for the study was obtained from the Institutional Review Board of Kaohsiung Medical University Hospital.

Consent for publication

Informed consent was obtained from the patient for the publication of this case report.

Availability of data and materials

The authors do not wish to share the patient's data. The privacy of this participant should be protected.

Funding

No funding sources contributed to this case report.

CRediT authorship contribution statement

Kuan-Hsien Wu: Writing – original draft, Data curation, Conceptualization. **Yen-Shuo Huang:** Writing – review & editing. **Ching-Chia Li:** Writing – review & editing, Conceptualization.

Declaration of competing interest

The authors declare no conflicts of interest.

Acknowledgements

The authors would like to acknowledge the Department of Pathology at Kaohsiung Medical University Hospital for their assistance.

Abbreviations

SEF	sclerosing epithelioid fibrosarcoma
CT	computed tomography
FISH	fluorescence in situ hybridization
NGS	next generation sequencing

References

1. Meis-Kindblom JM, Kindblom LG, Enzinger FM. Sclerosing epithelioid fibrosarcoma. A variant of fibrosarcoma simulating carcinoma. *Am J Surg Pathol*. 1995;19(9):979–993. https://doi:10.1097/00000478-199509000-00001.
2. Ossendorf C, Studer GM, Bode B, Fuchs B. Sclerosing epithelioid fibrosarcoma: case presentation and a systematic review. *Clin Orthop Relat Res*. 2008;466(6):1485–1491. https://doi:10.1007/s11999-008-0205-8.
3. Arbajian E, Puls F, Magnusson L, et al. Recurrent EWSR1-CREB3L1 gene fusions in sclerosing epithelioid fibrosarcoma. *Am J Surg Pathol*. 2014;38(6):801–808. https://doi:10.1097/PAS.0000000000000158.
4. Argani P, Lewin JR, Edmonds P, et al. Primary renal sclerosing epithelioid fibrosarcoma: report of 2 cases with EWSR1-CREB3L1 gene fusion. *Am J Surg Pathol*. 2015;39(3):365–373. https://doi:10.1097/PAS.0000000000000338.
5. Ertoy Baydar D, Kosemehmetoglu K, Aydin O, Bridge JA, Buyukeren B, Aki FT. Primary sclerosing epithelioid fibrosarcoma of kidney with variant histomorphologic features: report of 2 cases and review of the literature. *Diagn Pathol*. 2015;10:186. https://doi.org/10.1186/s13000-015-0420-z.
6. Ohlmann CH, Brecht IB, Junker K, et al. Sclerosing epithelioid fibrosarcoma of the kidney: clinicopathologic and molecular study of a rare neoplasm at a novel location. *Ann Diagn Pathol*. 2015;19(4):221–225. https://doi:10.1101/mcs.a006093.
7. Torabi A, Corral J, Gatalica Z, Swensen J, Moraveji S, Bridge JA. Primary renal sclerosing epithelioid fibrosarcoma: a case report and review of the literature. *Pathology*. 2017;49(4):447–450. https://doi:10.1016/j.pathol.2017.01.010.
8. Mok Y, Pang YH, Sanjeev JS, Kuick CH, Chang KT. Primary renal hybrid low-grade fibromyxoid sarcoma-sclerosing epithelioid fibrosarcoma: an unusual pediatric case with EWSR1-creb3l1 fusion. *Pediatr Dev Pathol*. 2018;21(6):574–579. https://doi:10.1177/1093526617754030.
9. Wang X, Wang J. Primary sclerosing epithelioid fibrosarcoma of the kidney: report of two additional cases with a clinicopathological and molecular cytogenetic study. *Exp Mol Pathol*. 2019;107:179–183. https://doi:10.1016/j.yexmp.2019.02.006.
10. Kurtz JL, Tan SY, Hazard FK. Sclerosing epithelioid fibrosarcoma of the kidney: first reported case in a young child. *Pediatr Dev Pathol*. 2021;24(2):148–153. https://doi:10.1177/1093526620977738.
11. Amin MB, Greene FL, Edge SB, et al. The Eighth Edition AJCC Cancer Staging Manual: continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. *CA A Cancer J Clin*. 2017 Mar;67(2):93–99. https://doi:10.3322/caac.21388.
12. Chien TM, Li CC, Li WM, et al. Significant prognosticators of upper tract urothelial carcinoma. *Urological Sci*. 2015;26(4):230–234. https://doi:10.1016/j.urols.2015.11.009.
13. Tai MC, Chung HJ, Wei TC, et al. Evaluation of peri-operative complications and outcomes of robot-assisted radical nephroureterectomy and bladder cuff excision in a tertiary center. *Urological Sci*. 2017;29(1):38–42. https://doi:10.1016/j.urols.2017.07.007.
14. Su CC, Liu CL, Lin CN, Lee YH, Shen KH. A rare, highly aggressive primitive neuroectodermal tumor of the kidney: case report and literature review. *Urological Sci*. 2012;23(2):58–60. https://doi:10.1016/j.urols.2012.03.001.