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Headlines

Summer 16 A newsletter for brain tumour patients and their families

MY STORY

The power of small deeds: The importance of 'showing up' when someone you know has a brain tumour

By Suzanne Heft

"YOU HAVE A BRAIN TUMOUR." If you've heard these words, then someone you care about has been given a diagnosis and sent on a terrible journey.

I know a little bit about this journey. In early 2014, my husband collapsed at work — a seizure, caused by an inoperable brain tumour. He spent the next year enduring gruelling radiation and chemotherapy while I struggled to support our family and raise our sons. As his primary caregiver I learned some of what it takes to survive.

My husband's brain tumour meant he could not drive, earn a living, read or write. Tasks like working a TV remote or checking voice mail became incredibly taxing. Radiation and chemotherapy altered his body. Though he remained courageous and deeply loving throughout his ordeal, his daily vitality was greatly diminished. My peace of mind evaporated.

Relatives, neighbours and friends asked: '*What can I do to help?*' People didn't know what to do. Many folks struggle with this. Here are my top suggestions:

1. Meals. Everyone has to eat and meal preparation is hard when you're sick. There is a great online scheduler for this purpose called Meal Train. www.mealtrain.com People sign up and send over meals, one week at a time. This generosity is an extraordinary blessing and supremely helpful. There is enormous life-affirming power in the act of helping to feed the sick.
2. Mail. Yes, honest to goodness, mail: cards, notes, or postcards. Reach out and remind the family that they are not alone. A dear friend sent my husband a greeting card every week for 8 months, with a silly joke inside each one. Each one made his day. Illness can be isolating. Mail helps the patient know he/she is 'still in the world.'
3. Music, books and treats. Send your sick loved one an iPod with playlists for those endless hours of chemo transfusions or waiting for blood-work. Buy an Apple TV, or a Netflix gift subscription or a boxed set of DVDs for sleepless nights and long days. Load up an MP3 player with audio books. Other treats might be a cosy pair of new slippers or pajamas, a robe, a soft blanket or throw, assorted teas and a new teapot, a bird feeder and bag of seed for the garden. The point is to be thoughtful. One friend stopped at my house without telling me and filled my planters with potted geraniums (knowing I had no time to do it myself!). A small infusion of beauty or comfort shows your caring and eases pain.
4. Time. Many tasks remain undone when illness descends upon a household: getting winter tires on, mowing grass, shovelling snow or cleaning eaves. Take these on. Make a schedule and solicit friends to carpool kids or walk the dog. Offer to manage communications: send out notes for the family or start a blog. Buy a caregiver a concert ticket or just give them 'the afternoon off' while you take their place sitting with the patient – so the caregiver gets a much-needed rest. Time is so precious. Give some back.

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2016 American Society of Clinical Oncology (ASCO) meeting

By Dr. Brian Thiessen,
Neuro-oncologist, Vancouver Centre

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY held their annual general meeting in Chicago in June 2016. This is the largest international cancer meeting and brings oncologists from all corners of the world to hear about new research in treating cancer. The neuro-oncology news was as usual a mixed bag which included practice-altering advances as well as a disappointing lack of updates on the status of several completed immunotherapy trials. There was no report on the phase 3 trials in the Rindopepimut vaccine or the DCVax vaccine. There was no update on polio virus. There were no outcome results on the phase 2 trial of the immune checkpoint inhibitor, nivolumab, although safety data were presented. So we are still in a holding pattern regarding any new information about this exciting avenue of cancer research.

But we did learn a few important things. The results from the Elderly Glioblastoma trial (CCTG CE6) performed by Canada and Europe were presented by Dr. James Perry from Sunnybrook Hospital in Toronto. The talk was even awarded a plenary presentation, which is very prestigious since only six presentations for all of cancer are granted plenary status. A plenary presentation is a meeting or session attended by all participants at a conference or assembly. The study showed that combining three weeks of radiotherapy with temozolomide chemotherapy was more effective than radiation alone in patients over age 65. This benefit was most pronounced in patients with tumours that showed a genetic defect called methylguanine methyltransferase (MGMT) promoter methylation, but even MGMT unmethylated tumours showed a small benefit. Prior to this study, it was uncertain a) whether older patients could tolerate the combined treatment and b) whether the combination would significantly add to survival. So this study will now change our pattern of practice and we will offer both radiotherapy and chemotherapy to almost all glioblastoma patients, regardless of age.

We also had an update from the ongoing CATNON trial. This study is looking at another group of brain tumour patients where the benefit of chemotherapy combined with radiotherapy is unknown. These are patients with grade 3 astrocytomas. The study compares radiotherapy alone to radiotherapy with temozolomide chemotherapy. The early data show that the addition of chemotherapy is also beneficial for these patients. Generally in BC, we were offering chemotherapy to this population anyway, so it is reassuring to know we've been doing the right thing all along.

There was also a somewhat controversial phase 3 EORTC trial 26101 for relapsed glioblastoma presented. This study looked at a combination of bevacizumab (an antiangiogenic agent that stops a brain tumour from making new blood vessels to feed itself) with lomustine, also known as CCNU (an older chemotherapy agent), versus lomustine therapy alone. The combination treatment delayed progression of the glioblastoma but it didn't alter overall survival of patients. The controversy in this trial stems from the fact that the patients on the lomustine alone arm only received 1 cycle of lomustine on average, and after stopping lomustine, 36% of them received bevacizumab. Given that so many patients ended up receiving both drugs, it's very hard to judge the effectiveness of either agent. In the end we can likely say that it matters less when you give bevacizumab, but that when you do choose to give it, it will hold off the tumour better than just chemotherapy.

Finally, results from a phase 2 trial done at the University of California in San Francisco were presented. This trial looked at giving temozolomide chemotherapy alone to patients with progressive low grade oligodendrogliomas. Two years ago we learned from the RTOG 98-02 trial that giving radiation with chemotherapy in low grade gliomas was superior to radiation alone. But questions about giving chemotherapy alone persisted. The California study showed that patients who received radiation combined with chemotherapy had a better response and lived longer than those who received chemotherapy alone.

Bottom line, from what we've learned at ASCO 2016: a combination of radiation and chemotherapy is the standard of care for virtually all glioma types. Now if only we had some answers regarding immunotherapy. Perhaps ASCO 2017 will provide these.

For previous ASCO Updates, see archived copies of Summer Headlines issues.

Editions of *Headlines* are also available as a pdf download on our website at:
www.bccancer.bc.ca/health-info/types-of-cancer/brain-central-nervous-system/headlines
If you would like to submit an article, ask a question, or serve on our patient and family editorial board, please contact Rosemary Cashman at rcashman@bccancer.bc.ca or 604 877 6072 (phone) 604 877 6180 (fax).

How the 2016 World Health Organization (WHO) classification affects the diagnosis and management of brain tumours

By Stephen Yip, M.D., Ph.D., FRCPC
Neuropathologist, Vancouver General Hospital and BC Genome Sciences Centre

THE WORLD HEALTH ORGANIZATION (WHO) provides an internationally recognized classification of brain tumours that is used by neuropathologists around the world to diagnose these diseases. Since the previous WHO update in 2007, there have been a number of significant advances in our understanding of the molecular characteristics and behaviour of certain types of brain tumours.

The most recent WHO Classification (WHO2016), released this year, is the result of two years of hard work by international experts in the fields of neuropathology, neuro-oncology and molecular pathology. WHO2016 combines new information about molecular characteristics and importantly, it also affects the way oncologists treat these diseases.

Examples of molecular characteristics include mutations in a gene called isocitrate dehydrogenase *(IDH1/2)*, or the loss of genetic material on chromosomes 1 and 19. Chromosomes are thread-like strands that come in pairs and contain the genes responsible for hereditary information. Most humans have 23 pairs and each strand has a short (p) and a long (q) arm. Characteristic changes in tumours affect how we diagnose the various types of gliomas, including astrocytoma, oligodendroglioma and glioblastoma.

In the past, classification of gliomas was based primarily on how tumour cells and tissue looked under a microscope ("histology") and how fast cells grew and how much tumour cells resembled or were different from the non-cancer cells of origin ("grade"). For gliomas, the main histological types have included oligodendrogliomas and astrocytomas. The grade of the tumour ranges from the most benign (grade I) to the most malignant (grade IV).

Brain tumours rarely metastasize or leave the central nervous system and are therefore not "staged" as other cancers are. Staging refers to how extensively the cancer has spread beyond the original site of disease. This occurs commonly with some cancers, like lung and breast, but very infrequently with brain cancer.

WHO grade II and III gliomas (also called infiltrating gliomas because of their tendency to invade brain tissue) include those with cells that look like astrocytomas or oligodendrogliomas. The majority of these carry *IDH1/2* mutations. In addition, many of these are characterised by a change in an amino acid in position 132 (R132H) in the *IDH1* gene. Amino acids are the building blocks of proteins and are found in every cell of the body. This change can be clearly identified by pathology testing and provides an accurate diagnosis of an infiltrating glioma.

Oligodendrogliomas were previously identified by the way the tissues looked, including a cellular appearance resembling "fried eggs," and a fine network of blood vessels that look like "chicken wire." However, diagnosis by these histological features alone failed to accurately predict how these tumours behaved. Oligodendrogliomas are expected to respond well to treatment, but sometimes they behave like more aggressive tumours. Some oligodendroglial tumours are characterized by changes in their genes. The loss of genetic material on the p arm of chromosome 1 and the q arm of chromosome 19 is associated with a tumour that does behave well; those tumours that do not have this loss of genetic material tend to behave more malignantly and do not respond as well to treatment. As a result of this discovery, a more accurate diagnosis can be made.

The WHO2016 classification system continues to include histological descriptions that have been used for the past 100 years, but it gives priority to more precise molecular characteristics such as the presence or absence of IDH mutation and the loss or retention of 1p19q chromosomal material. In the 2016 classification, there are three new subtypes of tumours:

1) IDH mutated, 1p19q- codeleted (which have the best response to treatment) ;

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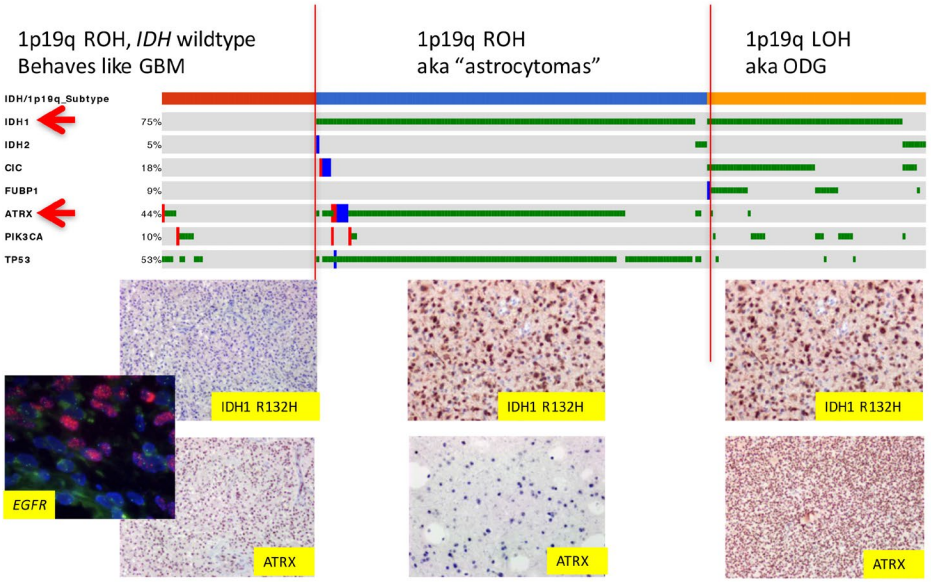
Molecular segregation of low grade gliomas



SAVE THE DATE: Sat., Oct. 29, 2016

Brain Tumour Information Day

BC Cancer Research Centre, Vancouver

More information to follow!

The power of small deeds

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5. Money. Many brain tumour patients become disabled and cannot earn a living. Costs pile high. Rehabilitative and occupational therapy or nursing care is not always affordable. Medications are costly. Consider raising funds to help the family involved. If you use easy online tools, someone like you can do this for them. www.gofundme.com is a great website that can easily be set up and 100% of donations are directed to the family. Word of mouth spreads quickly through workplaces, church groups and neighbourhoods. Be someone's angel. It's the best money you will ever spend.

Director Woody Allen once said: "80% of success in life is just showing up." There is no more important time to 'show up' than when someone has heard the words "You have a brain tumour." Show up, and your presence will embody these words: "*You're not alone.*"

Suzanne Heft is a mother of two boys, a professional fundraiser for educational causes and her husband Harold Heft, a distinguished scholar, poet and writer, died in 2015 from brain cancer at the age of 50. He was a patient at the Pencer Brain Tumour Centre at Princess Margaret Hospital in Toronto.

For other personal stories from the brain tumour community, see Headlines Spring 08, 11, 13, 14, 15; Summer 09, 10; Fall 11; and Winter 07.

WHO classification

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2) IDH mutated, 1p19q- retained (which have an intermediate response to treatment);
3) No IDH mutation (the worst responders, and the poorest prognosis).

"Mixed" gliomas, also called oligoastrocytomas, are no longer recognized.

These and other elements of the new classification system allow us to better predict a patient's prognosis and help us choose the most appropriate therapy for an individual patient. The diagnostic categories in WHO2016 have been adopted in B.C. and will become the new standard in pathology labs in brain tumour centres around the world.

For previous articles about neuropathology, see Headlines Summer 09 and 10.

Reference

Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, Ohgaki H, Wiestler OD, Kleihues P, Ellison DW (2016). The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathologica 131:803–820 DOI 10.1007/s00401-016-1545-1

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