A Registry for Central Nervous System Atypical Teratoid/Rhabdoid Tumor

INTRODUCTION

Atypical teratoid tumor/rhabdoid tumor (ATT/RT) of the central nervous system is an extremely rare and aggressive tumor of early childhood [1-6]. Because of both the rarity and the aggressive behavior of central nervous system ATT/RT, there is no standard therapy to recommend when faced with a patient with this tumor. Parents and treating physicians had to rely on anecdotal evidence at best. This rarity, and the poor outcomes with conventional infant brain tumor therapy, has resulted in a lack of clear treatment guidelines, and thus multiple approaches have been undertaken. It is for this reason that a registry of patients with CNS ATT/RT, their therapy, and their outcomes, was developed by Dr. Joanne Hilden MD, Dr. Jaclyn A Biegel Ph.D. and Jan Watterson BA. This registry was to create an outcomes database that would track patients through the continuum of the illness, and was to facilitate biology studies for this tumor through a linked but separate study.

ATT/RT was originally described as a variant of Wilms' tumor with rhabdomyosarcomatous features [7]. Subsequently the features differentiating ATT/RT from Wilms' tumor were clarified [8, 9]. Reports of extra-renal rhabdoid tumors ensued, with debate over a different or common cell of origin [10]. The association of renal and CNS ATT/RT [11] led to cytogenetic studies mapping abnormalities in tumors from both sites to a region on chromosome 22 [12] [13]. Molecular genetic studies have led to the identification of a putative tumor suppressor gene (INI1/hSNF5) at 22q11, and the current hypothesis is that mutations in this gene predispose children to the development of ATT/RT [14, 15]. While this represents tremendous progress, not all mutations have been elucidated, as 14% of cases studied have no identified mutation (Biegel communication at NCI workshop Jan 2001). Thus biologic and molecular genetic studies need to continue, and we are not yet able to design tumor-specific therapy.

In terms of treatment outcomes, the early literature reflects a time course from diagnosis to death of about 12 months in the great majority of patients with “standard” [5, 6, 16]. Subsequent reports document the use of more aggressive therapies (including surgery, chemotherapy with or without stem cell support, intrathecal chemotherapy, and early radiation), with some prolongation of the natural history of this tumor [1, 2, 3] [17]. From these reports it is not possible to clarify the role of a specific treatment modality, as many different regimens were used. This fact was born out in a workshop co-sponsored by the Pediatric
Brain Tumor Foundation and the National Cancer Institute[18]. The role of surgery has not been addressed in the literature nor has the role of radiotherapy or intrathecal chemotherapy for this tumor.

While the registry originated at Children’s Hospital in St. Paul, the main center for collection of data for the registry will now be the Cleveland Clinic Foundation due to Dr. Hilden’s relocation to Chair of the Department of Pediatric Hematology/Oncology. At the inception of the registry in 1995, expedited review at Children’s St. Paul IRB was accomplished. According to regulations acceptable at that time, some institutions did and some did not have IRB approval at their own sites.

**PURPOSE**

The purpose of this project is to collect information about the therapy and clinical course of patients with Teratoid/Rhabdoid tumor for a ATT/RT registry, so that in the future, the medical literature will include information about the treatment of this tumor, and about outcomes.

**METHODS**

When the diagnosis of Teratoid/Rhabdoid tumor is made, after written consent has been obtained, clinical information (such as age, sex, tumor size, X-ray reports, surgical reports, type of treatment given) from the child’s chart will be sent to the tumor registry, using data capture forms. The forms will be filled out so that only the child’s initials and date of birth are used, so that a child cannot be identified. The parents will not be contacted by the registry personnel, although there are cases where parents make the first contact with us.

Cases will be referred to the registry by either treating physician, evaluating pathologist, or by parent (through internet information sources regarding ATT/RT). In the case of parent referral, information will be obtained from the treating physician. Institutional IRB approval will be obtained from each institution participating in the registry. Our approach is to require that the diagnosis be confirmed by one of the pathologists who described this entity, Drs. Peter Berger, Lucy Rorke, or Bernd Scheithauer. Cases will be classified as ATT/RT if the initial diagnosis had been made or verified by one of the above pathologists. If this is not the case, Dr. Rorke will seek material for review.

A standardized data sheet will be provided to treating physicians listing the reports that are to be sent to the registry for abstraction. The registry will ask for radiology reports, operative notes, pathology reports, cytogenetics reports, discharge summaries, and treatment records in addition to patient demographics.
Registry personnel will abstract the information; follow-up information on surviving patients will be sought twice yearly from the treating physicians. We do so by initiating contact.

Therapy delivered to registry patients, primary and secondary resection of tumors, radiotherapy given, stem cell rescue, intrathecal chemotherapy will be documented in the registry. Recurrent or progressive disease, death from disease, status of alive with disease, toxicity, status of alive with no evidence of disease will also be documented in registry. Dr. Jacquelyn Biegel will independently ask physicians to obtain a separate informed consent from parents so archived or frozen tumor tissue can be sent to her for molecular genetic analysis. While parents are made aware by literature and by treating physicians that this is necessary testing for confirmation of diagnosis and to determine whether the disease is familial, our approach is to maintain a consent process that is separate from the registry.

REFERENCES


