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Significance of micro-RNA expression in patients with meningioma

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Abstract

Recent brain tumour research has shown abnormalities in gene expression as key features for almost all common brain tumours investigated. However, there is increasing evidence that epigenetic abnormalities are also crucial for tumorigenesis. Epigenetic abnormalities are heritable alterations affecting gene expression without changing the primary DNA sequence. Epigenetic abnormalities in meningiomas include abnormal microRNA expression, altered DNA methylation and histone and chromatin modifications. In this review we identify the role of altered expression of microRNA in the development and recurrence of meningioma. Based on the review of current literature, extensive knowledge of micro-RNA expression cannot only determine tumour recurrence and prognosis but also opens up new avenues for treatment.

Keywords: Brain tumor, Meningioma, miro-RNA, Epigenetics.

Introduction

Meningiomas represent the most frequent intracranial tumour entity of non-glial origin with an incidence of 15-20% among all primary intracranial neoplasms.[1,2] Studies show that altered micro-RNA (mi-RNA) expression in meningiomas may have them functioning as either oncogenes or tumour suppressor genes. Mi-RNAs bind complementary to one or more messenger RNA (mRNA) molecules resulting in post translational gene expression silencing and initiate the degradation or the inhibition of translation.[3] Here the authors review the evidence of the effect of altered mi-RNA expression in meningioma.

Review of Evidence

Mi-RNAs have a confirmed diagnostic and prognostic role in certain types of cancers and have recently become one of the most promising areas of neuro-oncology research, and may reveal possible targets for drug development and therapy. Zhi et al., in 2012 investigated the mi-RNA expression profiles in human meningiomas comparing levels of 200 mi-RNA from 110 meningioma samples to

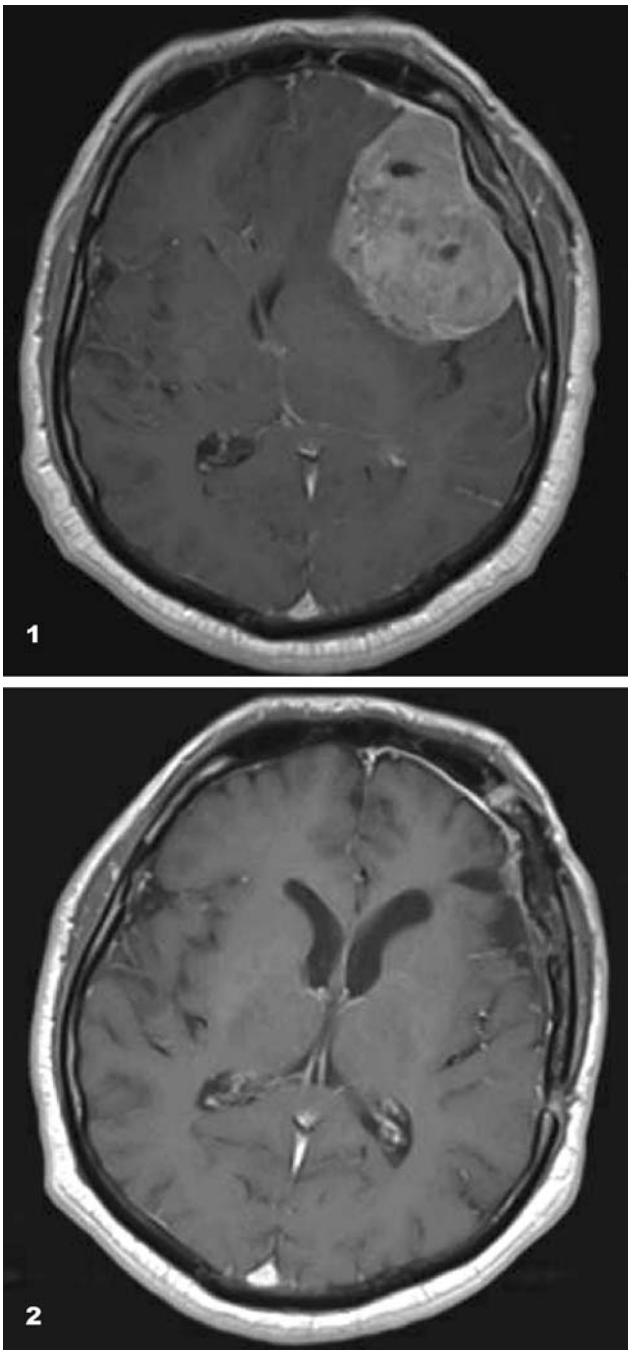

Figure-1 and 2: MRI T1WI post-contrast axial images show a large left convexity meningioma with mass effect and midline shift. Figure 2 is the post-operative MRI images showing complete excision and resolution of mass effect.

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mi-RNA expression profiles in 35 normal adjacent tissue (NAT).[4] They identified a molecular profile containing 14 specific mi-RNAs which distinguished meningiomas from NAT samples. Of these 14, they indicated three mi-RNAs (miR-190a, miR-29c-3p, miR-219-5p) which may have the potential to serve as novel prognostic indicators of meningioma. They further reported that high levels of miR-190a and low levels of miR-29c-3p and miR-219-5p were significantly correlated with elevated recurrence rate in meningioma patients.[4] We must add here that markedly elevated levels of miR-21 have been found in glioblastoma. Galani et al., in 2015 reported that atypical and malignant meningiomas had higher expression of both miR-21 and nestin levels compared to benign meningioma.[5] A positive correlation between miR-21 and nestin mRNA levels was also found.[5]

Significantly reduced miR-145 expression was seen in atypical and anaplastic tumours as compared to benign meningiomas. Moreover, meningioma cells with high miR-145 levels had impaired migratory and invasive potential in vitro and in vivo. PCR-array studies of miR145-overexpressing cells suggested that collagen type V alpha (COL5A1) expression is down regulated by miR-145 over expression. Accordingly, COL5A1 expression was significantly upregulated in atypical and anaplastic meningiomas.[6] Collectively, the data indicates an important anti-migratory and anti-proliferative function of miR-145 in meningiomas.

In addition, the use of artificial mi-RNA molecules as therapeutic agents is now under intense development. Such molecules are modified oligonucleotides that can either bind to a specific mi-RNA to enhance or reduce the expression of its targets.[7] Thus, mi-RNA expression can be altered in meningiomas with a prognostic relevance and may become a potential therapeutic target in the future.

Conclusion

Review of evidence identifies that expression of micro-RNA is involved in tumour pathogenesis. Multiple studies show the changes in micro-RNA expression and their effect on prognosis and recurrence. The identification of these micro-RNA can help in screening, treatment planning prognostication and counselling. It further opens up new avenues for research in meningiomas.

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