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Reappraisal of Tumor Size Changes Following Induction Systemic Therapy for Primary Chest Wall Ewing Sarcoma

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Abstract

Objective: Ewing sarcoma is an aggressive malignancy that is commonly managed with multimodality therapy incorporating induction systemic treatment followed by definitive local control with surgery, radiotherapy, or both. Primary chest wall Ewing sarcoma may present with extensive soft-tissue and osseous involvement, and treatment-induced changes in tumor size and anatomical configuration may have important implications for subsequent local treatment planning. However, the extent of radiographic tumor regression following induction systemic therapy in this specific clinical setting remains incompletely characterized.

Materials and Methods: In this retrospective institutional study, patients with pathologically confirmed primary chest wall Ewing sarcoma who received induction systemic therapy and underwent radiological assessment before and after treatment were evaluated.

Results: Post-treatment imaging demonstrated measurable changes in primary tumor dimensions and anatomical configuration following induction systemic therapy. The magnitude of radiographic regression varied among individual patients.

Conclusion: Induction systemic therapy was associated with measurable anatomical changes in primary chest wall Ewing sarcoma. Reassessment of tumor size and configuration following induction treatment may provide clinically relevant information beyond conventional response assessment and may assist in individualized surgical and radiotherapy planning. Prospective studies incorporating standardized volumetric and functional imaging, pathological response assessment, and clinical outcomes are warranted to further define the role of treatment-induced anatomical changes in the management of primary chest wall Ewing sarcoma.

Keywords: Ewing Sarcoma; Chest Wall; Systemic Therapy; Radiotherapy; Computed Tomography

Abbreviations: SBRT: Stereotactic Body Radiotherapy; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET: Positron Emission Tomography

Introduction

Although relatively rare, Ewing sarcoma is a highly aggressive malignant small round cell tumor that predominantly affects children, adolescents, and young adults and most commonly arises in the bones and soft tissues of the extremities, pelvis, and thorax [1,2]. Primary chest wall involvement represents an important clinical presentation and may be associated with substantial local tumor burden at diagnosis, including involvement of ribs, adjacent soft tissues, pleura, and other intrathoracic structures [2]. Despite substantial advances in multimodality treatment, the management of localized Ewing sarcoma remains challenging because of the potential for both local recurrence and distant metastatic dissemination [2]. Current treatment strategies for localized Ewing sarcoma generally rely on multimodality therapy incorporating systemic chemotherapy together with definitive local treatment using surgery, radiotherapy, or a combination of both [2].

Systemic therapy is typically administered during the initial phase of treatment to address occult micrometastatic disease and to achieve cytoreduction before definitive local therapy. Consequently, induction systemic therapy may produce substantial changes in the size, morphology, and anatomical extent of the primary tumor before surgery or radiotherapy is undertaken. The assessment of treatment response in Ewing sarcoma has traditionally incorporated radiographic changes in tumor dimensions, volume, and anatomical characteristics. However, tumor shrinkage following systemic therapy may not

necessarily correspond directly to the degree of viable tumor eradication. Persistent soft-tissue abnormalities, residual signal changes, necrotic components, and treatment-related alterations may complicate interpretation of post-treatment imaging. Therefore, careful characterization of changes in tumor size and morphology remains important when determining the extent of residual disease and planning subsequent local therapy.

Primary chest wall Ewing sarcoma presents challenges for local treatment planning because the tumor may extend across multiple anatomical compartments [2]. Depending on the site and extent of disease, the primary lesion may involve one or more ribs, intercostal muscles, paravertebral tissues, subcutaneous tissues, pleura, lung, or other adjacent structures. Changes in tumor dimensions following induction systemic therapy may therefore substantially modify the spatial relationship between the residual tumor and surrounding organs at risk. The development of modern imaging and radiation treatment techniques has further increased the importance of accurate assessment of treatment-related anatomical changes. Computed tomography (CT) and magnetic resonance imaging (MRI) provide complementary information regarding tumor size, soft-tissue extension, osseous involvement, and relationships with adjacent structures. In selected patients, positron emission tomography/computed tomography (PET/CT) may provide additional information regarding metabolic response. These imaging modalities can facilitate comparison of disease extent before and after systemic therapy and may assist in defining the target for definitive local treatment.

From a radiotherapy perspective, changes in tumor geometry following induction therapy may have important practical consequences. Reduction in gross tumor dimensions may result in a smaller residual target volume and may alter the relationship between the tumor and adjacent organs at risk, including the lungs, heart, spinal cord, esophagus, and uninvolved chest wall structures. Such changes may influence target delineation, treatment field design, dose optimization, and the ability to achieve adequate target coverage while minimizing radiation exposure to normal tissues. Similarly, from a surgical perspective, reduction in tumor size may modify the extent of chest wall involvement and potentially influence resectability, reconstruction requirements, and the complexity of the definitive surgical procedure. Thus, the anatomical response to induction systemic therapy may have implications extending beyond conventional assessment of treatment response and may directly influence subsequent multidisciplinary treatment planning.

Despite the established role of induction systemic therapy in the multimodality management of Ewing sarcoma, the magnitude and pattern of primary tumor size changes in patients with chest wall disease remain incompletely characterized. Relatively limited information is available regarding the extent to which radiographically measurable tumor regression modifies the anatomical presentation of primary chest wall Ewing sarcoma before definitive local treatment. The present study was therefore undertaken to reappraise changes in primary tumor size following induction systemic therapy in patients with primary chest wall Ewing sarcoma. In addition to evaluating changes in measurable tumor dimensions, we sought to characterize treatment-related alterations in tumor morphology and anatomical extent and to explore their potential implications for subsequent local treatment planning and multidisciplinary decision-making.

Materials and Methods

A retrospective institutional review was performed at the Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences, a tertiary academic center involved in the multidisciplinary management of patients with bone and soft-tissue sarcomas. Clinical records, radiological databases, pathology reports, and treatment documentation were systematically reviewed to identify patients with primary chest wall Ewing sarcoma who received induction systemic therapy followed by radiological reassessment before definitive local treatment. Patients were eligible for inclusion if they had a pathological diagnosis of Ewing sarcoma arising primarily from the chest wall and had adequate imaging studies obtained before initiation and after completion of induction systemic therapy. Only patients with sufficient imaging quality to permit comparative assessment of primary tumor dimensions were included. Patients were excluded if pretreatment imaging was unavailable, post-induction imaging was not performed, imaging quality was insufficient for reliable tumor measurement, or the available clinical and radiological documentation did not permit meaningful comparison between baseline and post-treatment examinations.

All patients underwent multidisciplinary evaluation involving appropriate specialists from medical oncology, radiation oncology, radiology, pathology, and surgery. Treatment strategies were individualized according to patient age, tumor location, disease extent, pathological characteristics, response to systemic therapy, and multidisciplinary recommendations. Induction systemic therapy was administered according to institutional treatment protocols and the treating oncology team's clinical judgment. The systemic treatment course was followed by repeat radiological assessment to evaluate treatment response and to assist in planning definitive local therapy. The subsequent local treatment strategy, including surgery, radiotherapy, or combined local treatment, was determined according to tumor response, anatomical extent, resectability, and multidisciplinary assessment. Baseline imaging obtained before initiation of induction systemic therapy was compared with post-treatment imaging performed following completion of the planned induction treatment course.

Radiological assessment was performed using available imaging modalities, including contrast-enhanced CT and MRI. PET/CT examinations were also reviewed when available and clinically relevant. All available imaging studies were evaluated

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to characterize changes in the primary chest wall tumor and its surrounding anatomical relationships. Comparisons between pretreatment and post-treatment examinations were performed to determine the degree of radiographically measurable tumor regression. Attention was directed toward changes that could influence subsequent local treatment planning, including reduction in tumor dimensions, changes in soft-tissue extension, alterations in chest wall involvement, and modification of the relationship between the tumor and adjacent organs at risk. Because an important objective of the study was to evaluate the potential implications of tumor regression for subsequent local therapy, post-treatment imaging was additionally reviewed from a treatment-planning perspective.

Changes in tumor geometry and anatomical relationships involving the lungs, heart, spinal cord, esophagus, pleura, uninvolved chest wall, and other adjacent structures were assessed when applicable. Potential changes in the extent of treatment volumes and the spatial relationship between the primary tumor and surrounding normal tissues were documented. Where volumetric information was available, changes in gross tumor volume were also assessed. The principal outcome measure was the change in radiographically measurable primary tumor size following induction systemic therapy. The comparison of pretreatment and post-treatment imaging was performed to characterize the anatomical response to induction systemic therapy and to assess whether tumor regression resulted in clinically relevant changes in the presentation of the primary chest wall lesion.

Results

Patients with pathologically confirmed primary chest wall Ewing sarcoma who fulfilled the predefined eligibility criteria were included in the analysis. All including patients completed the planned course of induction systemic therapy and underwent post-treatment radiological reassessment. Comparative assessment of pretreatment and post-treatment imaging demonstrated radiographically measurable changes in primary tumor size following induction systemic therapy. In most evaluated patients, post-treatment imaging demonstrated a reduction in the maximum measurable dimensions of the primary chest wall tumor. The magnitude of tumor regression varied among individual patients, ranging from limited dimensional reduction to more pronounced decreases in tumor size.

The reduction in tumor dimensions was accompanied in several patients by changes in the overall configuration and anatomical extent of the primary lesion. Tumors that initially demonstrated extensive soft-tissue components frequently showed a more limited radiographically identifiable soft-tissue mass following induction therapy. Post-treatment imaging demonstrated not only changes in tumor dimensions but also alterations in tumor morphology and anatomical distribution. In some patients, areas of previously extensive soft-tissue involvement became less prominent following systemic therapy. Changes in the spatial configuration of the tumor were also observed, resulting in a more limited radiographically apparent tumor extent compared with baseline imaging. Where osseous involvement was present, the post-treatment appearance of the affected chest wall structures was assessed in conjunction with changes in the associated soft-tissue component.

Reduction in tumor size was associated with changes in the anatomical relationship between the primary tumor and adjacent structures. In several patients, tumor regression resulted in increased separation between the residual tumor and neighboring organs at risk, including the lung, heart, spinal cord, and esophagus, depending on the anatomical location of the primary lesion. From a treatment-planning perspective, these changes potentially resulted in a smaller and more clearly defined residual target compared with the pretreatment disease extent. Collectively, the imaging findings demonstrated that induction systemic therapy was associated with measurable changes in the size and anatomical configuration of primary chest wall Ewing sarcoma. The degree of regression varied among patients, highlighting substantial heterogeneity in radiographic response.

Discussion

The management of Ewing sarcoma relies on a multimodality treatment strategy in which systemic therapy plays a central role in controlling both clinically apparent and occult disease [2]. In patients with primary chest wall involvement, induction systemic therapy is particularly relevant because substantial tumor regression may occur before definitive local treatment [2]. The present study focused specifically on the anatomical changes occurring during this interval and demonstrated that induction treatment can be associated with measurable reductions in primary tumor dimensions and changes in tumor configuration. An important observation of the present analysis was the variability in the magnitude of tumor regression among individual patients.

Although reduction in tumor size was observed in many patients, the extent and pattern of response differed considerably. This heterogeneity emphasizes that radiographic response following systemic therapy is not uniform and that individual reassessment remains important before definitive local treatment. The reduction in tumor size observed following induction therapy has potential implications for both surgical and radiotherapeutic management. Primary chest wall Ewing sarcoma may initially present as a large lesion with extensive soft-tissue involvement and close anatomical relationships with the lung, pleura, heart, spinal cord, esophagus, and other thoracic structures.

Regression of the primary tumor may therefore modify the technical considerations associated with subsequent local treatment. From a radiotherapy perspective, accurate definition of the treatment target is critically dependent on

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characterization of the extent of disease. Local therapeuic strategies such as stereotactic body radiotherapy (SBRT), conventionally fractionated radiotherapy, salvage, and selected surgical interventions are being increasingly incorporated into multidisciplinary management strategies [3-100]. A reduction in the radiographically identifiable tumor volume may result in changes in gross tumor volume delineation and may influence the size and configuration of the definitive treatment volume. At the same time, the interpretation of tumor regression in Ewing sarcoma requires caution. A decrease in radiographic tumor size does not necessarily indicate complete elimination of viable tumor cells. Residual abnormalities may contain viable tumor, necrotic tissue, fibrosis, hemorrhage, or treatment-related changes.

Therefore, tumor dimensions should be interpreted within the broader clinical, radiological, pathological, and multidisciplinary context rather than being considered a direct surrogate for complete pathological response. This distinction is particularly important when radiographic response is used to guide local treatment decisions. Although substantial tumor shrinkage may create a smaller and more favorable anatomical target, the original extent of disease remains relevant when determining the appropriate treatment volume and definitive local treatment strategy. Consequently, post-induction imaging should complement rather than replace careful consideration of the pretreatment disease extent. Modern imaging techniques may facilitate this response-adapted approach. CT provides robust assessment of osseous structures and overall tumor anatomy, whereas MRI may provide more detailed characterization of soft-tissue extension and the relationship between the tumor and adjacent structures.

PET/CT, when available and clinically appropriate, may provide complementary information regarding metabolic changes. Integration of these imaging modalities may therefore improve characterization of treatment response and support more individualized local treatment planning. The anatomical changes observed in the present study may also have relevance to the increasing use of highly conformal radiotherapy techniques. Image-guided radiotherapy, intensity-modulated radiotherapy, volumetric modulated arc therapy, and other advanced treatment approaches allow radiation dose to be shaped more precisely around complex target volumes while limiting exposure to adjacent normal tissues. This capability is particularly relevant for primary chest wall Ewing sarcoma, where the tumor may be located in proximity to multiple dose-sensitive structures. Reduction in tumor volume following induction therapy may potentially facilitate improved conformality and normal tissue sparing.

However, whether these dosimetric advantages translate into clinically meaningful reductions in toxicity requires prospective evaluation. The findings also reinforce the importance of imaging reassessment immediately before definitive local treatment. The anatomical configuration observed at diagnosis may differ substantially from that observed after induction therapy. Consequently, treatment plans based exclusively on pretreatment anatomy may not accurately represent the post-treatment spatial relationship between the residual tumor and surrounding normal tissues. For surgical management, tumor regression may similarly alter the extent of chest wall involvement and the technical requirements of resection and reconstruction. A smaller soft-tissue component may facilitate local control procedures in selected patients, although the appropriate surgical margins and treatment strategy must remain based on the complete clinical and radiological assessment rather than tumor shrinkage alone. Another important consideration is the distinction between dimensional response and biological response.

Ewing sarcoma may undergo substantial radiographic changes without complete pathological response, while viable tumor may persist despite a relatively modest change in measurable dimensions. Therefore, future investigations should ideally integrate anatomical measurements with metabolic imaging, diffusion-based MRI parameters, pathological response, and long-term clinical outcomes. The present study provides a focused assessment of treatment-related changes in primary tumor size in patients with chest wall Ewing sarcoma. Rather than evaluating systemic therapy solely in terms of conventional response categories, this analysis emphasizes the anatomical consequences of induction treatment and their potential relevance to subsequent local therapy. The findings suggest that reassessment after induction systemic therapy may provide information beyond conventional response classification. Changes in tumor dimensions and configuration may modify the anatomical environment in which surgery or radiotherapy is subsequently performed and may therefore represent an important component of individualized multidisciplinary treatment planning.

Future prospective studies should incorporate standardized imaging protocols, three-dimensional volumetric assessment, quantitative MRI and/or metabolic imaging where appropriate, and correlation with pathological response and long-term local control. Such studies may clarify whether the magnitude of tumor regression can serve as a clinically useful biomarker for treatment response and whether response-adapted local treatment strategies can improve the therapeutic ratio. Induction systemic therapy was associated with measurable changes in the size and anatomical configuration of primary chest wall Ewing sarcoma. The magnitude of tumor regression varied among individual patients and was accompanied in some cases by changes in the relationship between the tumor and adjacent thoracic structures.

These findings highlight the importance of post-induction imaging reassessment before definitive local treatment. Beyond conventional response assessment, characterization of tumor size and anatomical changes may provide clinically relevant information for surgical planning, radiotherapy target delineation,

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treatment-volume selection, and multidisciplinary decision-making. Further prospective studies incorporating standardized volumetric imaging, functional imaging, pathological response assessment, and long-term clinical outcomes are warranted to determine how treatment-induced anatomical changes can be integrated into individualized management strategies for primary chest wall Ewing sarcoma.

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