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Case Series

Unusual Clinical Presentations and Diagnostic Challenges of Pediatric Ewing's Sarcoma: A Case Series from a Tertiary Oncology Center

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Abstract

We present a case series of three pediatric patients diagnosed with Ewing's sarcoma at distinct anatomical sites—the scalp with intracranial extension, the forearm involving bone, and the lumbar region with metastatic spread. Each patient underwent a detailed clinical assessment, radiological imaging, histopathology, and immunohistochemistry for diagnosis. Treatment comprised a multidisciplinary approach including surgical resection, chemotherapy, and radiotherapy. Our findings highlight the diverse clinical manifestations, diagnostic challenges, and the critical role of early detection and individualized treatment strategies in optimizing outcomes for Ewing's sarcoma patients.

Keywords: Ewing's sarcoma, pediatric bone tumor, intracranial extension, metastasis, histopathology, immunohistochemistry, case series.

Introduction

Ewing's sarcoma, first described by James Ewing in 1921, is an aggressive bone and surrounding soft tissue malignancy predominantly affecting children and young adults.[1] It is the second most prevalent pediatric bone cancer, after osteosarcoma, with a survival rate of about 30-40%, depending on the metastatic status and tumor location at diagnosis.[2] Although the precise cellular origin of Ewing's Sarcoma is still unclear, it is generally believed to arise from mesenchymal or progenitor stem cells.[3]

Ewing's sarcoma is the second most common primary bone tumor in pediatric cancer patients and accounts for approximately 4% of pediatric malignancies.[4] The most commonly affected bones are the long bones of the extremities and pelvis, while the vertebrae are affected in < 5% of cases. Patients often present with non-specific symptoms, such as muscle aches, low back pain, and vague paresthesia, leading to diagnostic and treatment delays. Neurological symptoms can develop as a result of spinal cord compression in advanced cases.[5] Early identification and a multimodal treatment strategy including chemotherapy, radiotherapy, and surgery are essential for favorable survival outcomes.[6]

Diagnosing Ewing's Sarcoma remains challenging because of its overlapping histological features with other small round cell tumors. Histopathology usually shows small, round, blue cells with CD-99 antigen expression.[7,8] However, CD-99 is not exclusive to Ewing's sarcoma, as it is also expressed in other primitive neuroectodermal tumors. Imaging modalities such as MRI and CT help to assess lesion extent but are not diagnostic. Delayed symptom onset often results into late recognition of the disease.[9] This case series indicates the diagnostic challenges and the importance of a comprehensive treatment approach.

Methodology

This case series includes three pediatric patients diagnosed with Ewing's sarcoma at the Department of Pediatric Oncology, The Children's Hospital, Pakistan Institute of Medical Sciences (PIMS), Islamabad, who presented in May 2024, August 2024, and November 2024, respectively. Patients presented to us with progressively enlarging swellings in various anatomical locations. Each underwent detailed clinical assessment, radiological imaging, histopathological evaluation, and immunohistochemistry to confirm the diagnosis of Ewing's sarcoma. All three cases were presented at the Punjab Tumor Board Meeting held at the Agha Khan University Karachi, where individualized treatment strategies were formulated. Additional imaging studies included computed tomography (CT) scans and bone marrow biopsies. Surgical resection was undertaken in two cases, while the third patient was advised for surgery. This case series study follows the Preferred Reporting of Case Series in Surgery (PROCESS) 2023 criteria, ensuring adherence to methodological and ethical standards and guidelines.

Case Presentation

Case-I: Scalp Swelling with Intracranial Extension

An 11-year-old boy presented with a three-month history of a progressively enlarging scalp swelling, accompanied by low-grade fever and clinical pallor. MRI revealed an aggressive lesion in the occipital region with both extracranial and intracranial extension, causing compression of the cerebellum. Histopathological examination and immunohistochemistry confirmed the diagnosis of Ewing's sarcoma, with tumor cells showing strong positivity for CD-99, synaptophysin, and P-53. The case was reviewed in a multidisciplinary Punjab Tumor Board meeting, where a consensus-based treatment plan was formulated (Figure 1).

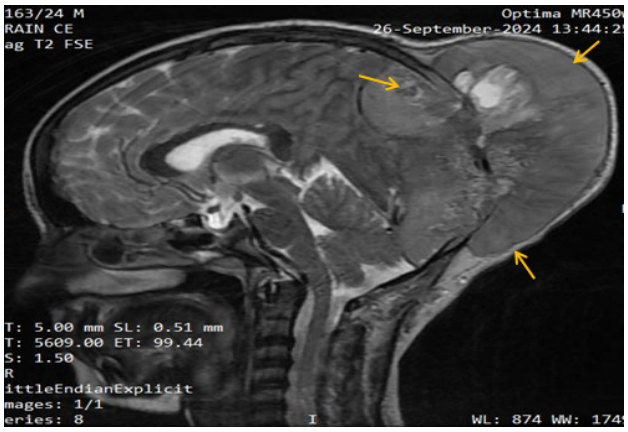

Figure 1: MRI of the brain shows an abnormal signal intensity mass lesion centered over the occipital region, producing a significant bulge in the overlying skin. The lesion causes erosion of the underlying occipital bone with intracranial extension into the posterior parietal and occipital regions, exerting extrinsic compression on the superior surface of the cerebellum.

Case-II: Forearm Swelling with Bone Involvement

A 10-year-old girl presented with a progressively enlarging swelling over the right forearm, developing gradually over the course of one year. MRI revealed a large, heterogeneously enhancing lesion involving the mid-shaft of the radius, with evidence of necrosis and surrounding soft tissue infiltration. Histopathological examination demonstrated sheets of small round blue cells, and immunohistochemistry was positive for NKX2.2, CD99, and focal synaptophysin, consistent with a diagnosis of Ewing's sarcoma. Surgical resection was carried out, involving removal of the proximal two-thirds of the radius. The estimated histologic treatment response was approximately 50%. The patient was subsequently scheduled to receive radiotherapy for local disease control (Figure 2).

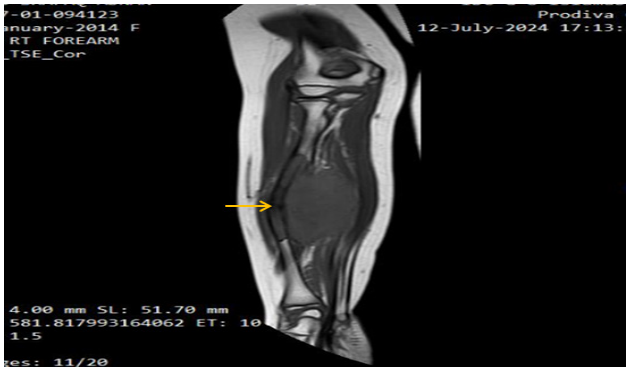

Figure 2: MRI of the right forearm showing a large, heterogeneously enhancing lesion with inner necrosis in the anteromedial cortex of the mid-shaft radius, bowing deformity, and a large soft tissue component

Case-III: Lumbar Swelling with Hematuria

A 3-year-old boy presented with a one-month history of a left-sided lumbar swelling, accompanied by an episode of hematuria. Imaging studies revealed a large, heterogeneous mass arising from the left kidney and extending across the midline. Histopathological examination showed a population of round to spindle-shaped tumor cells with pleomorphic nuclei. Immunohistochemical analysis confirmed the diagnosis of a BCOR-mutated Ewing-like sarcoma. Surgical excision revealed a well-defined, lobulated mass with tumor-free margins. The pathological assessment indicated a complete treatment response, with 100% tumor necrosis (Figure 3).

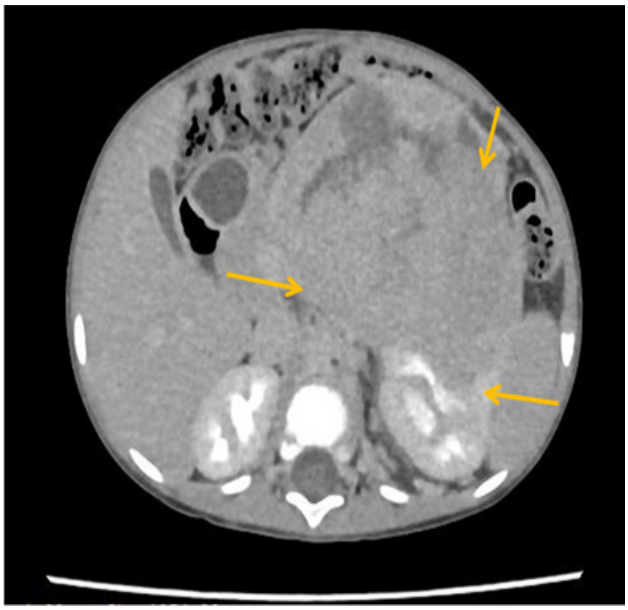

Figure 3: MRI of the abdomen reveals a large, heterogeneously enhancing mass measuring 9 × 7 × 8 cm arising from the left kidney. The mass contains necrotic areas and extends across the midline.

Discussion

Ewing's sarcoma poses a significant challenge in pediatric oncology due to its aggressive nature, diverse clinical presentations, and diagnostic complexity.[10] This case series highlights the distinct anatomical manifestations of Ewing's sarcoma and emphasizes the necessity for increased clinical suspicion, especially when faced with atypical or persistent symptoms in children and adolescents. Standard multimodal treatment protocols comprising chemotherapy, surgery, and radiotherapy were employed across all three cases; however, the varied tumor responses and progression patterns exposed the limitations of a uniform treatment strategy. Diagnosis in each case required the integration of histology, immunohistochemistry, and advanced molecular diagnostic tools, which remain inconsistently accessible in many regions of Pakistan. While CD99 is widely used as an initial marker, the growing utility of newer markers such as NKX2.2 and BCOR gene mutations[11] as reported in our third case, reflects a shift towards more precise, molecularly guided diagnosis and management.

This case series offers valuable insights into the multifaceted challenges of diagnosing and managing Ewing's sarcoma in low- and middle-income countries (LMICs) like Pakistan.

The first case's intracranial extension was exceedingly rare and difficult to diagnose due to its non-specific symptoms and the need for early neuroimaging. This observation aligns with findings from Altaf et al. (2023), who reported that late-stage cranial Ewing's sarcoma is mostly misdiagnosed due to limited awareness and access to neuroimaging. Both cases were marked by delayed neuroimaging, low clinical suspicion at the primary care level, and limited access to specialized services, resulting in diagnosis and treatment delays.[12] Similarly, Ahmed et al. (2019) examined that in peripheral hospitals across Pakistan, initial symptoms such as persistent headaches or localized swelling are often misattributed to benign causes, further delaying oncologic evaluation.[13]

In the second case, involving the forearm, surgical decisions were guided by the need to preserve limb function while ensuring oncologic control. Early multidisciplinary collaboration enabled limb-sparing surgery an outcome supported by Shah et al. (2019), who emphasize the importance of tumor board discussions and preoperative chemotherapy as key factors in achieving limb preservation.[14] Consistent with findings by Raza et al. (2021) at Aga Khan University Hospital, late-stage presentations frequently limit options for limb-sparing procedures, often necessitating amputation.[15] However, in our case, the successful preservation of the limb was significantly influenced by the early involvement of a multidisciplinary team and access to musculoskeletal imaging highlighting that timely collaboration can improve outcomes even in resource-limited settings.

The third case involved a renal Ewing-like sarcoma—an uncommon entity often misdiagnosed without molecular confirmation. Qureshi et al. (2019) and Ali et al. (2020) similarly reported primary renal and adrenal Ewing-like sarcomas in Karachi and Quetta, respectively—both presenting with vague abdominal symptoms and requiring comprehensive diagnostic workups.[16,17] Our case highlights the diagnostic ambiguity surrounding Ewing-like variants and underscores the critical role of molecular testing, including BCOR mutation analysis, in distinguishing them from classical forms. As Kamal et al. (2022) noted, BCOR-altered sarcomas may exhibit distinct responses to conventional chemotherapy and could require alternative or intensified treatment protocols.[18]

Across all three cases, delayed presentation emerged as a consistent challenge, echoing findings by Khan et al. (2020) and Farooq et al. (2017), who reported that over 60% of pediatric sarcomas in Lahore and Multan were diagnosed at advanced stages (III or IV).[19, 20] Contributing factors included poor health-seeking behavior, misdiagnosis at the primary care level, and inadequate access to neuroimaging and biopsy services in peripheral hospitals. To enhance early detection, awareness campaigns targeting primary healthcare providers, coupled with structured diagnostic algorithms for persistent pain or masses, are essential. Moreover, facilitating timely referrals to specialized oncology centers equipped with diagnostic imaging and multidisciplinary teams must become a policy priority.

This case series highlights the pivotal role of multidisciplinary collaboration and access to advanced diagnostics in the management of pediatric Ewing's sarcoma. The involvement of the Punjab Tumor Board was instrumental in recommending individualized treatment strategies for each patient, integrating the expertise of oncologists, radiologists, surgeons, and pathologists. As these cases illustrate, a coordinated, patient-centered approach can help overcome systemic limitations and improve survival outcomes. Moving forward, investment in regional diagnostic infrastructure particularly molecular pathology laboratories and institutionalizing multidisciplinary tumor boards nationwide could significantly increase the standard of care for pediatric sarcoma patients in Pakistan.

Conclusion

Ewing's sarcoma remains a challenging malignancy due to its various clinical presentations, diagnostic complexity, and aggressive nature of a disease. A detailed and comprehensive examination using histology, imaging, and molecular markers is essential. The findings emphasized for enhanced diagnostic access, multidisciplinary care, and, clinician awareness especially in resource-limited healthcare settings. Provision of imaging capabilities (e.g., PET scans, whole-body MRI) could improve staging and treatment planning in low income countries like Pakistan.

Authors' Contributions

RM led the manuscript drafting and literature review and contributed to case presentation development and analysis of diagnostic challenges. JJ assisted in assembling imaging data. NY reviewed, revised, and approved the final manuscript.

Conflict of Interest: The authors have no conflicts of interest.

Footnote: An informed consent was taken from the patients for the purpose of these case reports, without revealing their identity.

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