

Congenital Peripheral Primitive Neuroectodermal Tumor (pPNET)/Ewing's Sarcoma of the Upper Limb in a Neonate: A Rare Case Report

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ABSTRACT

Background: Ewing's sarcoma (EWS)/peripheral primitive neuroectodermal tumor (pPNET) is a rare, aggressive small-round-cell malignancy primarily of children and adolescents; congenital presentations are exceptional. We report a neonate with congenital pPNET of the arm.

Case presentation: A 24-day-old full-term female presented with a progressively enlarging left-arm swelling present since birth. Birth and maternal histories were unremarkable; no family history of genetic disease.

Clinical findings: Examination revealed a 6 × 6 cm soft, immobile posterolateral arm mass. Laboratory values were within normal limits.

Diagnostic assessment: Ultrasound showed a hypoechoic lobulated intermuscular lesion. MRI demonstrated a well-circumscribed T1 hypointense, T2/STIR hyperintense ovoid mass abutting but not invading adjacent structures. FNAC revealed sheets of small round blue cells. Excisional biopsy showed uniform small round cells; immunohistochemistry was CD99 and vimentin positive, desmin, myogenin, synaptophysin, S-100, EMA, and LCA negative. Cytogenetic/molecular testing was not performed due to resource constraints.

Therapeutic intervention: Radical surgical resection followed by four cycles of cisplatin and cyclophosphamide at 3-week intervals.

Follow-up and outcomes: Immediate postoperative imaging showed no metastasis; postoperative course was uneventful. Patient lost to follow-up after three months.

Conclusion: Congenital pPNET/EWS is extremely rare and aggressive. Diagnosis relies on histopathology and IHC when molecular tests are unavailable. Early recognition and multimodal therapy are critical, but prognosis in neonates remains guarded.

Keywords: Upper Extremity, Neuroectodermal tumor, Ewing Sarcoma, Newborn, Soft Tissue Neoplasms, Case Report

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INTRODUCTION

Ewing's sarcoma (EWS) and peripheral primitive neuroectodermal tumor (pPNET) are malignant small round cell neoplasms characterized on air dried smears by presence of malignant cells that are slightly larger than red blood cells, often forming cohesive sheets of uniform round cells.[1] The Ewing's sarcoma family of tumors include Ewing's sarcoma, peripheral primitive neuroectodermal tumor, neuroepithelioma, atypical Ewing's sarcoma and Askin's tumor.[2] It is more common in White individuals, especially of European descent, than Black and Asian populations.[3] Because of its resemblance to other small round cell tumors, it is important to differentiate it from other tumors of small round cell neoplasms, for which multimodal diagnostic approaches are needed. These tumors predominantly affect children and adolescents; occurrences in the neonatal period are exceedingly uncommon.[4] In our literature search, we found only 14 newborns diagnosed with congenital pPNET/EWS of soft tissue. The objective of presenting this case is that only one case of congenital pPNET/EWS arising in the upper limb of a neonate has been reported, by Shu-Guang Jin et al.[4]

CASE REPORT

A 24-day-old newborn female presented with a complaint of swelling in left arm since birth which was progressive in nature, in the Pediatric OPD. On history-taking, the patient's attendant confirmed that she was a full term, vaginal delivery with a swelling present on the left arm at the time of birth. The birth and maternal histories were uneventful and there was no family history of any genetic diseases. On examination, a soft, immobile swelling measuring 6X6 cm in the left arm was identified. An ultrasound showed a large hypoechoic lobulated lesion measuring 6X5 cm in intermuscular plane in posterolateral aspect of the left arm with thin internal septa; a probable diagnosis of soft tissue tumor was made on USG. On MRI, along the subcutaneous plane of left posterolateral arm a well circumscribed T1W hypo, T2W/STIR hyperintense mass lesion was seen. The le-

sion was ovoid in shape with peripheral capsule. Few thin internal septa were seen. The underlying bone and muscles were normal. Anteromedially, the mass abutted the brachial vessels; however, signal void was maintained. FNAC was performed and yielded blood-mixed aspirates, on microscopic examination smears were highly cellular, comprising small, round, monomorphic blue cells. These cells had a high nucleocytoplasmic ratio; nuclei were round to oval with finely dispersed chromatin and tiny, inconspicuous nucleoli. The cytoplasm was scant. The background was composed of RBCs. A cytological diagnosis of small round cell tumor was made. [Figure 1] Biopsy was advised for confirmation and further typing. Surgery was performed, and the tissue was sent for histopathological examination. Grossly, the cut surface was gray-white to tan with soft and fleshy consistency. Tissue was processed, and on microscopic examination, it showed uniform small round cells arranged in a sheet like growth pattern. These cells had high nucleocytoplasmic ratio; nuclei were round, with finely stippled chromatin, inconspicuous nucleoli and scanty cytoplasm. [Figure 2] On immunohistochemistry, tumor cells were CD 99-positive [Figure 3], vimentin-positive [Figure 4], desmin-, myogenin-, synaptophysin-, S-100, Epithelial membrane antigen- and leukocyte common antigen-negative. A diagnosis of pPNET/Ewing's sarcoma was made and molecular genetic assay was advised but ultimately omitted because it was unavailable at our institution and was financially prohibitive for this patient from a BPL background. After the diagnosis made based on histopathological examination along with immunohistochemistry, a radical surgical resection was performed which was followed by USG, MRI and CT scan; no evidence of metastasis was found. The postoperative course was uneventful. Due to infant's young age and organs immaturity, four courses of chemotherapy were started after 10 days of surgery in the oncology department with cisplatin and cyclophosphamide (once every 3 weeks). After 3 months, the patient was lost to follow-up and no further information or patient medical records were available. Table 1 is showing the patient chronological summary.

Table 1: Patient chronological summary

Time point	Clinical event/activity	Details/Findings
At birth	Baseline status	Patient born; left arm swelling
Pre-presentation/ initial	Clinical onset	Left arm swelling progressive in nature (since birth) and positive clinical findings (6×6 cm soft immobile posterolateral arm mass)
Diagnostic work up	Imaging and pathology	• First USG • First MRI • FNAC • Biopsy
Diagnosis	Histopathology and IHC	Confirmed histopathological and IHC diagnosis
Intervention	Radical surgery	Radical surgical resection performed
Post operative care	Restaging and treatment	• Post-op USG, MRI & CT-scan • Initiation of chemotherapy
After 3 months of follow up	Re-evaluation	• Follow up USG, MRI & CT-scan • Administration of adjuvant chemotherapy
Subsequent follow-up	Outcome status	Patient lost to follow up

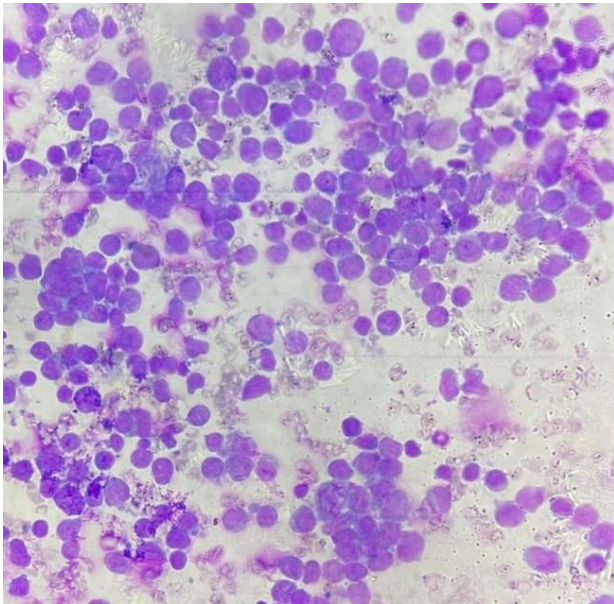


Figure 1: Giemsa-stained photomicrograph of small round cell tumor (400 X)

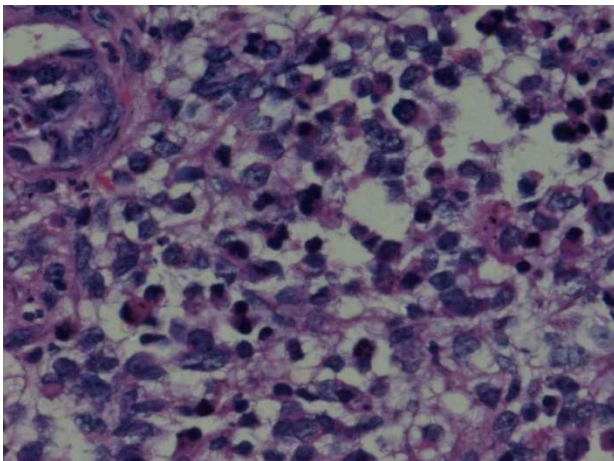


Figure 2: Hematoxylin and eosin-stained photomicrograph of pPNET/ Ewing's sarcoma showing uniform small round cells in sheet-like growth pattern with high N/C ratio (400 X)

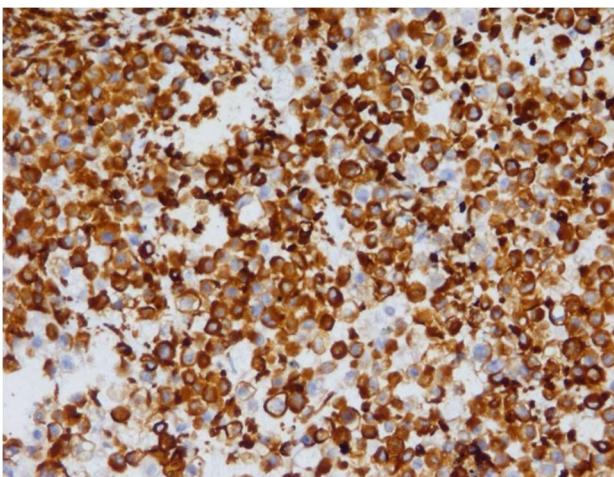


Figure 3: Diffuse membranous CD99 positivity in tumour cells (200X)

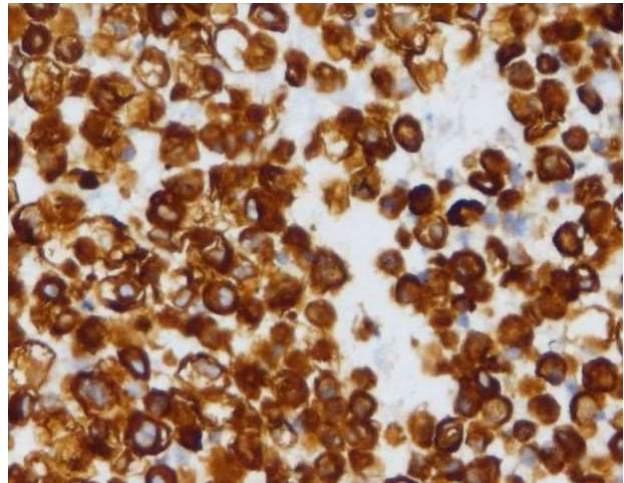


Figure 4: Diffuse cytoplasmic vimentin positivity in tumour cells (200X)

DISCUSSION

Peripheral PNET/Ewing sarcoma is an aggressive small-round-cell malignancy most commonly affecting children and adolescents and is only rarely present at birth.[5,6] Only 14 newborns with congenital EWS/pPNET of soft tissue have been reported in the literature. The estimated incidence of Ewing family tumors is low (approximately 0.1-0.4 cases per million), emphasizing the rarity of congenital presentations.[7,8] A study by Vasileva et al [9] suggested how a single-gene mutation alters embryonic cell-fate decisions to initiate devastating pediatric cancer, by using zebrafish genetic Ewing sarcoma model. In this study, evidence for a neural crest origin of this cancer was established. Neural crest-derived cells uniquely tolerate expression of EWSR1::FLI1, and targeted expression of EWSR1::FLI1 in these cells generates lethal Ewing sarcomas. Single-cell analysis of tumor initiation shows that EWSR1::FLI1 reprograms neural crest-derived cells to a mesoderm-like state, strikingly resulting in ectopic fins throughout the body. By profiling chromatin accessibility and genome-wide EWSR1::FLI1 binding, they find that the fusion oncogene hijacks developmental enhancers for neural crest to mesoderm reprogramming during cancer initiation. [9] The most commonly affected areas are the head, neck, trunk, upper and lower limbs. [10] The most common symptoms are a swollen mass, local pain and fever. Elevated ESR and leukocytes counts are also observed. Radiologic features are often nonspecific; therefore, definitive diagnosis relies on histopathology supported by immunohistochemistry and, where available, molecular confirmation of characteristic translocations. [11] Multimodal treatment - typically wide surgical excision combined with chemotherapy and, in selected cases, radiotherapy - represents the current standard of care for localized disease. [12] Standard Ewing sarcoma regimens (VDC/IE or VAIA protocol) are highly toxic for a neonate and are considered intolerable given the unique physiology of a neonate. Choosing cisplatin along with cyclophosphamide provided distinct clinical trade-off in

this case. [13] Dose reduction was done using Children's Oncology Group (COG) Infant Dosing Guidelines to protect the neonate from fatal systemic toxicity. Clinical management included, (1) Pharmacokinetic monitoring: Therapeutic drug monitoring (TDM) for cyclophosphamide metabolites to ensure clearance before administering subsequent doses. (2) Aggressive Supportive Care: Strict, continuous hydration protocols were ensured during cisplatin administration, and aggressive mesna uroprotection was employed for cyclophosphamide to protect the immature urinary tract. (3) Audiological Baseline: Cisplatin carries a high risk of ototoxicity, which can severely impact neurodevelopment; therefore, automated auditory brainstem response (AABR) was monitored closely between cycles.

Compared with other similar cases where some were managed with chemotherapy or radiotherapy alone, and others with surgery plus chemotherapy or radiotherapy, radical surgical resection followed by chemotherapy was performed in this case.

To date, only one newborn with congenital pPNET/Ewing's sarcoma of soft tissue in the arm has been reported by Shu-Guang Jin et al [4] in the literature. Reported neonatal outcomes vary, and prognosis is generally poor when presentation is congenital, highlighting the need for early recognition and aggressive management.

STRENGTH AND LIMITATIONS

This case is extremely rare and of clinical educational value. Multimodal diagnostic approach (FNAC, histopathology, IHC & radiology) for definitive diagnosis was followed & to differentiate it from other small round cell tumors.

First, molecular genetic testing was not performed to confirm the specific EWSR1 gene rearrangement, which limits definitive molecular confirmation of the diagnosis. Second, the patient was lost to follow-up at 3 months, and therefore, the long-term clinical outcome remains unknown, preventing a definitive assessment of treatment efficacy. Finally, as this was a single-case report, the findings cannot be generalized to the broader patient population, and causal inferences cannot be established.

CONCLUSION

Congenital pPNET/Ewing sarcoma is an uncommon and biologically aggressive tumor in neonates. When molecular diagnostics are unavailable, diagnosis depends on careful histopathological assessment and immunophenotyping. Prompt recognition and early multimodal therapy are essential, although neonatal cases often face a guarded prognosis.

Consent of participants: Information about the benefits and harm of the study, the usefulness of their participa-

tion, the confidentiality of the information and the right not to participate was given to the participant. A written informed consent was obtained from the patient's guardian for publication of this case report and accompanying images. All the procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation and with the Helsinki Declaration of 1975, revised in 2008.

Individual Author's Contribution: BS and RKS contributed to conceptualization, methodology, investigation, data curation, analysis, supervision, and writing - original draft and review & editing. Both authors read and approved the final manuscript and confirm that it represents their original work.

Declaration of Non-use of generative AI Tools: This article was prepared without the use of generative AI tools for content creation, analysis, or data generation. All findings and interpretations are based solely on the authors' independent work and expertise.

REFERENCES

- Kocjan G. Diagnostic dilemmas in FNAC cytology: small round cell tumors. In: Kocjan G, editor. Fine needle aspiration cytology: diagnostic principles and dilemmas. Berlin: Springer-Verlag; 2006. p.133-4.
- Okpokowuruk FS, Oloyede I. Congenital Ewing's Sarcoma in a neonate in Uyo - a case report. Pan Afr Med J. 2013;15:90. DOI: <https://doi.org/10.11604/pamj.2013.15.90.2219> PMID:24198886 PMCID:PMC3810286
- Jawad MU, Cheung MC, Min ES, Schneiderbauer MM, Koniaris LG, Scully SP. Ewing sarcoma demonstrates racial disparities in incidence-related and sex-related differences in outcome: an analysis of 1631 cases from the SEER database, 1973-2005. Cancer. 2009 Aug 1;115(15):3526-3536. DOI: <https://doi.org/10.1002/cncr.24388> PMID:19548262
- Jin SG, Jiang XP, Zhong L. Congenital Ewing's Sarcoma/Peripheral Primitive Neuroectodermal Tumor: A Case Report and Review of the Literature. Pediatr Neonatol. 2016 Oct;57(5):436-439. DOI: <https://doi.org/10.1016/j.pedneo.2013.11.002> PMID:24480101
- Teicher BA, Bagley RG, Rouleau C, Kruger A, Ren Y, Kurtzberg L. Characteristics of human Ewing/PNET sarcoma models. Ann Saudi Med. 2011;31(2):174-182. DOI: <https://doi.org/10.4103/0256-4947.78206> PMID:21422656 PMCID:PMC3102479
- Ewing J. Classics in oncology. Diffuse endothelioma of bone. James Ewing. Proceedings of the New York Pathological society, 1921. CA Cancer J Clin. 1972; 22(2):95-98. DOI: <https://doi.org/10.3322/canjclin.22.2.95> PMID:4622125
- Shrateh ON, Jobran AW, Owienah H, Sweileh T, Abulihya M, Natsheh MA, et al. Primary extraskelatal Ewing sarcoma of the foot with extensive skeletal and pulmonary metastasis: a rare case report. Ann Med Surg (Lond). 2022;82:104752. DOI: <https://doi.org/10.1016/j.amsu.2022.104752> PMID:36268294 PMCID:PMC9577863
- Abboud A, Masrouha K, Saliba M, Haidar R, Saab R, Khoury N, et al. Extraskelatal Ewing sarcoma: diagnosis, management and prognosis. Oncol Lett. 2021;21(5):354. DOI: <https://doi.org/10.3892/ol.2021.12615> PMID:33747211 PMCID:PMC7967932
- Vasileva E, Arata C, Luo Y, Burgos R, Crump JG, Amatruda JF. Origin of Ewing sarcoma by embryonic reprogramming of neural

- crest to mesoderm. *Cell Rep.* 2025 Oct 28;44(10):116376. DOI: <https://doi.org/10.1016/j.celrep.2025.116376> PMID:41072418
10. WHO Classification of Tumours Editorial Board. Soft tissue and bone tumours. 5th ed. Lyon (France): International Agency for Research on Cancer; 2020. (World Health Organization classification of tumours, volume 3).
 11. Vural C, Uluoglu O, Akyurek N, Oguz A, Karadeniz C. The evaluation of CD99 immunoreactivity and EWS/FLI1 translocation by fluorescence in situ hybridization in central PNETs and Ewing's sarcoma family of tumors. *Pathol Oncol Res.* 2011;17(3):619-625. DOI: <https://doi.org/10.1007/s12253-010-9358-3> PMID:21267687
 12. Marec-Bérard P, Chotel F, Claude L. PNET/Ewing tumours: current treatments and future perspectives. *Bull Cancer.* 2010 Jun;97(6):707-713. DOI: <https://doi.org/10.1684/bdc.2010.1120> PMID: 20497910
 13. Veal GJ, Errington J, Sastry J, Chisholm J, Brock P, Morgenstern D, et al. Adaptive dosing of anticancer drugs in neonates: facilitating evidence-based dosing regimens. *Cancer Chemother Pharmacol.* 2016 Apr;77(4):685-692. DOI: <https://doi.org/10.1007/s00280-016-2975-0> PMID:26875154 PMCID:PMC4819938