Gliomatosis Cerebri: An Enigmatic Pattern of Growth

Feature Article by Tab Cooney, M.D., Pediatric Neuro-Oncology, Dana-Farber/Boston Children’s Cancer and Blood Disorders Center, Harvard School of Medicine

Introduction
The term ‘gliomatosis cerebri’ was first introduced in 1938 and describes an extensive pattern of glioma spread throughout the brain – at least three lobes or more. Up until 2016, gliomatosis cerebri (GC) was considered a diagnosis all to its own. However, over time we have realized that GC occurs across different types of diffuse glioma. There are no histologic or molecular features, as far we know, that distinguish gliomas with a GC growth pattern from other types of glioma. GC was therefore removed as a diagnosis from the revised 2016 WHO classification of Tumors of the Central Nervous System (CNS) [1]. Seen in both adults and children, best estimates suggest glioma with a GC growth pattern occurs in approximately 40 people every year, although efforts to capture this data are sorely lacking. It remains unclear why some gliomas develop a GC growth pattern, and much more research is needed.

For important background information on pediatric low-grade and high-grade gliomas including diffuse glioma, please review the insightful articles on this website.

Presentation
Gliomas with a GC growth pattern can spread to other areas of the CNS quickly and deeply, but they do not travel outside of the CNS (Figure 1). Symptoms, therefore, depend on the tumor’s location and the patient’s age. Some possible symptoms include seizures, fatigue, mood changes, changing in thinking and memory, and headaches [6]. On an MRI, the pattern usually shows no obvious mass, but rather widespread abnormality. Sometimes, a tumor mass exists with a widespread fluffy looking tumor pattern.

(continued on page 2)
Cont.....Gliomatosis Cerebri

Treatment
There is no standard of care for gliomas that have a GC growth pattern. Since removing all the tumor is impossible, surgery has usually been limited to biopsy to determine the tumor type. As with all types of high-grade or diffuse glioma, gliomas with GC growth pattern may respond well to radiation therapy, but patients should discuss the full risks and benefits with their healthcare team, as radiation to a large volume of brain tissue puts normal brain tissue at risk for problems. Clinical trials with chemotherapy, targeted therapy, and/or immunotherapy may be available and can be a possible treatment option. To date, there are no clinically directly therapies specifically for GC.

Novel Discoveries
Efforts to evaluate cellular evolution, the tumor microenvironment, and neuronal circuitry are bringing us closer to understanding the GC phenomenon, and glioma invasion in general. It is now recognized that the nervous system plays an important role in the growth of cancers such as glioma [2]. Glioma cells can plug into – and feed off – the brain’s neuronal network. The connection between glioma cells and neurons, if better understood, may help explain the travel pattern of gliomatosis cerebri. Efforts to characterize immune cell infiltration are just beginning for pediatric and adult high-grade glioma, and much more work is needed to understand whether the type of immune infiltration affects growth pattern [3].

Canine Gliomatosis Cerebri
The medical community has long recognized the need to collaborate across disciplines to understand and ultimately cure rare diseases. In more recent years, we have broadened our reach across species. At present, veterinarians and human medical doctors are collaborating on an NIH-funded clinical trial in which the same immunotherapy, the oncolytic virus M032, is being used to treat people and dogs with glioma (NCT02062827). Gliomatosis cerebri is a well-described phenomenon in dogs, and many cases have been published in medical literature over the last couple decades (Figure 2) [4]. It is likely we will soon hear of joint translational and clinical efforts to investigate GC in human and canine patients.

Figures

Figure 1. George et al, J Child Neu-ro, 2015. Axial FLAIR MRI of a 19- year-old gliomatosis cerebri patient [5].

Figure 2. Schweizer-Gorgas et al, Vet Radiol Ultrasound, 2018. Transverse T2-weighted image of diffuse gliomatosis cerebri in a canine (Continued on page 3)
The International Gliomatosis Cerebri Platform

Bolstered by the support and enthusiasm from several patient advocacy groups, an international network of experts studying and treating GC developed the International Gliomatosis Cerebri Platform in 2020. The Platform serves as a center of communication for translational scientists and is developing as a central resource of clinical and biological information from GC patients across the world. The Platform’s long-term goals are to establish and maintain a highly collaborative, global research infrastructure dedicated to pre-clinical and clinical projects related to gliomatosis cerebri.

For more information, please visit the website: https://gliomatosis.dana-farber.org/

A Call to Action

The rarity and poor prognosis make gliomatosis cerebri a highly challenging phenomenon to understand. Indeed, understanding why and how gliomatosis cerebri occurs will require concerted effort from all stakeholders—patients and families, advocacy organizations, and physician researchers. Scientists will need to pool their resources across laboratories, institutions, and continents. As the present has provided us with the novel sequencing tools, global communication methods, and a collaborative mindset, we hope the future will hold the cure for those with gliomatosis cerebri.

References:

Upcoming Events 2020

Childhood Brain Tumor Conference: Education and Updates
(TBD—June date change due to COVID-19)
Our website will have updates and other information soon. We have an excellent speaker line-up.

CBTF Party 2020
Glenview Mansion, Rockville—Saturday, December 5, 2020
We hope to see you in December!

Fundraising events and donations are significant to our ability to fund excellent research and programs. Thank you for your support!

Thank you so much!
Be AMYazing, Reston Youth League—2020 Virtual Duathlon
FD Associates, Inc.
Roger and Bashi Packer
Saint John Paul II School—Run with the Saints

Special thanks from CBTF to the research and medical community for their dedication.

CBTF Sponsorships:
2020 -19th International Symposium on Pediatric Neuro-Oncology
2020 Funded grants to be announced in the next newsletter edition.
Here I am so all alone, sitting here with no one home
Another day with nothing to do, Oh how I wish I was like you
I am so bored I’m writing this poem, Oh how I wish I was not home
School is where I am supposed to be, not in the hospital collecting pee
Cancer sucks it makes me mad, I wake up feeling so, so sad
And when it’s done, I can’t wait to run, run, run

Poem by Lenn, written as a child when on treatment, now an adult.

Run with the Saints Fall Festival (Continued from page 1)

On October 26, 2020 the 21st Run with the Saints (RWTS) Fall Festival honoring Lauren Lockard was held at Saint John Paul II (St.JPII), Houston, Texas. The proceeds from this event directly benefits the Childhood Brain Tumor Foundation and St.JPII.

This event has been held annually to honor the memory of Lauren Lockard, a brave, fun-loving, and talented student who loved athletics. The festival brought Lauren’s family, friends, and faculty together with activities such as the 5K and Kids’ race, Trunk or Treat, and a Pumpkin Patch. The attendees always have a wonderful time. The planning committee and volunteers seek sponsors and spread the word to rally supporters.

The Childhood Brain Tumor Foundation is forever grateful to St.JPII, the staff, organizers, and supporters for raising funds for CBTF and the school. Thank you!!

Please support the Childhood Brain Tumor Foundation
Visit our GIVE ONLINE donation button:
https://www.givedirect.org/donate/?cid=1605
Be part of the solution in helping fund vital research initiatives for cures!

In Honor of

CBTF Advisors
Ella Day
Jackson Dundon
Sam Lunn
Alicia Gonzalez
Roger and Bashi Packer

CBTF Advisory
Cooper Ian Raleigh
Coach Jimmy Rizzo
Vincent Sanudo
Kathy Triebwasser
Camden Wiseman
The Childhood Brain Tumor Foundation is dedicated to funding research for all pediatric brain tumor types. Please contact us if you have any questions: cbtf@childhoodbraintumor.org To make a donation to our cause, visit our secure website: www.childhoodbraintumor.org

The Annual Superheroes 5K and Kids’ Run 2020, originally planned for April, is being held in July as a virtual race due to the COVID-19 concerns. [https://tinyurl.com/5kCBTF20](https://tinyurl.com/5kCBTF20)

Currently we have 13 great teams and we are excited to have their support! In our next issue we hope to share some of the photos and stories from our participants.

**Virtual Teams 2020**

Run for Robert
Team Awesome Alicia
Heads Up!
Team Camden
Team Maya
Tay’s Team
Superkidz
Brain Tumor Trouncers
TEAM GEOFF
MCPS Athletic Directors
Team Yehudis
Speedsters
Team Rebecca

Thank you to our friends who donate through workplace charitable giving campaigns this year. It was a pleasure meeting some of you at the CFC fairs!

The Childhood Brain Tumor Foundation, friends and families are very appreciative of your support.

(National) CFC 12035

Charity Campaign and other independent campaigns have also been very supportive. We appreciate the support we are given. Thank you!

Maryland Charity Campaign

The Childhood Brain Tumor Foundation participates in the Combined Federal Campaign (CFC) and Maryland Charities.

Campaign donations may be made for the United Way (UW) through the “donor option” or “donor choice.” Please check with your employer in reference to UW campaigns. You may write us in.

ISPNO 2020, VIRTUAL 5K, Give2Charity, Resources

ISPNO 2020

The 19th International Symposium on Pediatric Neuro-Oncology

The Childhood Brain Tumor Foundation is a SILVER sponsor for the 19th International Symposium on Pediatric Neuro-Oncology. Meeting date has changed and the ISPNO will now be held, **December 11 to December 13, 2020** in Karuizawa, Nagono, Japan.

As always the ISPNO brings together clinicians, researchers, allied health professionals, and experts.

HELPFUL RESOURCE LINKS

**Pediatric Brain Tumors (PubMed),**
by Drs. Elizabeth Wells and Roger Packer

**Memorial Sloan Kettering Kids—Pediatric Brain Tumors**
[https://tinyurl.com/y7fhk4k](https://tinyurl.com/y7fhk4k)

**A.D.D. Warehouse**
GIVE2CHARITY

Help children with brain tumors.

We need your support.

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prognosis and quality of life for children suffering from
brain tumors. Every dollar that raises money to improve.

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or volunteer services. To help with our operations.

Please let us know by e-mail if your address has changed.

Their generous support is deeply appreciated.

Thank you to the Rocking Moon Foundation.

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Table of Contents.

Next Issue: Feature article, Grants funded in 2020.

Our new website is open.

Page 1: Survivors' Forum: In Honor of Survivors. Thank you.

Page 2: Upcoming events: 5K Run with the Saints.

Page 3: ISPNO, CFC, Virtual 5K Teams, Give2Direct, Resources

Page 4: Survivor Profile: Tab Cooney

Page 5: Survivor Profile: Colleen Snyder

Survivor Profile: Jeanne P. Young

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