Abstract 11

Image Analysis in Neuropathology: Hue-Saturation-Intensity vs. Colour Deconvolution

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doi: 10.1017/cjn.2019.265

As image analysis expands into clinical and basic applications it is important that users be aware of opportunities and limitations. A common image analysis workflow involves the digitization of stained tissue sections into a red-green-blue (RGB) colour model for quantitative interpretation. Upstream of the digital image, quality and variability can be degraded at each step (tissue handling, fixation, sectioning, staining, image acquisition). Digital image analysis presents additional steps where variables can affect data quality. Image analysis platforms are not uniform. Aside from interface preferences, some introduce unintended variability due to their processing architecture that may not be obvious to the end-user. One important component of this is colour space representation: hue-saturation-intensity (HSI) vs. colour deconvolution (CD). A potential weakness of analyses within the HSI colour space is the mis-identification of darkly stained pixels, particularly when more than one stain is present. We were interested to discover whether HSI or CD provided greater fidelity in a typical immunoperoxidase/hematoxylin dataset.

Fifty-nine samples were processed using HSI- and CD-based analyses. Processed image pairs were compared with the original sample to determine which processed image provided a more accurate representation. CD proved superior to HSI in 94.9% of the analyzed image pairs. Where the option exists, CD-based image analysis is strongly recommended.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. To describe differences between HSI and CD colour spaces
2. To explain limitations in the use of HSI-based analyses
3. To be aware of recent developments in CD-based platforms

Session 3: Tumour neuropathology

Abstract 12

NTRK2 Fusion Driven Pediatric Glioblastoma: Identification of key molecular drivers by personalized oncology

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doi: 10.1017/cjn.2019.266

We describe the case of an 11-month-old girl with a rare cerebellar glioblastoma driven by a *NACC2-NTRK2* (Nucleus Accumbens Associated Protein 2-Neurotrophic Receptor Tyrosine Kinase 2) fusion. Initial workup of our case demonstrated homozygous *CDKN2A* deletion, but immunohistochemistry for other driver mutations, including IDH1 R132H, BRAF V600E, and H3F3A K27M were negative, and ATRX was retained. Tissue was subsequently submitted for personalized oncogenomic analysis, including whole genome and whole transcriptome sequencing, which demonstrated an activating *NTRK2* fusion, as well as high PD-L1 expression, which was subsequently confirmed by immunohistochemistry. Furthermore, *H3* and *IDH* demonstrated wildtype status. These findings suggested the possibility of treatment with either NTRK- or immune checkpoint- inhibitors through active clinical trials. Ultimately, the family pursued standard treatment that involved Head Start III chemotherapy and proton radiotherapy. Notably, at most recent follow upapproximately two years from initial diagnosis, the patient is in disease remission and thriving, suggesting favorable biology despite histologic malignancy. This case illustrates the value of personalized oncogenomics, as the molecular profiling revealed two actionable changes that would not have been apparent through routine diagnostics. *NTRK* fusions are known oncogenic drivers in a range of cancer types, but this is the first report of a *NACC2-NTRK2* fusion in a glioblastoma.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Explore the current molecular landscape of pediatric high grade gliomas
2. Recognize the value of personalized oncogenomic analysis, particularly in rare and/or aggressive tumors
3. Discuss the current status of NTRK inhibitor clinical trials

Abstract 13

Update on the national survey on molecular diagnostics in CNS tumors

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doi: 10.1017/cjn.2019.267

There have been significant changes in the diagnostic criteria for diffuse gliomas in the 2016 WHO CNS tumor classification, with the incorporation of molecular criteria into a number of definitions. This has placed a greater emphasis on the availability of key immunohistochemical and molecular tests. In order to determine the effect that these changes have had on

neuropathology practice and the access of different centres to these tests, we designed a survey that was sent to all members of the Canadian Association of Neuropathology member list in the fall of 2017. This survey asked a number of questions relating to the approach to glioma diagnosis, immunohistochemical/molecular test ordering patterns, in-house test availability, and need to send out for testing. In this presentation we will present preliminary results from this survey, with a focus on institutional testing capabilities. This provides a valuable resource that could ultimately need to a national database of immunohistochemical and molecular test availability for each neuropathology centre.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Review the key molecular markers in the diagnosis of adult gliomas and methods of testing for them
2. Discuss the effect that the 2016 WHO CNS tumor update has had on clinical practice in Canada

Abstract 14

Role of MacroH2A2 in the glioblastoma stem cell epigenome

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doi: 10.1017/cjn.2019.268

Glioblastoma is the most common primary malignant brain tumour in adults, and remains uniformly lethal. These tumours contain a subpopulation of glioblastoma stem cells (GSCs) that drive tumour recurrence and drug resistance. We find that MacroH2A2 is a histone variant that can stratify glioblastoma patients, with higher levels of this histone variant associated with better patient prognosis. Knockdown of macroH2A2 in GSCs is associated with increased self-renewal and an increased expression of stemness genes by RNA-seq. Our preliminary results suggest that macroH2A2 is a novel biomarker for glioblastoma and that macroH2A2 loss is a marker of GSC stemness and a poor prognostic marker in glioblastoma. This work identifies loss of macroH2A2 as a feature of GSCs and provides a framework for therapeutic modulation of this histone variant.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Explain the role of epigenetics in glioblastoma pathophysiology

Abstract 15

Cerebellar glioblastoma: a clinicopathologic series of 16 cases

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doi: 10.1017/cjn.2019.269

Due to their rareness, it is not known if the clinicopathological features of cerebellar glioblastomas (cGBMs) are different from supratentorial GBMs (sGBMs). We reviewed all 16 cases of cGBMs (total GBMs: 1350) at St. Michael's Hospital over 18 years and assessed their clinicopathologic features. The mean age at diagnosis was 57 years. The most common presentations were headache (56%) and gait instability (56%). The majority (81%) of cGBMs were hemispheric while 19% involved the midline. There was radiologic evidence of brainstem infiltration at presentation in one case. Radiologically, peritumoral edema (63%) and heterogeneous contrast enhancement (50%) were common. Histologically, cGBM showed leptomeningeal involvement in 10/12 of cases. Uncommon histologic variants included 3 giant cell GBMs, a gliosarcoma, and a tumor with Rosenthal fibres and eosinophilic granular bodies. IDH1 R132H mutation was detected in 3/14 cases, a rate much higher than sGBMs. Additionally, 7/11 tumors had widespread p53 immunopositivity suggestive of TP53 mutation which is in accordance with previous reports in the literature. Of 9 cases tested, none had histone H3 K27M or G34R/V mutation. In summary, cGBMs have unique features that distinguishes them from sGBMs.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Identify the clinicopathological features of cerebellar GBMs including major molecular alterations
2. Compare cerebellar and supratentorial GBMs and describe the distinguishing features of each type of tumor

Session 4: Infectious/Immune mediated Neuropathology and Neuromuscular Neuropathology

Abstract 16

Mycobacterium chimaera encephalitis following cardiac surgery in three adult immunocompetent patients: first detailed neuropathological report.

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