CNS 2018 ANNUAL MEETING
HOUSTON, TEXAS
OCTOBER 6-10, 2018

Proteomic Analysis of Atypical Meningiomas to Identify Biomarkers for Distinguishing Radiotherapy Responders from Non- Responders

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Introduction

Adjuvant radiation therapy is often recommended for the treatment of refractory atypical meningiomas. However, literature suggest that the benefit of radiotherapy is ambiguous. While some meningiomas are radioresistant, there appears to be a subset of tumors that are biologically predisposed to respond well. It is imperative to develop a new diagnostic method that may distinguish between meningiomas that will respond to radiotherapy from those that will not. We hypothesized that proteomic analysis of proteins derived from meningiomas will identify novel biomarkers which will distinguish radiotherapy responders from non-responders.

Methods

A search in the neurosurgical oncology database revealed 354 patients that were treated with radiation therapy for meningiomas between 2006 and 2015. Of these, we identified a unique subset of patients (n=21) who undergone a sub-total resection surgery (Simpson IV) for parasagittal atypical meningiomas prior to having undergone radiotherapy for progressive disease. Time to progression (TTP) was calculated and bottom-up spectrometry proteomic analysis of surgical specimens was done.

Results

The median TTP of atypical meningioma following radiotherapy was 35.8 months (range, 7-108 months). Bottom-up spectrometry proteomic analysis of 3,349 proteins identified 57 distinguishing short TTP (median 8 months, range 7 - 8 months; n=3) from long TTP (median 52 months, range 50 - 108 months; n=3) atypical meningiomas. An Ingenuity® Pathway Analysis of these 57 proteins, identified pathways associated with inflammatory response (score 64) and DNA replication and repair (score 32) as the most enriched pathways. Of these 57 proteins, four proteins with high correlation coefficient score between expression level and TTP were chosen as putative biomarkers.

Learning Objectives

By the conclusion of this session, participant should be able to discuss that 1) response of atypical meningiomas to radiation therapy is not uniform, 2) Biomarkers may distinguishing between radiotherapy responders and non-responders.

Conclusions

The response of atypical meningiomas to radiation therapy is not uniform. Proteomic analysis of surgical specimens identified biomarkers capable of distinguishing between radiotherapy responders and non-responders. Further validation is needed in a larger cohort.