Current practice of cancer predisposition testing in pediatric patients with CNS tumors

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Background

Pediatric central nervous system tumors (CNSTs)

- Recent studies have found that **approximately 8.6% of all pediatric patients with CNSTs have underlying hereditary cancer predisposition.**
- Pediatric CNSTs are known to be associated with many hereditary syndromes, including:
  TP53, FAP, NF1, NF2-related schwannomatosis, Lynch syndrome/cMMRD), TSC, Gorlin syndrome, etc.

Current CNSTs germline testing guidelines

- Current guidelines are pathology specific, which is limiting compared to broader germline testing guidelines for adult-onset cancers with similar genetic predisposition (8-10%).
- " Pediatric Central Nervous System Cancers " (July 2022) is the first attempt at national guidelines, but only discusses pediatric diffuse high-grade gliomas.
- Despite the clinical significance of identifying a hereditary cancer syndrome and the growing evidence of their prevalence, **there is a lack of national consensus on the optimal germline testing approach.**

Objectives

Describe the current practice of oncology and genetics providers **when assessing pediatric patients with CNSTs for genetic predisposition** at many clinical sites across the Unites States in terms of:

- Provider roles in germline testing process
- How testing decisions are made
- The process of ordering germline testing

Methods

The Institutional Review Board of Cincinnati Children's Hospital Medical Center granted exemption of approval for this study.

Inclusion Criteria

- Oncology and genetics providers in the U.S. who identify as providing clinical care to pediatric patients with CNSTs.

Data Collection

- Redcap survey emailed to NSGC, ASPHO and an email list of 25 neuro-oncology providers created by the research team open from 8/3/2022 to 9/30/2022.

Data Analysis

- Descriptive statistics were used to describe the study population as frequency(proportion).
- Survey responses were analyzed by medical specialty or by expertise (i.e. average annual patients with CNST treated).
- The following responses were removed from the association analysis: I am unsure, I am not the provider that performs this role and missing responses.
- All analyses were performed using SAS 9.4 (SAS Institute, Inc.; Cary, NC).
- A p value less than 0.05 was used to indicate the statistical significance without correction on multiple testing given the exploratory nature of the study.

Demographics

Total participants: 60

- Gender: Females= 48(81); Male=10(17); Non-binary=1(2)
- Race: White= 47(78); Asian= 12(20); Ashkenazi Jewish= 1(2)
- Ethnicity: Hispanic/LatinX= 4(7); Non-Hispanic/LatinX= 55(93)

Respondent specialty and expertise

Average number of pediatric patients with CNST treated per year	
<25	25 (42)
26-50	13 (22)
51-75	9 (15)
76-100	5 (8)
>101	8 (13)
Year graduated with terminal degree	
<2000	11 (19)
≥2000	48 (81)
Medical specialty	
Pediatric oncologist	10 (17)
Pediatric neuro-oncologist	21 (35)
Genetic counselor	26 (43)
Geneticist	2 (3)
Region of workplace	
West	8 (15)
Midwest	22 (41)
Northeast	7 (13)
South	17 (31)

*Data presented as frequency(percent)

Results: Provider roles

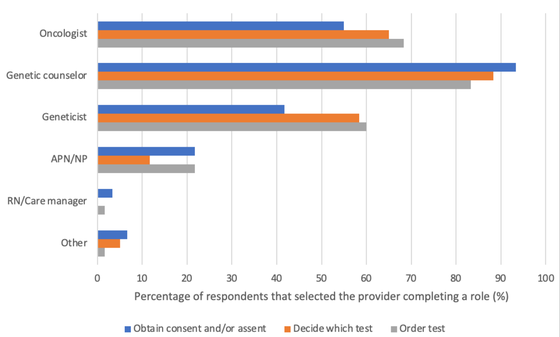

Figure 1 Provider roles in the germline testing process for pediatric patients with CNST.

Genetic counselors and pediatric oncologists are completing most of the germline testing roles

Other providers reported by respondents:

- Physician assistants with genetics certification
- Clinical research coordinators

Results: Germline testing decisions

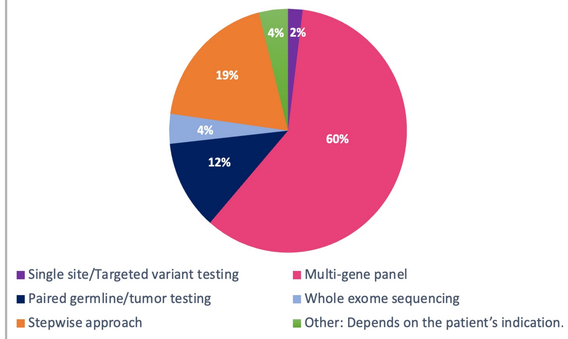

Figure 2 Most often germline test ordered for pediatric patients with CNSTs

Red flag diagnoses

- The following survey item assessed 18 CNSTs in total.
- Listed below are CNSTs that are **more commonly associated with genetic predisposition, yet still lacking consensus** on offering genetic testing among respondents.

In the absence of suspicious family history, ***for which indications/diagnosis do you offer germline testing*** *for a pediatric patient with a CNST? Select all that apply.*

	Genetics N=28	Ped-neuro onc N=21	Ped-onc N=10	P value
Choroid plexus carcinoma	21 (75)	19 (90)	6 (60)	0.15
Hemangio-blastoma	17 (61)	9 (43)	5 (50)	0.48
Medullo-blastoma	18 (64)	13 (62)	2 (20)	0.050
Schwanno ma	21 (75)	14 (67)	5 (50)	0.34
ATRT	21 (75)	17 (81)	7 (70)	0.78
High grade glioma	18 (64)	9 (43)	3 (30)	0.13

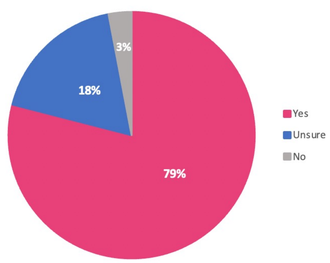

Figure 3 At your institution, are genetics providers a part of the multidisciplinary team that provides care to pediatric patients with CNSTs?

- Of the respondents that selected yes or unsure (N=47), **33% selected that all** pediatric patients with CNSTs referred for or offered genetics services

Future Directions

1. **Further explore the role of other providers** treating pediatric patients with CNSTs, particularly obtaining consent/assent and deciding which testing to order.
2. **Investigate the optimal germline testing approach** for pediatric patients with CNSTs to inform creation of guidelines.
3. **Establishment of national guidelines** to address inconsistencies in access and practice of genetics care across institutions **by serving as a universal genetics resource** for non-genetics professionals.

Conclusions

Provider roles and the process of ordering testing:

- **Multiple providers are involved** in different steps of the germline testing process for pediatric patients with CNSTs, with genetic counselors and pediatric oncologists completing most of these roles.

Testing decisions

- Most oncology and genetics providers reported ordering muti-gene panels.
- The circumstances (i.e. universal testing vs pathology guidelines) and diagnoses influencing when providers would offer testing **varied among and between** oncology and genetics providers.
- **More neuro-oncologists identified pathology guidelines** as influential in testing decisions, paralleling the integration of molecular tumor testing into patient care, particularly for medulloblastomas and high-grade gliomas.

Testing decisions: Red flag diagnoses

- Even for CNST indications serving as more obvious red flags for testing, there was variability in providers' decisions to offer germline testing **indicating inconsistencies in the genetics care of pediatric patients with CNSTs**.
- Most surprisingly, there was **a lack of consensus even among genetics professionals** for CPCs (which uniquely do have national guidance housed in adult HBOC NCCN guidelines for testing regardless of age and family history).
- Consistent genetics care is essential for vulnerable, rare pediatric populations like CNSTs.

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