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Rhabdomyosarcoma and It's Risk Factors in Adults

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Abstract

Rhabdomyosarcoma (RMS) is a pediatric soft tissue sarcoma and represents a high-grade neoplasm of skeletal myoblast-like cells. A gradual improvement in understanding of physiology has helped optimize clinical care. Two main subtypes of RMS. Originally characterized by features of optical microscopy. Driven by fundamentally different molecular mechanisms, it poses a variety of clinical challenges. Curative therapies depend on control of the primary tumor. It can occur in many different anatomical locations. Combat common ailments known or suspected to be present in all cases. Refined risk stratification for children with RMS includes a variety of clinical, pathological and molecular characteristics; this information is used to guide the application of multifaceted treatments. Such treatments have historically included both cytotoxic chemotherapy and ionizing radiation or both. This introduction describes the current understanding of the epidemiology of RMS. Factors of clinical care, including disease susceptibility factors; disease mechanisms; and diagnosis. Risk-based care for newly diagnosed and recurrent disease. Prevention and treatment of late complications in survivors.

Keywords: Rhabdomyosarcoma; Soft tissue sarcoma; Translocation-driven neoplasms

Introduction

Soft tissue sarcomas account for approximately 7% of childhood cancers and 1% of adult cancers1. About half of pediatric patients with soft tissue sarcoma have rhabdomyosarcoma (RMS) [1]. It is a high-grade malignant neoplasm in which cancer cells tend to differentiate myogenically. There are two main RMS subtypes, 'alveolar' RMS (ARMS) and 'embryonic' RMS (ERMS), which are driven by fundamentally different mechanisms. Achieving a cure requires control of primary tumors, which can arise from various anatomical sites, by surgical resection and/or ionizing radiation, and eradication of systemic metastases by intensive chemotherapy; Both subtypes present significant clinical challenges. Survival rates for many children with RMS have improved dramatically over the past 30 years [2]. This is evidenced by the development and conduct of a series of clinical trials conducted nationally or internationally as collaborative groups in North America and Europe. Moreover, advances in molecular biology and genetics have also enabled a better understanding of RMS pathogenesis. These approaches continue to provide platforms for improving diagnosis, disease classification, patient risk stratification, and treatment strategies [3].

ARMS and ERMS have emerged as two major RMS subtypes based on light microscopic characterization of cells distributed around an open central space or resembling immature skeletal myoblasts. This distinction is associated with balanced chromosomal translocations where ARMS affects chromosomes 2 or 1 and 13 (referred to herein as t(2;13) and t(1;13)) [4]. This was supported by the finding that there are often As detailed below, a small but significant proportion of patients with ARMS do not have these translocations, and these tumors are biologically and clinically similar to her ERMS. The World Health Organization (WHO) also recognizes two rarer RMS subtypes. Polymorphic RMS is a morphological variant of RMS that usually occurs in adults. As in ERMS, the unifying molecular genetic abnormality in pleomorphic RMS is not yet clear. A spindle cell/sclerosing RMS variant is observed in children [5]. Tumors originating in the head and neck appear to have more specific somatic mutations and have a poorer prognosis.

The disease classification of RMS subtypes was further refined by the identification of 'fusion-positive' (FP) and 'fusion-negative' (FN) RMS [6]. Molecular biological approaches and next-generation DNA and RNA sequencing have shown that ARMS-associated translocations generate novel fusion proteins involving the pair box proteins PAX3 or PAX7 and the forkhead box protein O1 (FOXO1).

With the exception of polymorphic RMS, which occurs in adults, most experts believe that RMS in childhood is best explained by a confluent state [7]. This introduction follows this convention, but uses ARMS and ERMS as descriptors when describing pathology reports and previous studies based on these classifiers.

Despite many advances, the chances of recovery for children with extensive metastatic and recurrent disease are still very small can cause life-threatening acute poisoning and sometimes life-changing late effects.

Risk Factors

Unlike osteosarcoma and Ewing's sarcoma (two other fairly common pediatric soft tissue sarcomas), no genome-wide association studies have been published for RMS. Furthermore, although whole-exome and whole-genome sequencing have identified somatic mutations in the RMS, few studies have characterized the role of germline DNA in disease susceptibility. Defining risk factors for rare cancers, which occur in 4-5 cases per million people, remains a challenge [8]. However, there is a large body of literature supporting the hypothesis that genetic susceptibility and environmental factors play a role in the development of RMS.

Genetic Risk Factors

Numerous reports have shown that children with certain genetic

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disorders are more likely than their unaffected peers to develop RMS. The most common syndromes in children with ERMS include Li-Fraumeni syndrome (germline mutation of her TP53, a tumor suppressor) [9]. Neurofibromatosis type I (NF1 gene deletion); Costello syndrome (HRAS mutation); Noonan syndrome (germline genetic variant that activates the RAS-MAPK pathway); Beckwith-Wiedemann syndrome and DICER1 syndrome (reproductive cell DICER1 mutation). However, based on small clinical studies, it is estimated that only about 5% of patients with RMS have a concomitant germline susceptibility syndrome. Interestingly, predisposition syndrome seems to occur more frequently in her ERMS patients than in ARMS patients [10]. This finding appears to be in contrast to experimental studies showing that germline loss of a specific tumor suppressor promotes PAX3-FOXO1-driven neoplasia in a genetically engineered mouse model.

Environmental Risk Factors

Several environmental exposures and other factors are associated with RMS risk in children. Many published reports are based on large case-control epidemiologic studies of RMS made possible by the former Intergroup Rhabdomyosarcoma Study Group (IRSG) and the current Children's Oncology Group (COG). North American RMS children [11]. Between April 1982 and July 1988, 322 RMS patients aged 20 or younger at diagnosis and her 322 sex-, age-, and race-matched controls were enrolled in this study.

Molecular Differences between Subtypes

RMS-specific fusion genes can be detected in clinical biopsies by RT-PCR and fluorescence in situ hybridization (FISH) assays. These assays show that 60% of ARMS patients express PAX3-FOXO1, 20% express PAX7-FOXO1, and 20% are FN [12]. A small subset of ARMS patients lack detectable PAX3-FOXO1 or PAX7-FOXO1 fusion proteins, such as PAX3-FOXO4 or PAX3-NCOA1 (NCOA1 encodes nuclear receptor coactivator 1) has a new variant of the clinical or biological consequences of these variants are unclear. Nucleic acid sequencing showed that FN ARMS patients did not express the fusion protein, instead exhibiting tumor cell genetic alterations resembling ERMS tumors, including whole chromosomal gains, recurrent point mutations, and p15.5 allele loss. it was done. In addition, genome-wide mRNA expression studies showed that ERMS and FN-ARMS tumors have highly similar expression profiles [13], which differ from those of PAX3-FOXO1-positive and PAX7-FOXO1-positive ARMS tumors. These studies therefore provide genetic evidence for combining ERMS and FN-ARMS tumors into a single FN-RMS subset and PAX3-FOXO1- and PAX7-FOXO1-positive ARMS tumors into distinct FP-RMS subgroups [14].

Over the past 30 years, our understanding of the pathophysiology of RMS has become increasingly sophisticated, and these discoveries have enabled more definitive clinical diagnosis and prognostic assessment that will help develop more precise therapeutic approaches [15]. These focused or experimental approaches aim to improve outcomes in patients with poor prognosis and severe acute and ongoing treatment-related effects in individuals likely to be cured by standard approaches.

Conclusion

The next step towards precision medicine involves developing robust, objective and accessible biomarkers that are highly predictive of response to targeted therapies. The main challenges of RMS are highlighted above. Especially in fusion-driven RMS is the lack of highly repetitive target protein-coding genes. Current efforts targeting resequencing of primary RMS biopsy specimens more precisely define the frequencies of previously identified somatic variants. Correlation of these variants with clinical features such as age, anatomical localization and outcome should lead to a better understanding of tumor biology and allow for better risk stratification. However, finding targeted oncogenic drivers unrevealed by nucleic acid sequencing will likely require integrative computational analyzes that specifically consider changes in gene expression caused by epigenetic reprogramming.

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