Commentary Article

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RNAs Participate in Regulating the Cellular Metabolism of Sarcoma

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Description

According to published research, specialized sarcoma centers provide the best care for sarcoma patients. In order to achieve optimal management, a multidisciplinary team must contribute to the formulation of the diagnosis and treatment sequence, taking into account a variety of clinical and pathologic factors. The purpose of this systematic review was to determine how radiotherapy at specialized sarcoma centers affected outcomes. The population, intervention, comparison, and outcome model was used in a systematic review. From 1990 to February 2022, publications evaluating the local control, survival, and toxicity of radiotherapy at specialized sarcoma centers were searched for in the Medline, Embase, and Cochrane Central databases. There were a total of 21 studies included, including 17 studies with cancer registry data and 4 retrospective comparative studies. When radiotherapy is supported through, but may not necessarily be delivered at specialized sarcoma centers, four studies reported the local recurrence endpoint when radiotherapy was part of limb conservation treatment. They also demonstrated better conformity to clinical practice guidelines and an improved local recurrence free rate. Only one retrospective study looked specifically at toxicity and found that patients who received preoperative radiotherapy at community centers were more likely to have a major wound complication than patients who received radiotherapy at a specialized sarcoma center. There were 14 studies that looked at overall survival, and 12 of them showed that patients treated at specialized sarcoma centers had significantly better 5-year overall survival. However, the specific impact of radiotherapy provided at sarcoma centers was not clear. For improved oncological outcomes, sarcoma patients should be managed by specialized sarcoma centers. As part of the limb conservation treatment at a specialized sarcoma center, radiotherapy is associated with a lower rate of wound complications and may contribute to improved oncological outcomes.

Neuroblastoma

Sarcomas, which account for about 1% of all cancers in humans, have a poor response to treatment and a high rate of recurrence. In sarcomas, metabolic reprogramming plays a significant role in the development of the tumor. There is growing evidence that non-coding RNAs (ncRNAs) play a role in regulating the cellular metabolism of sarcomas, which makes it easier to understand how treatment-resistant tumors develop. The implications of these findings for the onset and progression of sarcoma are discussed in this overview of the regulatory roles of metabolism-related ncRNAs. Sarcomas frequently exhibit dysregulation of metabolism-related ncRNAs, which is linked to decreased survival rates. Abnormal expression of ncRNAs related to metabolism has been linked to the development of aggressive sarcomas and affects cellular metabolism, such as glucose, lipid, and mitochondrial metabolism. Dysregulated metabolism-related ncRNAs' potential as biological biomarkers for disease diagnosis and prognosis prediction, as well as therapeutic targets for treating refractory sarcomas, are discussed in this review, along with recent advances in their roles in sarcoma development and stemness. In pediatric solid tumors like Ewing sarcoma, rhabdomyosarcoma, and neuroblastoma, nanoparticle albumin-bound paclitaxel (nab-paclitaxel) exhibits potent preclinical anticancer activity, but responses in clinical trials have been modest. We set out to discover a rational biomarker-based method for selecting suitable patients for this treatment in this study. Nab-paclitaxel's efficacy was tested on 27 patient-derived xenografts (PDX), which included 14 Ewing sarcomas, 5 rhabdomyosarcomas, and a number of other pediatric solid tumors.

In rhabdomyosarcomas (four of five) and Ewing sarcomas (four of 14), the response rate (partial or complete response) was remarkable. The expression of the Secreted Protein Acidic and Rich in Cysteine (SPARC), chromosomal stability of cancer cells, and ant apoptotic members of the B-cell lymphoma-2 (Bcl-2) family of proteins like Bcl-2, Bcl-xL, Bcl-W, and Mcl-1 were some of the predictive factors of response to nab-paclitaxel that we looked at. Positive correlations were found between SPARC protein (immunoblotting) expression and gene expression, while negative correlations were found between Bcl-2 expression and nab-paclitaxel efficacy in PDX Ewing sarcoma. Particularly robust was the negative correlation between Bcl-2 immunoblotting activity and signal ($r=0.8352$; $P = 0.0007$; correlation (Pearson). As a result, we looked into pharmacological ways to stop Bcl-2 from working against nab-paclitaxel. In highly resistant Bcl-2-expressing Ewing sarcoma PDX, the activity of nab-paclitaxel was found to be enhanced by the Bcl-2 inhibitor venetoclax. Overall, our findings suggest that Bcl-2 inhibitors could enhance the activity of nab-paclitaxel in Bcl-2-expressing Ewing sarcoma and

that low Bcl-2 expression could be used to select patients with Ewing sarcoma who are responsive to this treatment.

Quantitative Information

Ewing sarcomas are mesenchymal tumors that can be very different from one another. They can grow in bone or soft tissue and mostly affect children, teens, and young adults. It is the second most common malignant bone sarcoma, after osteosarcoma. Metastatic and relapsed Ewing sarcomas typically have a poor prognosis and frequently recur, resulting in high mortality and morbidity rates. Patients with Ewing sarcoma continue to have a poor overall survival rate, highlighting the urgent need to quickly translate new therapeutic approaches. The most important goal is to target the EWR1/FLI1 fusion protein, which is the primary genetic anomaly and master regulator of Ewing sarcoma and is present in 80–90% of Ewing tumors. The genomics and proteomics of Ewing sarcoma signaling, as well as the ways in which it affects the tumor microenvironment and the progression of the disease, are discussed in greater detail in this review. It also explains how some of the underlying oncogenic characteristics of Ewing sarcoma have been explained by recent technological advancements. The current review looked at both current and potential experimental therapies that target multiple signaling pathways that are involved in the progression of Ewing sarcoma and improve patient survival and quality of life. Patients might see these treatments as the new standard of care in the future. Especially in children, CIC-rearranged round cell sarcomas are uncommon and poorly understood. To further characterize the various presentations, surgical and medical management, and metastatic potential of these tumors, it is essential to distinguish this from the more common Ewing's sarcoma. We present the first case of pediatric CIC-rearranged round cell sarcoma that presented as a rapidly expanding, painless neck mass in a 13-year-old female and was treated with surgical excision, chemotherapy, and radiation. This is the sixth documented case of CIC-rearranged round cell sarcoma. This pathology's existing literature is also reviewed. Germline mutations in Cancer Predisposition Genes (CPGs) may result in Soft Tissue Sarcomas (STS).

Understanding the pathogenesis of the disease and the requirements for its treatment, in our opinion, necessitates elucidating the germline sarcoma predisposition. Participation in surveillance programs may enable earlier tumor detection, earlier treatment initiation, and improved outcomes in the long run. Pathogenic or likely pathogenic variants in CPGs were found in 7–33% of patients who had been diagnosed with soft-tissue sarcoma and examined as part of published germline sequencing studies. Most likely) pathogenic germline variants were found in BRCA1/2, NF1, and TP53. Soft tissue sarcomas have been linked to germline variants in CPGs, and we also discuss locally aggressive and benign soft tissue tumors that are strongly linked to cancer predisposition syndromes in this review. Additionally, we talk about suggestions for diagnostic germline genetic testing. Any child, adolescent, or adult diagnosed with STS should have their routine clinical workup and care included in the consideration of testing for sarcoma-predisposing germline variants, taking into account the implications for the entire family.