SESSION 1: Tumour Neuropathology

ABSTRACT 1

Pathological features determining recurrence and radioresistance in cerebral atypical meningioma

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We examined recurrence after gross total resection (GTR) or subtotal resection (STR) at St. Michael's Hospital, Toronto, of 181 cases of atypical meningioma (WHO grade II). In the entire group, Kaplan-Meier survival curves showed that combined necrosis and brain invasion was the feature associated with the worst outcome, followed in order by necrosis, histological variants (clear cell, rhabdoid, and chordoid), high mitotic count, and brain invasion. The highly significant difference between necrosis and brain invasion and necrosis was seen only in patients receiving GTR, and lost in those treated with STR. Adjuvant radiotherapy was associated with worse outcome, more so in patients receiving GTR. In the presence of high mitotic count (defined as >4/10HPF) radiation did not affect recurrence, but necrosis and specially combined necrosis and brain invasion magnified the apparent deleterious effect of adjuvant radiotherapy. In the presence of brain invasion, radiotherapy's small effect did not reach significance. Since patients were not randomized to adjuvant radiotherapy, these results should not be construed as indicating that this treatment is injurious. It can be stated that in the presence of necrosis and particularly necrosis and brain invasion, but not brain invasion alone, or high mitotic count, atypical meningiomas are more resistant to any possible beneficial effect of radiation in delaying recurrence.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Describe histological and treatment factors determining recurrence in atypical meningioma.
2. List histological factors associated with radioresistance in atypical meningioma.

ABSTRACT 2

A Machine Learning Analysis of TCGA Expression Data to Finding Signatures for "Normal-Like" IDH-WT Diffuse Gliomas with a Longer Survival

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Classification of primary CNS tumours is currently achieved by complementing histologic analysis with molecular information, in accordance with the WHO guidelines, and aims at providing accurate prognosis and optimal patient management. cIMPACT-NOW update 3 now recommends grading diffuse IDH-wild type astrocytomas as grade IV glioblastomas if they bear one or more of the following molecular alterations: EGFR amplification, TERT promoter mutation, and whole-chromosome 7 gain combined with chromosome 10 loss.

In this reanalysis of the Cancer Genome Atlas (TCGA) glioma expression datasets, we identified 14 IDH-wt infiltrating astrocytic gliomas displaying a "normal-like (NL)" transcriptomic profile associated with a longer survival rate. Some of these tumours would be considered as GBM-equivalents with the current diagnostic algorithm. A k-nearest neighbors model was used to identify 3-gene signatures able to identify NL IDH-WT gliomas. Genes such as C5AR1 (complement receptor) SLC32A1 (vesicular gamma-amino-butyric acid transporter), and SMIM10L2A (long non-coding RNA) were overrepresented in these signatures which were validated further using the Chinese Glioma Genome and Ivy Glioblastoma Atlases. They showed high discriminative power and correlation with survival. This finding could lead to the validation of an immunohistochemical or PCR test which would facilitate classification of IDH-WT astrocytomas with unclear histological grading. Furthermore, associated signaling pathways might represent novel treatment targets for aggressive tumours.

LEARNING OBJECTIVES

This presentation will enable the learner to:

1. Reconsider recent updates in the WHO classification of infiltrating gliomas.
2. Discuss advanced bioinformatics profiling of the brain cancer transcriptome.

ABSTRACT 3

Cerebrospinal fluid flow cytometry: utility in central nervous system lymphoma diagnosis

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Flow cytometry of the cerebrospinal fluid (CSF) is used in isolation or as an adjunct to cytology to increase the sensitivity of detecting primary central nervous system (CNS) lymphoma. We aim to evaluate the sensitivity of CSF flow cytometry as a diagnostic tool for primary CNS lymphoma in patients presenting with undifferentiated neurologic symptoms. We retrospectively reviewed all CSF samples received by the Calgary Laboratory Services Flow Cytometry Laboratory from 2012- 2015. Clinical data, laboratory investigations, radiologic imaging studies, and pathological data were analyzed. Clinical review extended to 2 years post CSF flow cytometric testing. The number of samples of CSF flow cytometry that were positive for a hematological malignancy was 43/763 (5.6%). The overall sensitivity of the test was 69.4%. A positive result was more likely to occur in patients with a prior history of a hematological malignancy or abnormal enhancement on MRI (p<0.0001). CSF flow cytometry was negative in all patients who did not have a previous hematological malignancy or abnormal enhancement on MRI (n = 247). CSF flow cytometry has a limited role in screening for primary CNS lymphoma, unless a strictly endorsed testing algorithm is applied. It is, however, an invaluable tool in evaluating CNS involvement in patients with a previous diagnosis of hematolymphoid malignancy or abnormal enhancement on MRI.