International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 11, November 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.11.2024.25

REVIEW ARTICLE

Primary Renal Ewing's Sarcoma In Adults, Series Of Three Cases And Systematic Review Of Literature

[1]Arshi Beg, [2]Mujahid Ahmad Mir, [3]Qurat Ul Ein, [4]Anuj Kumar Yadav

[1]Oncopathology Paras Central Lab Gurugram, India
[2,4]Urology Park Advanced Speciality Hospital Sector 47, Gurugram, India
[3]Department of Human Genetics, Guru Nanak Dev University, Amritsar, Punjab, India

Corresponding author
Mujahid Ahmad Mir
Urology Park Advanced Speciality Hospital Sector 47, Gurugram, India
Email: mujahidmir414@gmail.com

Received Date: 16 September, 2024 Accepted Date: 19 October, 2024

ABSTRACT

Background: Primary renal Ewing's sarcoma (EWS) is unusual in adults. Diagnosis is usually made on histopathological examinationation supported by immunohistochemistry. We aimed to review the clinical and histopathological data of patients with renal EWS and review the available literature. **Methods:** we reviewed our database from January 2015 to june 2024 to include all the cases of primary EWS of the kidney. Later on we performed systematic literature review to identify all the relevant series on renal EWS. **Results:** A total of three patients including two men and one woman were managed during the above mentioned period. Out of these two patients had venous tumour thrombus and none had metastasis at diagnosis. All patients underwent elective radical nephrectomy, two patients received adjuvant chemotherapy while none was subjected to radiotherapy (RT). On Immunohistochemistry (IHC), CD99 and NKX2.2 were positive in all the patients. All patients are alive without disease at a follow up ranging from 6 months to 25 months. In our review 17 studies were included, 29.88% of the patients had metastatic disease and 15.6 % had locally advanced disease at diagnosis. Average overall survival was 33.5 months. CD99 and FLI1 were positive in 95.6% and 85.7%, respectively. **Conclusion:** Primary renal EWS remains a pathological diagnosis and IHC has an important place in its diagnosis. Locally advanced and metastatic disease is common at diagnosis leading to overall poor survival.

Keywords: Ewing's sarcoma, renal tumour, immunohistochemistry, radical nephrectomy, multimodal treatment

INTRODUCTION

Ewing's Sarcoma (EWS) of the kidney is a rare and aggressive malignancy that originates from the neuroectoderm, accounting for only 1% of sarcomas[1]. The incidence of primary renal EWS is highest in children and young adults, with a median age of diagnosis of 15-20 years[2]. This tumour is characterized by its unique histological features, including a proliferation of uniformly small round cells with inconspicuous nucleoli and scant clear to pale cytoplasm, and a sheet-like growth pattern[3]. The pathogenesis of EWS is still unclear, but it is thought to be related to chromosomal translocation of EWSR1[4,5]. The EWSR1-FLI1 fusion protein has been shown to activate the expression of genes involved in cell proliferation and survival, while inhibiting the expression of genes involved in cell differentiation and apoptosis. This leads to uncontrolled cell growth and resistance to apoptosis, contributing to the development of EWS. Additionally, the EWSR1-FLI1 fusion protein has been shown to inhibit the expression of genes involved in DNA repair, leading to genetic instability and further contributing to the development of EWS. Recent studies have identified several molecular subtypes of EWS, including the EWSR1-FLI1 fusion protein subtype, which is the most common subtype. Other subtypes include the EWSR1-ERG fusion protein subtype and the EWSR1-ETV1 fusion protein subtype. These molecular subtypes have been shown to have different clinical and pathological features, and may require different treatment approaches.

The clinical presentation of renal EWS can be non-specific, and may include abdominal pain, hematuria, weight loss, fatigue, and fever. A palpable mass may also be present in the abdomen. The symptoms of renal EWS can be similar to those of other renal tumours, making diagnosis challenging[6]. The differential diagnosis of renal EWS includes other tumours that can present with similar symptoms, such

DOI: 10.69605/ijlbpr_13.11.2024.25

as renal cell carcinoma, Wilms tumour, rhabdoid tumour, and neuroblastoma. These tumours can be distinguished from renal EWS based on their histological features and molecular characteristics. The diagnosis of EWS of the kidney is often challenging due to its rarity and the lack of specific clinical and radiological features. Imaging studies, such as computed tomography (CT) and magnetic resonance imaging (MRI) may show a renal mass with heterogeneous enhancement, but these findings are non-specific and can be seen in other renal tumours[7,8]. Therefore, a biopsy is often necessary to establish a definitive diagnosis. The diagnosis is confirmed by molecular genetic studies, such as fluorescence in situ hybridization (FISH), reverse transcription polymerase chain reaction (RT-PCR), and next-generation sequencing (NGS)[9,10,11,12].

The current management of renal EWS includes surgical resection and/or radiotherapy, and adjuvant chemotherapy[13]. Systemic treatment is usually composed of multiagent chemotherapy cycles of vincristine, doxorubicin, and cyclophosphamide (VDC) alternating with cycles of ifosfamide and etoposide (IE)[14]. In some cases, patients may require additional treatment, such as radiation therapy to control local disease, targeted therapy to inhibit specific molecular pathways involved in the development and progression of EWS, and immunotherapy to stimulate the immune system to attack cancer cells. In recent years, there has been growing interest in the development of targeted therapies for EWS, including inhibitors of the erythroblast transformation specific (ETS) family of transcription factors, inhibitors of the PI3K/AKT signaling pathway, inhibitors of the MAPK signaling pathway, and other molecular targets[15]. These therapies aim to target specific molecular pathways involved in the development and progression of EWS, providing a more effective and less toxic treatment option for patients.

In this study, we present our experience of primary renal EWS over the past nine years. Clinical and pathological data of all the patients diagnosed with renal EWS were reviewed in this study. We also present a systematic review and pooled analysis of the published studies on renal EWS. Our aim is to contribute to the existing knowledge on this rare and aggressive tumour, with the hope of improving diagnosis, treatment, and patient outcomes.

MATERIALS AND METHODS

we performed a retrospective search of our database from January 2015 to June 2024 to include all the cases of primary EWS of the kidney diagnosed during the above-mentioned period. We could retrieve only two more patients with same diagnosis in the above mentioned time period. Departmental review committee clearance (UROL- 75/2023) was obtained before starting this study. Clinical and pathological characteristics of all the patients were traced from hospital records. All patients were contacted telephonically and were called for follow-up visit. Slides and blocks were reviewed by a senior pathologist. Paraffin-embedded sections were examined for IHC staining.

Using search engines PubMed and embase with key words “Ewing's sarcoma,” OR “Ewing sarcoma” OR “Primitive neuroectodermal tumour” AND Kidney, relevant articles were searched. The Last systematic search was done on 05 June 2024. Filters applied were Human, English language and Adult 19+ years. Titles and abstracts of these articles were reviewed for inclusion and exclusion criteria. Case reports, review articles and case series with less than 3 patients (arbitrarily) were excluded while as studies presenting histopathological and clinical data exclusively on renal EWS tumours were included. We also searched the references of the articles selected for full review. Full text review was done for articles included in the study and data regarding various clinical and pathological parameters were extracted and tabulated.

Data were extracted by two reviewers (AB and MAM) from the studies included in final analysis on predefined templates. A pooled analysis of the clinical, pathological, treatment related data was performed. All the related data was entered into a personal computer on Microsoft excel sheet and analysed. While doing the pooled analysis, weighted average of the individual summary statistics was calculated.

RESULTS

Our case series

We retrieved the data of 3 patients of primary renal EWS who were managed at our centre during above mentioned period of time. Demographic, clinical, radiological and histopathological findings of our patients are summarised in table 1. The average age at diagnosis was 35.3 years ranging from 21 years to 52 years and gender ratio was 2:1 with male predominance. The average maximum tumour dimension was 10 cm (range 9 to 12 cm). Radiologically, the presentation is not distinguishable from other kidney tumours as depicted in ultrasound and computed tomography (CT) pictures **(Figure 1a, 1b, 1c)**. Two of our patients had right sided tumours involving mid pole and lower pole of the kidney with renal vein thrombus detected at evaluation. None of our patients had metastasis at diagnosis. All the patients underwent elective radical nephrectomy with uneventful postoperative course. Two of our patients received adjuvant chemotherapy in the form of 3 alternating cycles of VAC and IE (vincristine [V], Adriamycin [A], cyclophosphamide [C], ifosfamide [I], and etoposide [E]) However, patient 1 refused to receive chemotherapy postoperatively and is under close follow up. The range of follow up in our case series is 6 months to 25 months and all the three patients were living without disease at last follow up **(table 1).**

DOI: 10.69605/ijlbpr_13.11.2024.25

Histopathological and immunohistochemistry features

In patient 1**,** on gross examination, a friable tumour (9x7.5 cm) with variegated appearance was seen in the lower and mid pole of left kidney with capsular involvement (**Figure 2**). Histopathological examination showed diffuse sheets of monotonous small round cells. Pseudo-rosettes were seen, and focal necrosis was noted. Entrapped renal tubules were also observed (**Figure 3a, 3b**). The tumour cells showed diffuse membranous CD99 staining. The tumour cells were strongly and diffusely positive for NKX2.2, focally for desmin. However, CK, Myogenin, Myo-D1, WT1, and CD45 were negative. INI 1 was retained in the tumour cells. Diffuse CD99 and NKX2.2 confirmed the diagnosis of ES/PNET in all of our patients (**Figure 4a, 4b**). Rest of the results of IHC staining is presented in **Table 3.** Intra-operatively, lymph node sampling was done in all 3 patients and was positive in none. In view of diffuse NKX2.2 positivity and non-affordability, EWSR1 rearrangement by FISH was not done in any of our cases. The case series emphasizes that while the imaging characteristics are non-specific, immunohistochemistry is crucial for differential diagnosis due to the tumour's histological similarity to other renal round cell tumours.

Literature review

With the help of keywords and filters described matching our inclusion and exclusion criteria mentioned above our search from PubMed, and EMBASE yielded 17 studies[16-32] for final analysis. Data from all these 17 studies was extracted and tabulated in pre-defined format. All the studies included in the final analysis were retrospective studies reporting outcomes in more than 3 patients.

Average age was 30.8 years with gender ratio askew towards males. Overall, pain in abdomen was the most common presenting feature (59%) followed by blood in urine (36.5%) and palpable swelling (32%). Patients having metastasis at diagnosis were 29.88% and 15.6% of patients had locally advanced disease. Tumour venous thrombus was seen in 41.9% of the patients. Mean tumour size was 12.6 cm **(Table 2)**. Local disease control was obtained through radical nephrectomy in 98.26% of the patients. Most of the patients received adjuvant chemotherapy and only few received neoadjuvant chemotherapy. Radiotherapy was used only in 13.57% of the patients. Average overall survival was 33.5 months **(Table 2).** CD99 and FLI1 were positive in 95.6% and 85.7%, respectively. FISH (fluorescence in situ hybridisation) for t (11; 22) (q24; q12) was positive in 89.5% of the patients. Immunohistochemical data are presented in **Table 3**.

Table 1: Demographic, clinical, radiological and histopathological findings of patients with Ewing sarcoma of kidney

PARAMETER		CASE 1	CASE 2	CASE 3
Age (years)		21	52	32
Gender		M	F	M
Presentation		Left Flank pain Nausea and emesis	Right flank pain Hematuria Palpable mass	Right flank pain
Radiology features	Size of tumour in centimetres	9.2	12	9
	Location of tumour	Mid and lower pole of the left kidney	Mid pole of right kidney	Lower pole of right kidney
	Tumour thrombus within renal vein/IVC	Absent	Present	Present
	Metastasis at the time of diagnosis	Nil	Nil	Nil
Treatment		Radical nephrectomy	Radical nephrectomy +CT (VAC+IE)	Radical nephrectomy + CT (VAC+IE)
Histopathological examination	Histomorphology	Diffuse sheets of monotonous small round cells. Pseudo-rosettes present; Focal necrosis seen; Entrapped renal tubules were observed	Sheets of uniform round cells with focal rosettes	Sheets of uniform round cells with wide areas of necrosis
	Extension of tumour	Confined to kidney; capsule involvement present; Adrenal free	Confined to kidney; capsule free; Adrenal free	Confined to kidney; capsule free; Adrenal free
	Lympho-vascular space invasion	Not evident	Not evident	Present

DOI: 10.69605/ijlbpr_13.11.2024.25

	Lymph node status	Free (0/3)	Free (0/4)	Free (0/2)
IHC data		CD99+ NKX2.2+, CK-, Myogenin-, Myo-D1-, NSE- WT1-, CD45-	CD99+; NKX2.2+, FLI1+ Myo-D1-, NSE- WT1-, CD45-	CD99+; NKX2.2+, FLI1+ Myo-D1-, NSE- WT1-, CD45-
Follow-up period (months)		6	13	25
Current status		LWOD	LWOD	LWOD

Abbreviations: CD, Cluster differentiation; FLI1, Friend leukaemia virus integration 1; NSE, neuron-specific enolase; WT1, Wilms tumour; LWOD, Live without disease.

TABLE 2.Clinical data derived from the systematic review

Study	Number of patient	Mean age (years)	M:F	Clinical presentation (n)	Mean Tumour size (cm)	Metastasis diagnosis	Locally advanced at diagnosis	Venous thrombus	Underwent radical nephrectomy	Chemotherapy	Radiotherapy	Overall survival (n)
Jimenez, USA: 2002 (16)	11	34	6:5	Flank pain (6),Mass (3),Hematuria(3)	11.8 (9)	1/8 LN	0/8	2/11	NA	8/8	3/8	21.6(8)
Thyavihally, India: 2008 (17)	16	29.2	NA	NA	NA	5/16 lungs (2),liver (1),lung and LN (1),LN only (1)	1/16	NA	13/16	16/16	9/16	44(16)
Karpate, india :2012 (18)	34	23.7	21:23	Flank pain (18),Mass (10),Hematuria(9)	12.5(22)	3/17	0/17	NA	NA	NA	NA	NA
zollner,Germany :2013 (19)	24	27.2	15:9	Flank pain (4),Mass (1),Hematuria(4)	11.3(19)	9/24	NA	7/16	NA	17/17	1/17	NA
Rowe, USA:2013 (20)	10	24.1	4:6	NA	NA	4/10	0/10	NA	9/10	NACT 7/10	NA	NA
Teegavarapu,USA :2014 (21)	6	35	4:2	Pain (5) Mass (2) Haematuria (2)	13.3	2/6	3/6	5/6	6/6	5/6	1/6	19(6)
Murugan,USA :2017 (22)	13	33.4	11;2	Flank pain (9),Mass (1),Hematuria(4)	12.1(12)	6/13	NA	5/13	9/13	13/13	0	36.5(13)
Huang China: 2013 (23)	23	31	13:10	Flank pain (10),Hematuria(8)	NA	2(LN)/23	NA	NA	21/23	NACT 5, adjuvant 14	1/23	35.2(18)
Seth,	8	30.	5:3	Pain (5)	12.	5/8(LN	3/8	NA	7/8	5/8	0/8	20(8

DOI: 10.69605/ijlbpr_13.11.2024.25

India :2016 (24)		7		Mass (8)	6	5)						)
Sun, China :2018 (25)	3	35.7	3:0	Flank pain (3),Mass (2)	14.1	1/3(BONE)	1/3	1/3	2/3	3/3	1/3	NA
Murat Sari, TURKEY:2020 (26)	7	29	6:1	Flank pain (5), fever (3),hematuria (1)	10.6	6/7 (lungs4 , RPLN 2)	NA	5/7	5/7	2/7	0/7	12.09(5)
Lei Liang,china :2020 (27)	12	38.3	5:7	Flank pain (3),Mass (4)	11.25(7)	2/7	1/17	3/7	6/7	5/7	1/7	10(7)
Gopal Sharma, India :2021 (28)	8	33.5	4:4	Pain (8/8) Mass (8/8) Haematuria (4/8)	NA	2/8(ln)	NA	4/8	8/8	6/8	2/8	42.6(6)
Xianwen Hu, china:2022 (29)	6	30.5	4:2	flank pain (6),Hematuria(1)	11.02	1/6 (LN (1) bone (1)	2/6	0/6	6/6	6/6	0/6	NA
Sanjiban PATRA, INDIA: 2022 (30)	4	28.7	3:1	Flank pain (3),Mass (2),Hematuria(1)	9.3	2/4(Lung,Bone)	0/4	2/4	4/4	NACT 2,adCT 2	0/4	19.5(3)
Ankit kumar Sharma, india:2022 (31)	3	29.3	2:1	Flank pain (1),Mass (1),Hematuria(1)	10.1	0/3	1/3	1/3	3/3	3/3	0/3	NA
Niramya J. Pathak, india:2024 (32)	8	26.5	7:1	Flank pain (6),Mass (2),Hematuria(1), incidental (1)	11.9	1/8	5/8	4/8	8/8	8/8	0/8	22.3(7)
Present study:2024	30.57	2:1	Pain (3) Mass (1) Hematuria (1)	10	0/3	0/3	0/3	3/3	1/3	0/3	NA	**Present study:2024**
pooled analysis	199	30.8		Pain (68/115)59 %Mass (37/115)32 %Haematuria (42/115)36.5%	12.6	52/174 (29.88 %)	17/109 (15.59%)	39/93 (41.93%)	113/115 (98.26 %)	128/150	19/140 (13.57 %)	35.5 (97)

DOI: 10.69605/ijlbpr_13.11.2024.25

TABLE 3. Immunohistological data of the patients included in systematic review

Study	CD 99	NKX2.2	FLI1	CD56	NSE	synaptophysin	chromogranin	s-100	WT-1	Vimentin	translocation t(11,22)(q24;q12)
Jimenez, USA: 2002 (16)	11/11	NA	5/8	NA	NA	NA	NA	NA	0/11	NA	NA
Thyavihally, India: 2008 (17)	16/16	NA	NA	NA	0/16	0/16	NA	0/16	NA	NA	5/5
Karpate, india :2012 (18)	32/34	NA	NA	NA	9/12	1/8	0/5	1/4	0/8	8/14	14/16
zollner,Germany :2013 (19)	20/20	NA	NA	NA	7/10	NA	NA	13/16	NA	12/13	10/12
Rowe, USA:2013 (20)	10/10	NA	NA	NA	NA	NA	NA	NA	NA	NA	7/7
Teegavarapu,USA :2014 (21)	6/6	NA	6/6	4/6	4/6	2/6	1/6	3/6	NA	5/6	6/6
Murugan, USA :2017 (22)	11/13	NA	NA	NA	NA	0/13	0/13	NA	0/13	0/13	8/10
Huang China: 2013 (23)	NA	NA	NA	NA	NA	NA	NA	NA	N	NA	NA
Seth, India :2016 (24)	21/23	NA	NA	3/7	6/6	5/13	NA	NA	NA	7/8	NA
Sun, China :2018 (25)	6/8	NA	NA	NA	6/8	NA	NA	NA	2/8	6/8	1/1
Murat Sari, TURKEY: 2020 (26)	3/3	NA	NA	NA	1/3	NA	NA	1/3	NA	2/3	NA
Lei Liang,china :2020 (27)	7/7	NA	NA	2/7	4	6/7	1/5	1/7	0/3	6/7	NA
Gopal Sharma, India :2021 (28)	12/12	NA	12/12	NA	NA	NA	NA	NA	NA	NA	NA
Xianwen Hu, china:2022 (29)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Sanjiban PATRA, INDIA:2022 (30)	4/4	4/4	4/4	NA	NA	1/4	1/4	NA	0/4	NA	NA
Ankit kumar Sharma,india:2022 (31)	3/3	NA	3/3	NA	NA	NA	NA	NA	NA	3/3	NA

DOI: 10.69605/ijlbpr_13.11.2024.25

Niramya J. Pathak, india:2024 (32)	8/8	NA	NA	NA	NA	NA	NA	5/8	NA	3/8	NA
Present study:2024	3/3	2/3	2/3	NA	NA	NA	NA	NA	NA	NA	NA
pooled analysis	173/181 (95.6%)	6/7 (85.71%)	32/36 (88.88%)	9/20(45%)	37/65 (56.92%)	15/67 (22.38%)	3/33 (9.09%)	24/60 (92.30%)	2/47 (4.25%)	52/83 (62.65%)	51/57 (89.47%)

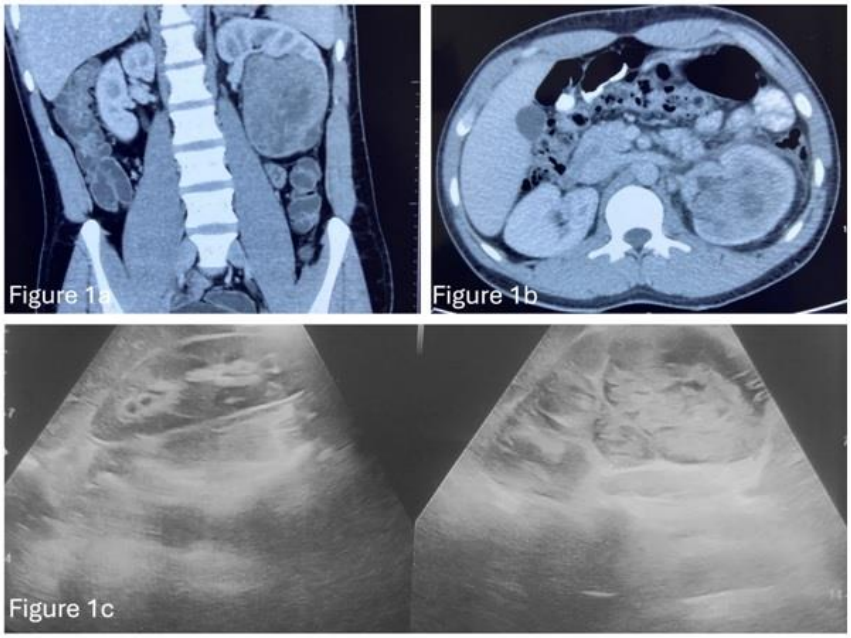

Figure 1a, 1b (CT Scan) and 1c (ultrasound): shows large solid heterogeneously enhancing mass in mid and lower pole of left kidney.

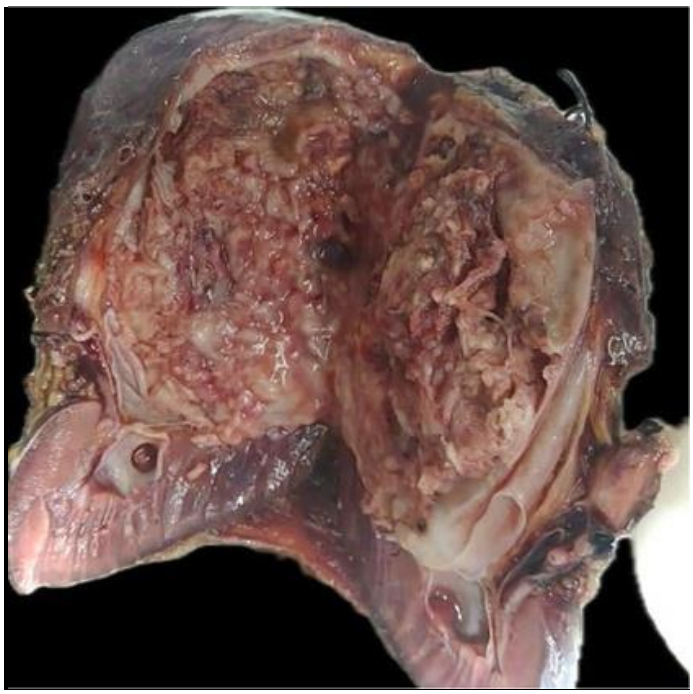

Figure 2: Radical nephrectomy specimen shows a variegated, grey brown tumour in the mid and lower pole with areas of necrosis and hemorrhage seen.

DOI: 10.69605/ijlbpr_13.11.2024.25

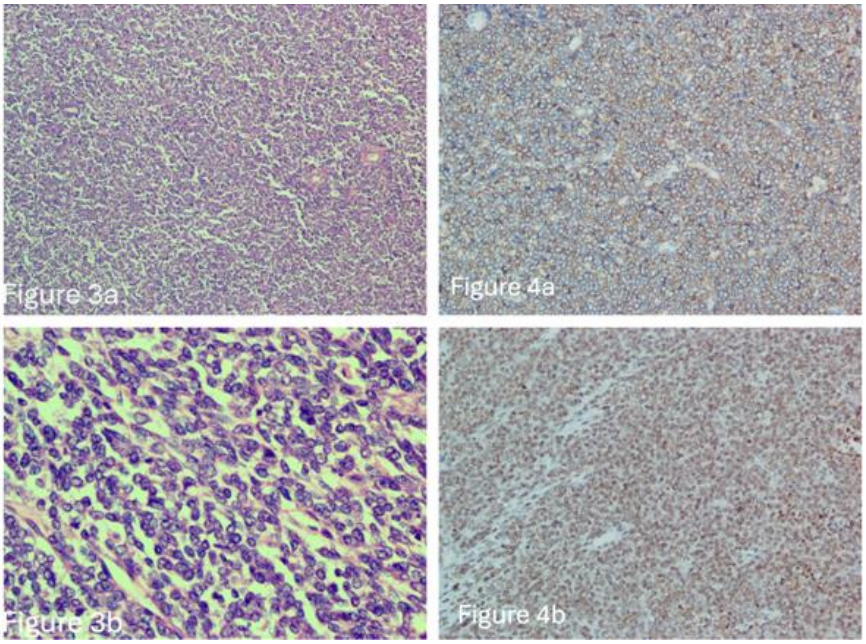

Figure 3a and 3b shows low and high power H&E images depicting diffuse sheets of monotonous round blue cells. Figure 4a show diffuse CD99 membraneous staining and Figure 4b shows diffuse nuclear positivity for NKX2.2.

DISCUSSION

First reported in 1975 by Seemayer et al[33]renal EWS is a rare and aggressive tumour, with approximately 200 cases documented in literature. Understanding the rarity of the disease and scarcity of data available, our study endeavours to recapitulate the available clinical and pathological data in the literature. In addition, we also provide our experience of three such patients.

In our case series, men were affected more frequently than women and Flank pain was the most common presentation. These findings are similar to our literature review. Patients in our study are older with mean age of 35 years as compared with systematic search result **(Table 2).**

Renal EWS is purely a "pathological diagnosis" as even with the best radiological investigations a definitive diagnosis is not possible. Irregular septa like structures, multifocal or diffuse haemorrhage and necrosis and weak enhancement on CT imaging were the characteristics described by Lee et al[34] to differentiate renal EWS from RCC. Histomorphological examination usually shows a large tumour mass with areas of necrosis and haemorrhage, classically depicting small blue round cells arranged in sheets or rosettes with high nucleocytoplasmic ratio, high mitotic index and hyperchromatic nuclei.

Renal Ewing's sarcoma stain positive for CD99[11]. CD45 and Friend leukaemia virus integration 1 (FLI1) help to set apart renal EWS and Wilms' tumour. In our series we performed IHC staining for NKX2.2 along with CD99, synaptophysin, NSE, S-100, FLI1, CD56, chromogranin and WT1 to help EWS differentiate from Wilms' tumour, rhabdomyosarcoma (RMS) and non-Hodgkin lymphoma (NHL) Although not definitive, diffuse and strong membraneous CD99 staining and NKX2.2 staining confirm the diagnosis of renal Ewing's sarcoma. CD99 and NKX2.2 were positive in all (3/3) patients in our series. In our review data synaptophysin, chromogranin and S100 were positive in 22.38%, 9.09% and 92.30% respectively. WT1 was positive only in 4.25% % of the patients **(Table 3).** Chromosomal translocation t (11; 22) (q24; q12) resulting in the fusion gene EWS/FLI1 is distinctive for EWS[35].The data from our review showed 89.47% positivity for this translocation **(Table 3)**

Owing to the rarity of primary renal Ewing's sarcoma, a standardized treatment protocol has not been established. A multimodality approach with debulking surgery (radical nephrectomy), chemotherapy with or without radiotherapy is followed for the treatment of renal EWS by most of the authors. The standard chemotherapy regimen includes a three-drug combination of vincristine, doxorubicin, and d-actinomycin, along with the addition of alternating cycles of etoposide and ifosfamide. Overall survival in our review was 35.5 months. Risi et al[35] reported an overall survival of 26.5 and 24 months in patients with metastatic disease supporting the excellent response to adjuvant chemotherapy. Adjuvant radiotherapy can be offered in case of incomplete resection, positive resection margins, or recurrence. Follow-up with laboratory and imaging tests are essential to assess recurrence and metastasis. Regular follow-up is crucial to detect any signs of recurrence or metastasis early, which can improve the chances of survival. Several other treatment options are being explored for patients with renal Ewing's sarcoma. Several targeted therapies have been shown to be

DOI: 10.69605/ijlbpr_13.11.2024.25

effective in the treatment of renal Ewing's sarcoma, including inhibitors of the ETS family of transcription factors and inhibitors of the PI3K/AKT signaling pathway. Immunotherapy including checkpoint inhibitors and cancer vaccines may also being tried. Stem cell transplantation is also being explored as a treatment option for patients with renal EWS.

CONCLUSIONS

To conclude, primary renal EWS is a rare disease with a scarce statistics regarding its management. Principally, renal EWS is a pathological diagnosis with IHC being pivotal in its diagnosis. Early diagnosis with complete resection and adjuvant chemotherapy may improve the overall survival. The available literature favours multimodality treatment including radical resection of primary tumour with chemotherapy in the adjuvant or neoadjuvant setting as the preferred management approach for primary renal EWS patients.

REFERENCES

1. Asiri, M., Al-Sayyad, A., et al. Renal primitive neuroectodermal tumour in childhood: case report and review of literature. Canadian Urological Association Journal 2010; 4(6): E158-E160.
2. Ellinger J, Bastian PJ, Hauser S, Biermann K, Muller SC. Primitive neuroectodermal tumour: rare, highly aggressive differential diagnosis in urologic malignancies. Urology 2006;68(2):257-262.
3. Das, S., Aggarwal, G., Gupta, S., & Midha, D. Primary renal Ewing's sarcoma in an adult: an enigma. Innovations in Surgical Science 2021; 6(1): 2022- 22.
4. Ellinger, J., Bastian, P. J., Hauser, S., Biermann, K., & Müller, S. C. Primitive neuroectodermal tumour: rare, highly aggressive differential diagnosis in urologic malignancies Urology 2006; 68(2): 257-262.
5. Funahashi, Y., Hattori, R., Yamamoto, T., Mizutani, K., Yoshino, Y., Matsukawa, Y., Sassa, N., et al. Ewing's sarcoma/primitive neuroectodermal tumour of the kidney. Aktuelle Urologie 2009; 40(4): 247-249.
6. Hakky, T. S., Gonzalvo, A. A., & Lockhart, J. L. Primary Ewing sarcoma of the kidney: a symptomatic presentation and review of the literature. Therapeutic Advances in Urology 2013; 5(3): 153-159.
7. Bray, G., Nesbitt, A., Maré, A., Willis, T., & Tracey, C. Primary Ewing sarcoma of the kidney presenting as hematuria in a pregnant woman – A case report highlighting the diagnostic and therapeutic dilemmas of the condition in pregnancy. Urology Case Reports 2023; 46: 102308.
8. Ekram, T., Elsayes, K., Cohan, R., & Francis, I. Computed tomography and magnetic resonance features of renal Ewing sarcoma. Acta Radiologica 2008; 49(9): 1085-1090.
9. Karpate, A., Menon, S., Basak, R., Yuvaraja, T. B., Tongaonkar, H. B., & Desai, S. B. Ewing sarcoma/primitive neuroectodermal tumour of the kidney: clinicopathologic analysis of 34 cases. Annals of Diagnostic Pathology 2012; 16(4): 267-274.
10. Kang, S. H., Perle, M. A., Nonaka, D., Zhu, H., & Chan, W. Primary Ewing sarcoma/PNET of the kidney: fine needle aspiration, histology, and dual colour break apart FISH Assay. Diagnostic Cytopathology 2007; 35(6): 353-357.
11. Llombart-Bosch, A., & Navarro, S. Immunohistochemical detection of EWS and FLI-1 proteins in Ewing sarcoma and primitive neuroectodermal tumours: comparative analysis with CD99 (MIC-2) expression. Applied Immunohistochemistry & Molecular Morphology 2001; 9(3): 255-260.
12. Marley, E. F., Liapis, H., Humphrey, P. A., et al. Primitive neuroectodermal tumour of the kidney—another enigma: a pathologic, immunohistochemical, and molecular diagnostic study. American Journal of Surgical Pathology 1997; 21(3): 354-359.
13. Mukkunda, R., Venkitaraman, R., Thway, K., Min, T., Fisher, C., Horwich, A., & Judson, I. Primary adult renal Ewing's Sarcoma: a rare entity. Sarcoma 2009; 504654.
14. Parham, D. M., Roloson, G. J., Feely, M., Green, D. M., Bridge, J. A., Beckwith, J. B., et al. Primary malignant neuroepithelial tumours of the kidney: a clinicopathologic analysis of 146 adult and pediatric cases from the National Wilms' Tumour Study Group Pathology Center. American Journal of Surgical Pathology 2001; 25(1): 133-146
15. Strauss SJ, Berlanga P, McCabe MG. Emerging therapies in Ewing sarcoma. Curr Opin Oncol. 2024;36(4):297-304.
16. Jimenez RE, Folpe AL, Lapham RL, Ro JY, O'Shea PA, Weiss SW, Amin MB. Primary Ewing's sarcoma/primitive neuroectodermal tumour of the kidney: a clinicopathologic and immunohistochemical analysis of 11 cases. Am J Surg Pathol. 2002 ;26(3):320-7.
17. Thyavihally YB, Tongaonkar HB, Gupta S, et al. Primitive neuroectodermal tumour of the kidney: a single institute series of 16 patients. Urology. 2008;71:292-296.
18. Karpate A, Menon S, Basak R, Yuvaraja TB, Tongaonkar HB, Desai SB. Ewing sarcoma/primitive neuroectodermal tumour of the kidney: clinicopathologic analysis of 34 cases. Ann Diagn Pathol. 2012 ;16(4):267-74.
19. Zöllner SK, Amatruda JF, Bauer S, Collaud S, de Álava E, DuBois SG, Hardes J, Hartmann W, Kovar H, Metzler M, Shulman DS, Streitbürger A, Timmermann B, Toretsky JA, Uhlenbruch Y, Vieth V, Grünewald TGP, Dirksen U. Ewing Sarcoma-Diagnosis, Treatment, Clinical Challenges and Future Perspectives. J Clin Med. 2021 14;10(8):1685.
20. 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 tumours. Urology 2013;81(2):347-353.
21. Teegavarapu PS, Rao P, Matrana MR, et al. Outcomes of adults with Ewing Sarcoma Family of Tumours (ESFT) of the kidney: a singleinstitution experience. Am J Clin Oncol. 2017;40:189-193.
22. Murugan P, Rao P, Tamboli P, Czerniak B, Guo CC. Primary Ewing Sarcoma / Primitive Neuroectodermal Tumour of the Kidney: a clinicopathologic study of 23 cases. Pathol Oncol Res. 2018;24:153-159.
23. Huang J, Zhang J, Dong B, et al. Primitive neuroectodermal tumour of the kidney: a single-institute series of six patients from China. Urol Int. 2013;90:174-178.

DOI: 10.69605/ijlbpr_13.11.2024.25

24. Seth A, Mahapatra SK, Nayak B, Saini AK, Biswas B. Primitive neuroectodermal tumours of kidney: Our experience in a tertiary care centre. Indian J Cancer 2016;53:109-112.
25. Sun Q, Miao B, Lao X, Yuan P, Cai J, Zhan H. Primitive neuroectodermal tumour of the kidney at the advanced stage: a case series of eight Chinese patients. Mol Clin Oncol 2018;8:743-748.
26. Sari M, Ekenel M, Ozluk M, Basaran M. Clinical and Pathological Features of Ewing Sacoma Family Tumours in Uro-oncology: A Single-Institute Experience. EJMI 2020; 4(2): 247-252.
27. Liang L, Song H, Ma B, Zhang Z, Zhu K, Li Q, Zhou C, Li A, Liu J, Zhang Q, Zhu S, Zhang Q. Renal Ewing's sarcoma/primitive neuroectodermal tumour (PNET): a case series of 7 patients and literature review. Transl Androl Urol 2021;10(2):548-554.
28. Sharma G, Kakkar N, Singh SK, Parmar K, Sharma AP , Mavuduru R. Primary primitive neuroectodermal tumour of the kidney in adults: Experience of managing 12 cases with systematic review and pooled analysis of literature. Int J Clin Pract 2021; 75: e14971.
29. Hu X, Li D, Cai J. Experience of CT diagnosis and management of primary renal Ewing's sarcoma: A retrospective analysis of 6 cases and a literature review. Medicine (Baltimore) 2022 ;101(49): e32189.
30. Patra, S., Trivedi, P. Primary Ewing sarcoma of the kidney: A series of four cases. Malays J Pathol 2022); 44(1): 93-9.
31. Sharma, A., Kuppurajan, N., Anandan, M. et al. Primitive neuroectodermal tumour of the kidney: an experience of three cases. Afr J Urol 2022; **28**: 37.
32. Pathak, Niramya J; Singh, Abhishek G; Surwase, Pavan J.; Agrawal, Sahil A.; Ganpule, Arvind P.; Sabnis, Ravindra B.; Desai, Mahesh R.. Primary Ewing sarcoma/primitive neuroectodermal tumours of the kidney: Case series of eight cases from a single center with follow-up details. Indian Journal of Urology2024; 40(3): 185-190.
33. Seemayer TA, Thelmo WL, Bolande RP, Wiglesworth FW. Peripheral neuroectodermal tumours. Perspect Pediatr Pathol 1975; 2:151-172.
34. Lee H, Cho JY, Kim SH, Jung DC, Kim JK, Choi HJ. Imaging findings of primitive neuroectodermal tumours of the kidney. J Comput Assist Tomogr 2009; 33:882-886.
35. Risi, E., Iacovelli, R., Altavilla, A., et al. Clinical and pathological features of primary neuroectodermal tumour/Ewing sarcoma of the kidney. Urology2013; 82(2): 382-386.