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Initiative of the Children's Oncology Group on Rare Tumors: The First Lessons Learned and Their Effect on Plans for the Future

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Abstract

When the National Wilma Tumor Study Group, the Intergroup Rhabdomyosarcoma Study Group, the Pediatric Oncology Group, and the Children's Cancer Group merged in 2000, it gave the newly formed Children's Oncology Group a chance to investigate uncommon cancers that had not been the subject of organized evaluation within the framework of a cooperative group. The rare tumor committee was established by the COG in 2002 and consists of four subcommittees. The brief tumor subcommittee's period of experience is described in this article. We have observed low registration rates within the COG registry and low participation rates in open banking, biology, and first-line therapeutic studies during the initial implementation of this strategy. We have been able to come up with new ways to increase clinical trial enrolment and registration rates thanks to this initial experience. With these new plans, it is hoped that we will be able to learn more about the biology of young patients with rare cancers and improve their treatment outcomes. Additionally, our initial experience has demonstrated the potential strength of global cooperation and collaboration.

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Introduction

Given that childhood cancer is considered a rare disease, the definition of a rare pediatric tumor is complex [1]. Indeed, a rare disease is one that affects fewer than 200,000 Americans annually, as defined by the Rare Disease Act of 20021. However, based on data from the National Cancer Institute's Surveillance Epidemiology and End Results Program, this definition would exclude the thyroid carcinoma and melanoma, the two rarest tumors found in children and adolescents, with incidence rates of 5.7 and 6.0 per million per year, respectively [2]. The neoplasms that are typically categorized as other malignant epithelial neoplasms and melanomas in the International Classification of Childhood Cancer subgroup XI of the SEER database have been selected as the definition of infrequent tumors in the context of a pediatric population for the purposes of this article [3]. Adrenocortical carcinoma, thyroid carcinoma, nasopharyngeal carcinoma, malignant melanoma, skin carcinoma, no melanoma skin cancers, and various other types of carcinoma are among this histologist. Controlled clinical trials in a multicenter setting are not possible due to sample size constraints, and a low prevalence of epithelial rather than mesenchyme origin in patients younger than years is one of the common features of these tumors [4].

Materials and Method

The formation of the Children's Oncology Group's Rare Tumor Committee

Children's Oncology Group was poised to be an invaluable resource and catalyst for the study of these tumors by developing a structure that could enhance clinical trial enrolment of pediatric patients with neoplasms that had not been the subject of organized prospective or even retrospective, evaluation [5]. As the only pediatric National Cancer Institute–sponsored cooperative group in North America, Children's Oncology Group enrolled 80% of eligible children with cancer on study [6]. The rare tumor committee was established by the COG in 2002 and consisted of three subcommittees: subcommittees for infrequent tumors, germ cell tumors, and liver tumors. In 2008, a subcommittee within this initiative was formed to focus on the

investigation of retinoblastoma, a different rare cancer [7]. The remaining sections of this report will focus on the difficulties that the infrequent tumor subcommittee has encountered over the course of the past six years as well as the strategies that are being considered and put into action to address the difficulties that arise when studying this category of childhood diseases.

Streamlining Research on Rare Tumors

The COG Data Center should receive a report from each member institution for each new cancer diagnosis. In addition, consent is sought for the COG Data Center to receive confidentially secured identifying information. The obligation to register in a formal capacity only became mandatory in [8]. The planning of epidemiologic, biologic, and therapeutic trials for this patient population could be made easier with active participation in this registry, which could provide invaluable information regarding the incidence and number of new patients with rare tumors. We have chosen, for the purposes of this publication, to review the information that is available for four histologic subtypes of infrequent childhood cancers in order to highlight our experience with the COG registry: adrenocortical carcinoma, thyroid carcinoma, nasopharyngeal carcinoma, and melanoma [9]. Our analysis demonstrates that, based on the estimates from the SEER database, the COG registry should have received 9,756 registrations for these four tumors in patients younger than 20 years old from January 2002 to December 2007. We then compared the actual number of registrations for these four tumors in patients younger than 20 years old in the COG registry with the expected number of patients with the same diagnosis and over the same time period.8 On the other hand, only 686 registrations were kept track of [10]. From 1992 to 1997, a population-based study by either the Children's Cancer Group or the Pediatric Oncology Group calculated age-adjusted registration rates for patients with cancer under the age of 20 in the United States and Canada. This value is comparable to that found in that study. According to our experience, the patient's age and histologic subtype appear to influence the disease registration rates. Only 5% of the expected number of patients predicted by the SEER database had melanoma or thyroid carcinoma. On the other hand, during this time period, nearly one third of anticipated cases of nasopharyngeal carcinoma and two thirds of adrenocortical carcinoma were recorded.

Conclusions

The COG rare tumor initiative, on the other hand, has provided unprecedented opportunities for international collaboration. Given the very different molecular genetic lesions in these tumors in North American patients compared to Latin American patients, recruitment of several very large pediatric cancer centers in Brazil, where the incidence of adrenocortical carcinoma is much higher, has increased clinical trial participation, captured valuable biologic specimens, and provided unique opportunities for genetic epidemiology research. Collaboration with large pediatric cancer programs in India and South America, where retinoblastoma prevalence is significantly higher than in the United States, has resulted in similarly significant increases in study enrolment. In addition to allowing the export of clinical trial techniques and expertise to developing nations, expanded international outreach efforts in other categories of rare tumor types affecting children and adolescents will provide a solution to accrual. The increased group-wide participation in the COG's mandatory pediatric cancer research registry, the Childhood Cancer Research Network, is likely to increase participation in rare tumor registries. The impact of this new strategy is being looked at right now. Differential reimbursement rates for rare tumor registration and specimen submissions, in addition to additional per-case reimbursements for clinical trial enrolments, may help institutional study sites address resource constraints and increase enrolment in rare tumor clinical trials across all age groups. Additionally, using COG's AYA committee to mediate effective collaborations with adult cooperative groups could result in increased older patient registry enrolment and clinical trial participation.

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