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Special Therapy and Psychosocial Needs Identified in a Multidisciplinary Cancer Predisposition Syndrome Clinic

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Abstract

Identification of patients with cancer predisposition syndromes (CPSs) can provide vital information to guide care of an existing cancer, survey for future malignancy, and counsel families. The same underlying mutation responsible for a CPS may also result in other phenotypic abnormalities amenable to therapeutic intervention. The purpose of this study was to examine patients followed in our multidisciplinary CPS clinic to determine the prevalence and scope of medical and psychosocial needs. Data from a baseline evaluation of a single-center patient registry was reviewed. Eligible patients included those with a known or suspected CPS. Over three years, 73 patients consented and had successful follow-up. Utilization rate of special therapies, defined as speech (ST), occupational (OT), and/or physical therapy (PT), in the CPS population was 50.7%, significantly higher than a representative sample of children with special needs. Prevalence of 504/IEP (Individualized Education Plan) utilization was 20.5%. Patients with CPSs have a high prevalence of medical and psychosocial needs beyond their risk for cancer, for which early screening for necessary interventions should be offered to maximize the patient's developmental potential. Future research is needed to further define the developmental and cognitive phenotypes of these syndromes, and to evaluate the effectiveness of subsequent interventions.

Keywords

support care; cancer predisposition syndromes; oncology

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Conflicts of Interest

The authors have no conflicts of interest to disclose.

INTRODUCTION

While pediatric cancer predisposition syndromes (CPSs) account for a minority of pediatric cancers, recent reports have found that up to 33% of pediatric cancer survivors meet criteria for genetic evaluation.[1,2] Recognition of these syndromes is critical to optimize care and provide individualized counseling for the affected patients and their families. Much of the investigation devoted to these syndromes relates to their diagnosis, genetic basis, cancer risk, and preventative/therapeutic interventions in relationship to syndrome specific malignancies. However, there are many examples where in addition to cancer susceptibility, the causative genetic mutations may predispose the patient to a variety of phenotypic abnormalities that are clinically significant.

The standard of care for most CPSs is surveillance for malignancy with frequent screenings during the patient's interval of risk. There has been less attention devoted to identifying other physical, cognitive, and emotional difficulties that may be associated with the CPS and may require early intervention.[3,4] For example, Down syndrome is a CPS associated with an increased risk of leukemia, but clinicians recognize that management of these patients requires a much more involved approach than genetic evaluation and cancer screening. Recognizing this potential need, our institution established a multidisciplinary cancer predisposition clinic that engaged a variety of specialized health professionals including oncologists, geneticists, genetic counselors, child psychologists, social workers, audiologists, speech therapists, occupational and physical therapists. This model mirrored a pre-established program that had been in existence for several years for our pediatric cancer survivors. The goals of this clinic were threefold: 1) Determine susceptibility to cancer of referred patients and their relatives, 2) Implement diagnostic surveillance methods to optimize early detection and treatment of future malignancy, 3) Provide comprehensive care to help meet the wide scope of needs due to phenotypic manifestations of their syndrome, or late effects from a cancer or its treatment. The current report characterizes the features of this diverse population and quantifies the need for specific therapeutic interventions.

MATERIALS AND METHODS

Patient selection

A patient registry was created in 2013, after study approval by our university's Institutional Review Board. Recruitment was conducted from patients directly referred to our cancer predisposition clinic, or patients with a preexisting treating relationship with either the Hematology/Oncology or Genetics divisions. Eligible patients included those with a known or suspected CPS. Of note, patients with Down syndrome and Neurofibromatosis are served by specific clinics at our institution, and are therefore not included in this study. Additionally, at the time of data collection all patients with Li-Fraumeni syndrome seen at our institution were either at end of life or undergoing therapy, and were therefore not actively followed in our clinic. All patients were <18 years of age.

Clinical Data Collection

Participation involved parental completion of an initial survey that broadly screened for the presence of any clinical difficulties experienced by this population. Select elements of the Childhood Cancer Survivor Study (CCSS) initial long-term follow up survey, the Pediatric Symptoms Checklist (PSC), and the Beckwith Wiedemann Syndrome Questionnaire were utilized as they provided a comprehensive survey of questions to capture the scope of potential problems for this patient population. The CCSS questionnaire was developed to assess the physical, cognitive, and emotional health of childhood cancer survivors, and provides a comprehensive screening tool to a broad scope of physical, cognitive and emotional problems.[5] The Pediatric Symptoms Checklist (PSC) is a brief screening questionnaire used by pediatricians and other health professionals to identify psychosocial problems in children.[6] An abnormal score above the cutoff (24 for children age 3–5, 28 for children age 6–18) suggests the need for further evaluation by a qualified health professional. The Beckwith Wiedemann Syndrome (BWS) Questionnaire characterizes the cardinal features of BWS, and was administered to patients with BWS or Isolated Hemihyperplasia (IHH).[7] In subsequent visits, the CCSS Long-Term Follow up survey and the Pediatric Symptom Checklist were re-administered, not more frequently than once a year to identify the development of new issues. The patient's clinical records were also reviewed at each visit to collect demographic information and medical history.

Statistical Analysis

Data was recorded in REDCap (Research Electronic Data Capture) software, a web-based platform for collection and management of research data.[8] Special therapies were defined as ST, OT, or PT. Prevalence of therapy needs, intellectual disability, learning disability, need for 504/Individualized Educational Program (IEP), behavioral disorders, and mood disorders was collected from parental reporting on the initial questionnaire form, and summarized using descriptive statistics. Answers on the questionnaire of "Don't Know" or those left blank were treated as "No" for this analysis. Malignancies, prior surgeries, and ICD-10 codes for comorbid medical conditions were collected from chart review.

The proportion of patients with abnormal screening scores on the PSC was compared to that of a large pediatric primary care survey (12%, n=18,045 patients).[9] The proportion of patients with a 504 or IEP was compared to the national average in public schools, reported in the 2013–2014 Civil Rights Data Collection (CRDC) survey (14%, n=50,035,744).[10] A two-sided, one-sample test for difference of binomial proportions was used to compare these proportions. Need for special therapy was compared with two nationally representative surveys, the 2011–2012 National Survey of Children's Health (NSCH), and the 2009–2010 National Survey of Children with Special Health Care Needs (NS-CSHCN). The NSCH was a cross-sectional telephone survey of children aged 0–17, with a sample size of 95,677 completed interviews.[11] Need for special therapy in this sample was defined as "need or use of special therapy such as occupational, physical or speech therapy due to health conditions lasting 12 months or longer."

The NS-CSHCN was a cross-sectional telephone survey of children aged 0–17 with a certain set of qualifying conditions, and a total sample of 40,242 interviews.[12] Children qualified

based on experiencing one of five health consequences due to a health condition that had lasted or was expected to last 12 months. These five consequences were 1) Use or need of prescription medication; 2) Above average use or need of medical, mental health or educational services; 3) Functional limitations compared with others of same age; 4) Use or need of specialized therapies (OT, PT, speech, etc.); 5) Treatment or counseling for emotional or developmental problems. A two-sided, one-sample test for difference of binomial proportions was used to compare the need for special therapies in the CPS sample with the NSCH and NS-CSHCN populations. Analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). The threshold of statistical significance was defined as $\alpha=0.05$.

RESULTS

Demographics

A total of 110 patients were seen during the study period (February 2012 to June 2015). Of these, 73 patients consented and had successful follow-up. Eight patients were consented but never completed the initial questionnaire. Demographic and clinical data from the study population are given in Table I. Medical characteristics and specific therapy needs for this population are listed in Table II. Fifty-eight patients had valid PSC questionnaires for analysis (13 patients were too young, 2 had too many missing answers (4 or more items left blank)). The prevalence of intellectual disability was 6.85%, with 13.7% reporting a learning disability and 20.5% with an established 504/IEP plan at their school. Utilization of therapy services was high, with 28.8% of patients receiving OT, 37% receiving PT, and 30.1% receiving ST. The average number of medical problems reported was 2.74 per patient (2.69 in patients with history of malignancy, and 2.77 in patients without). The rate of abnormal screening on the PSC questionnaire (8.62%) was not significantly different than that found in primary care settings (12%, p= 0.43). The rate of 504/IEP utilization (20.5%) was higher, but not significantly different than the national average in public schools (14%, p=0.11)

Taking the utilization of any special therapies (OT, PT, ST) together, 50.7% of the CPS population was engaged with at least one of these services. This was significantly higher than the needs in both NSCH (4%) and NS-CSHCN (26.6%) surveys (Table III, $p < 0.0001$ for both). Thus, patients who were served by our CPS clinic had a substantially greater need for services than the general population and a representative sample of children with special needs, despite a referral pattern that was focused on cancer screening.

DISCUSSION

Research has shown the importance of a multidisciplinary approach to hereditary cancer management, involving genetic assessment and tumor screening. For example, Villani et al. demonstrated that a biochemical and imaging screening protocol could increase tumor detection and decrease mortality in patients with Li-Fraumeni syndrome.[13] Our institution established a cancer predisposition clinic with the intention of providing a comprehensive medical home to serve our CPS patients. While investigation in this field has been devoted to the genetic assessment and cancer screening for these syndromes, this is the first study to analyze the scope of medical, neurocognitive, and emotional phenotypes of this population.

Our clinic population was considerably diverse, representing over 14 different CPSs. Overall, there was high medical need, reflected by the number of comorbid medical conditions (2.74) even though less than half of the cohort (39.7%) had a prior diagnosis of malignancy. In terms of special needs, prevalence of 504/IEP (20.5%) and special therapy utilization (50.7%) were notably high. In particular, the need for special therapies was significantly higher than a representative sample of children with special health care needs. Special therapy utilization among patients with BWS or IHH was 51.4%, even though these patients had much lower prevalence of malignancy (10.8%) compared to other diagnoses seen in our clinic (70.3%). This result lends further evidence to recent reports that patients with BWS may be at risk for neurodevelopmental difficulties in contrast to prior assumptions.[14] Patients with CPSs may benefit from therapeutic services for a variety of reasons. These include effects of a cancer (e.g. OT for a retinoblastoma patient), a cancer's treatment (e.g. PT for a patient with chemotherapy-related neuropathy), or a phenotypic manifestation of their syndrome (e.g. ST for a BWS patient with macroglossia). While more research is needed to demonstrate the specific benefits of these services in this population, this study suggests that patients with a CPS are at high risk for requiring a variety of services that may not be evident without broad screening, independent from their history or risk of malignancy. Early screening combined with timely interventions such as OT, PT, ST, and special education accommodations have been shown to improve outcomes for children with a variety of conditions, including developmental delay and autism.[15,16]

There are several limitations to this study. Most variables were based on parental reporting. Also, we were not able to collect specific ST, OT, and PT evaluations for each patient since these services were not all obtained within our health network. Future efforts will focus on more extensive characterization of the nature and scope of these deficits and to assess the impact of implemented therapies on outcomes. Further limitations may have led to a selection bias in our population. As a tertiary medical center, we are often referred more complex patients, and healthier patients with CPSs may not seek care in our clinic. Also, some CPSs may have subtle manifestations and may not come to the attention of our clinic. Thus, patients with fewer medical needs may fail to be recognized as having a CPS and may have milder phenotypes or fewer medical needs. Further expansion of this cohort will hopefully give us better insight into the variability and spectrum of these clinical observations.

In summary, this report suggests patients with CPSs have several associated medical and neurocognitive difficulties which may not be directly associated with a cancer diagnosis. Children with a known or suspected CPS may benefit from coordinated care that incorporates genetic work-up, malignancy screening, and comprehensive evaluation for special needs. Future research is needed to further delineate optimal service evaluation and treatment in this diverse patient population.

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Table I:

Patient Demographics

Total patients with CPS	Number	Percentage (%)
	73	
Age at survey completion		
0–6	42	57.6
7–12	22	30.1
13–18	9	12.3
Gender		
Male	43	58.9
Female	30	41.1
Ethnicity		
Caucasian	59	80.8
African American	13	17.8
Other	1	1.40
Diagnosis		
IHH*	23	31.5
BWS	14	19.2
Pleuropulmonary Blastoma	8	11
Personal and Significant Family History of Malignancy	6	8.22
Retinoblastoma	6	8.22
Von Hippel-Lindau	4	5.48
Peutz-Jeghers	2	2.74
Hereditary Neuroblastoma	2	2.74
Cowden	1	1.37
Familial Adenomatous Polyposis	1	1.37
Gorlin	1	1.37
Wilms-related	1	1.37
Lynch syndrome	1	1.37
Bannayan-Riley-Ruvalcaba	1	1.37
Noonan syndrome	1	1.37
PI3CKD disorder	1	1.37

* IHH: Isolated Hemihyperplasia

Table II:

Characteristics and Therapy Needs of CPS patients

	Number	Percentage (%)
Medical and Cognitive Characteristics		
Intellectual Disability	5	6.85
Learning Disability	10	13.7
Mood Disorder	1	1.37
Behavioral Disorder	3	4.11
Medical Conditions (mean, per patient)	2.74	NA
Malignancy (Y/N)	29	39.7
Therapy Needs		
OT	21	28.8
PT	27	37.0
ST	22	30.1
504/IEP	15	20.5
Cancer Treatment		
Surgeries (mean, per patient)	2.79	NA
Exposed to Chemotherapy	24	32.9
Exposed to Head/Neck Radiation	6	8.22
PSC	58	
Positive score	5	8.62

Table III:

Therapy Needs Comparison with the NSCH and NS-CSHN

	Special Therapies[a] (%)
CPS	50.7
NSCH[*]	4
NS-CSHCN[#]	26.6

[a]Special Therapies= Physical, Occupational, or Speech Therapy

[*]CPS needs vs. NSCH, $p < 0.0001$

[#]CPS needs vs. NS-CSHCN $p < 0.0001$