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Case Report

Aggressive Ewing Sarcoma of the Mandible in a Child: A Case Report

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ABSTRACT

Ewing sarcoma is a highly aggressive malignant bone tumor which most commonly arises in the long bones and pelvis of adolescents and young adults. Craniofacial involvement, particularly of the mandible, is extremely rare and may mimic odontogenic or inflammatory lesions, leading to diagnostic delay. We report the case of a 14-year-old girl with histologically confirmed Ewing sarcoma of the left mandible. Clinical and initial radiological findings suggested an aggressive mandibular lesion with locoregional extension. For comprehensive baseline evaluation, an ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) was performed. It demonstrated intense metabolic activity of the mandibular mass, consistent with high tumor aggressiveness, while excluding cervical, thoracic, abdominal, and skeletal metastases. This case underlines the crucial role of ^{18}F-FDG PET/CT not only in the initial staging of Ewing sarcoma but also in the differential diagnosis of atypical mandibular swellings in children and adolescents. By combining functional and anatomical data, PET/CT improves diagnostic confidence, guides therapeutic planning, and contributes to prognostic assessment in such uncommon presentations.

Keywords: Ewing sarcoma, mandible, child, FDG PET/CT

Introduction

Ewing sarcoma is a primary malignant bone neoplasm of uncertain origin which was first described by James Ewing in 1921 (1). It is a highly aggressive, small round blue cell tumor which typically arises from bone and, less frequently, from soft tissues (2). It represents approximately 10-15% of all primary bone malignancies in children and adolescents (3). The tumor most often involves the pelvis, femur, tibia, or humerus. Craniofacial localization is rare, accounting for only 1-4% of cases (4). Within the craniofacial skeleton, mandibular involvement is particularly uncommon, representing approximately 0.7% of all Ewing sarcoma sites (5), and it may easily be mistaken for odontogenic or inflammatory conditions. Such non-specific presentations

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often result in delayed diagnosis, which can adversely affect prognosis. Comprehensive and early imaging is therefore essential to establish the extent of the disease and guide multidisciplinary management, which usually combines neoadjuvant chemotherapy, surgery, and/or radiotherapy. In this context, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has emerged as a valuable diagnostic tool. In addition to its high sensitivity for detecting metabolically active lesions, it provides a whole-body overview which is crucial for differential diagnosis, initial staging, restaging, and response assessment. We report the case of a 14-year-old girl with mandibular Ewing sarcoma, an exceptionally rare presentation. This case underscores the importance of including Ewing sarcoma in the differential diagnosis of mandibular swellings in adolescents and highlights the pivotal role of ^{18}F-FDG PET/CT in both the diagnostic work-up and staging process. The aim of this report was to illustrate the diagnostic challenges posed by mandibular Ewing sarcoma and to emphasize the contribution of ^{18}F-FDG PET/CT in the staging and management of this rare localization.

Case Report

A 14-year-old girl presented with progressive swelling and pain localized on the left side of her face, which had been evolving over the prior few weeks. Clinical examination revealed a firm, tender mass in the left mandibular region. There were no signs of cervical lymphadenopathy, fever, weight loss, or other systemic symptoms. An initial contrast-enhanced CT scan revealed a large, destructive lesion of the left mandible associated with soft tissue invasion. Incidentally, a solitary 8 mm pulmonary nodule was also identified in the right upper lobe, raising concerns of possible metastatic spread. Histopathological analysis of a biopsy taken from the mandibular mass confirmed the diagnosis of Ewing sarcoma. Microscopically, the tumor consisted of small round blue cells with scant cytoplasm and hyperchromatic nuclei. Immunohistochemistry demonstrated diffuse membranous positivity for cluster of differentiation 99 and nuclear positivity for Friend leukemia virus integration 1. Markers for lymphoma (leukocyte-common antigen), rhabdomyosarcoma (desmin, myogenin), and carcinoma (cytokeratin) were negative, thereby supporting the diagnosis of Ewing sarcoma. In order to complete the initial staging and evaluate the extent of the disease, a whole-body ^{18}F-FDG PET/CT was performed. It demonstrated a markedly hypermetabolic mass involving both the horizontal body and ascending ramus of the left mandible (Figure 1). The lesion measured approximately 73×73 mm in axial dimensions and extended vertically over 111 mm. It exhibited a very high maximum

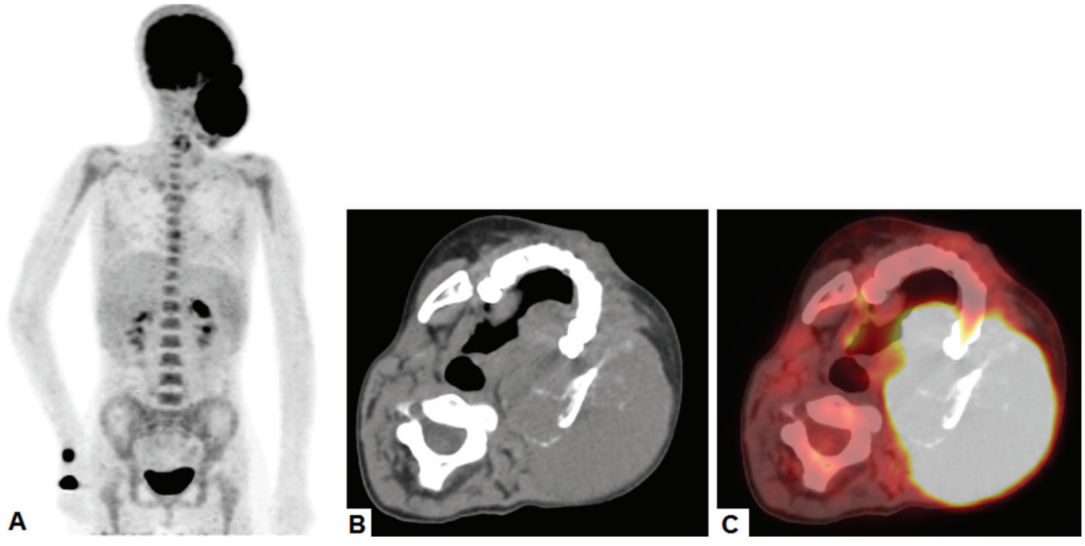

Figure 1. A: Maximum intensity projection image from the ^{18}F-FDG PET scan showing intense hypermetabolic activity in the left mandibular region, consistent with a large primary tumor, without evidence of distant metastatic uptake. **B:** Axial CT scan at the mandibular level revealing a large destructive mass involving the left mandibular body and ramus, with cortical bone lysis and extension into adjacent soft tissues. **C:** Axial fused ^{18}F-FDG PET/CT image demonstrating intense FDG uptake within the mandibular lesion (SUV_{max} 19.9), with a central photopenic area suggestive of necrosis and infiltration of surrounding tissues, including the left maxillary sinus and parapharyngeal space, showing intense hypermetabolic activity in the left mandibular region, consistent with a large primary tumor, without evidence of distant metastatic uptake.

^{18}F-FDG PET/CT: ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography, SUV_{max}: Maximum standardized uptake value

standardized uptake value (SUV_{max}) of 19.9, reflecting intense metabolic activity. The tumor had a heterogeneous appearance with a central photopenic area suggestive of necrosis. It infiltrated the surrounding soft tissues, including the left maxillary sinus, the left parapharyngeal space, and extended anteriorly to the region of the external auditory canal. However, there was no involvement of the cranial vault. No abnormal FDG uptake was noted in cervical, supraclavicular, mediastinal, hilar, or abdominal lymph nodes. Importantly, the 8 mm pulmonary nodule identified on CT showed no FDG uptake, lowering the suspicion of metastatic disease. No other hypermetabolic foci were observed in the lungs. The liver, spleen, pancreas, adrenal glands, and gastrointestinal tract appeared metabolically unremarkable. Skeletal evaluation revealed no FDG-avid bone lesions suggestive of metastasis. A diffuse and mildly heterogeneous increase in bone marrow activity was noted in the spine, pelvis, and proximal long bones, with a peak SUV_{max} of 4.9 in the thoracic vertebrae. This pattern was interpreted as reactive bone marrow activation, commonly observed in pediatric patients or in the context of systemic inflammation. Overall, PET/CT confirmed the presence of an aggressive, metabolically active mandibular tumor with extensive local spread but no evidence of distant metastasis. These findings established the initial staging and supported the decision to begin curative-intent treatment. The patient subsequently received neoadjuvant chemotherapy according to the standard protocol, including vincristine, doxorubicin, cyclophosphamide, ifosfamide, and etoposide. Despite the initiation of treatment, the disease progressed rapidly, and the patient's clinical condition deteriorated. She unfortunately died three months after the initial diagnosis.

Written informed consent was obtained from the patient's legal guardians for the publication of this case report and all accompanying clinical information. Assent was also obtained from the 14-year-old patient in accordance with ethical guidelines.

Discussion

Mandibular Ewing sarcoma is considered an exceptionally rare presentation within the spectrum of head and neck localizations, with only a limited number of case reports and small series described in the literature (2,4). This scarcity underlines the importance of detailed clinicopathological and imaging descriptions to guide both differential diagnosis and management. The non-specific clinical presentation often mimics odontogenic infections or benign jaw lesions, which may delay diagnosis and compromise prognosis. In our patient, the lesion was initially suggestive of an odontogenic process, emphasizing the need to include Ewing sarcoma in the differential diagnosis of mandibular swellings in adolescents. From a radiology and nuclear medicine perspective, ^{18}F-FDG PET/CT was pivotal. The intense metabolic activity and extensive local invasion it demonstrated were crucial findings which supported the diagnosis of a highly aggressive tumor rather than an odontogenic or inflammatory condition. As well as this diagnostic contribution, PET/CT provided a comprehensive baseline evaluation by excluding nodal, visceral, and skeletal metastases. Previous studies have shown that ^{18}F-FDG PET/CT can reveal additional metastatic sites not detected by conventional imaging in up to 21% of patients (6). Furthermore, its ability to quantify metabolic activity adds prognostic value by correlating with tumor aggressiveness and potential treatment response (7). The management of Ewing sarcoma is based on internationally established protocols, largely derived from cooperative group studies such as the Children's Oncology Group, the European Ewing Tumor Working Initiative of National Groups (EURO EWING), and the National Comprehensive Cancer Network (NCCN) guidelines. Current standards recommend a multimodal approach combining systemic multi-agent chemotherapy with local control by surgery and/or radiotherapy. First-line chemotherapy typically alternates vincristine, doxorubicin, and cyclophosphamide with ifosfamide and etoposide over 6-12 cycles (8), a regimen which has significantly improved survival compared to historical treatments. Surgical resection with negative margins remains the preferred option for local control whenever feasible, while radiotherapy is an effective alternative or adjunct in anatomically complex regions such as the head and neck (9). Modern radiotherapy modalities, including intensity-modulated radiotherapy and proton therapy, are recommended to optimize tumor targeting while limiting toxicity to surrounding critical structures, especially in children and adolescents (10). According to both NCCN and EURO EWING recommendations, management should be coordinated within a multidisciplinary team and ideally delivered in specialized sarcoma centers in order to maximize oncologic outcomes and preserve function. Recent advances are also exploring targeted and innovative therapies. Agents directed against molecular pathways such as the insulin-like growth factor 1 receptor and poly adenosine diphosphate-ribose polymerase inhibitors have shown encouraging activity in early trials (11). Immunotherapy approaches, including checkpoint inhibitors, are under investigation but are limited by the

typically low mutational burden of Ewing sarcoma (12). The prognosis of Ewing sarcoma is strongly influenced by the presence of metastases at diagnosis and by the tumor's histological response to chemotherapy. Patients with localized disease treated with intensive multimodal therapy achieve 5-year survival rates of approximately 70% (13). Nevertheless, mandibular involvement poses unique challenges related to anatomical complexity and the risk of delayed diagnosis, both of which may adversely affect outcomes. Histological response to neoadjuvant chemotherapy is also an important prognostic factor, correlating with long-term survival (14). Looking ahead, the future management of Ewing sarcoma is increasingly oriented toward personalized medicine. Genomic profiling may help identify actionable mutations and guide targeted therapies, moving beyond conventional cytotoxic regimens (15). Combination approaches incorporating chemotherapy with novel targeted agents or immunotherapy are currently under investigation and may enhance treatment responses (16). In parallel, advances in imaging, including PET tracers beyond FDG, and liquid biopsy technologies hold promise for earlier detection of residual or recurrent disease. Equally important are strategies to optimize functional and psychosocial rehabilitation, particularly for adolescent patients, in order to improve their quality of life after treatment. Overall, despite significant progress in multimodal therapy, the prognosis of mandibular Ewing sarcoma remains guarded, especially in those cases with delayed diagnosis or poor therapeutic response.

Conclusion

Mandibular Ewing sarcoma is an exceptionally rare and diagnostically challenging entity. ^{18}F-FDG PET/CT plays a pivotal role in its initial evaluation, not only by confirming the extent of locoregional disease and excluding distant metastases, but also by contributing to the differential diagnosis in adolescents presenting with atypical mandibular lesions. By providing comprehensive staging information, PET/CT helps guide therapeutic decisions and supports individualized, multidisciplinary management. Continued advances in imaging and treatment strategies hold the promise of improving outcomes in such uncommon and aggressive malignancies.

Ethics

Informed Consent: A written informed consent form was taken from the patient and family in order to publish this case.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.B., R.B., H.M., C.E.M, A.D., Concept: Y.B., A.D., Design: Y.B., A.D., Data Collection or Processing: Y.B., R.B., H.M., C.E.M., Analysis or Interpretation: Y.B., Literature Search: Y.B., Writing: Y.B.

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