1H magnetic resonance spectroscopy detects differences between metastatic and localised medulloblastoma in children

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AIM

To establish the differences in metabolite concentrations between metastatic and non-metastatic medulloblastoma using in vivo ^{1}H magnetic resonance spectroscopy and relate the metabolite levels to tumour proliferation rate.

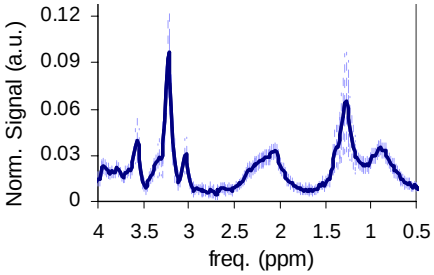
BACKGROUND

Medulloblastoma is the most common malignant brain tumour of childhood. The prognosis varies widely depending on clinical and pathologic characteristics of the tumour but most importantly the presence or absence of metastases. Currently it is unknown whether tumours presenting with metastatic disease are biologically different from those which are localised. There have been several studies correlating ^{1}H MRS with prognosis in mixed populations of brain tumours and a common finding is that a high total choline/creatine ratio confers a poor prognosis[1]. This finding is thought to be related to the presence of an increased concentration of total choline resulting from rapid cell turnover. However, single tumour groups have not been investigated in detail and little has been reported on the relationship between ^{1}H MRS and commonly used histopathological indices.

METHODS

Single voxel ^{1}H MRS using PRESS at an echo time of 30ms was carried out on a Siemens Symphony 1.5T scanner prior to surgery on 9 children with medulloblastoma. The voxel was placed within the tumour visualised on T1 weighted images post gadolinium contrast administration. A water unsuppressed signal was acquired for use in post processing and quantitation. Metabolite concentrations were determined by fitting a linear combination of individual metabolite spectra to the frequency spectrum using LCModel. Metastatic disease was taken as the presence on MRI of abnormal tissue outside the primary site. All patients had the diagnosis confirmed by histology and Ki 67 immuno-staining was performed as a marker of cell proliferation.

Fig 1. ^{1}H MRS for medulloblastoma (solid line: mean, dashed lines: standard deviation)



RESULTS

An average frequency spectrum for the tumours together with standard deviations is given in fig 1. Concentrations of creatine (Cr), taurine (Tau), syalloinositol (Scyllo) and a peak at 3.8ppm tentatively assigned to guanidoacetate (Gua) are significantly higher in those with metastases (see fig 2).

Fig 2. Concentrations of metabolites in metastatic and non metastatic tumours. Error bars: SE of mean.

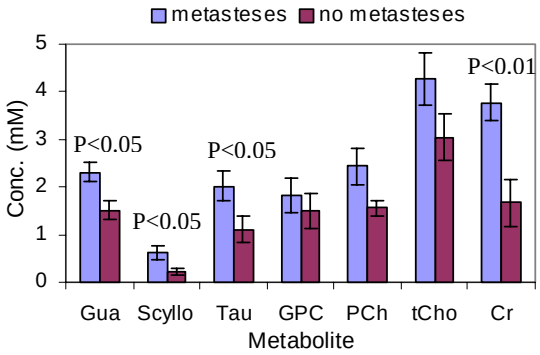
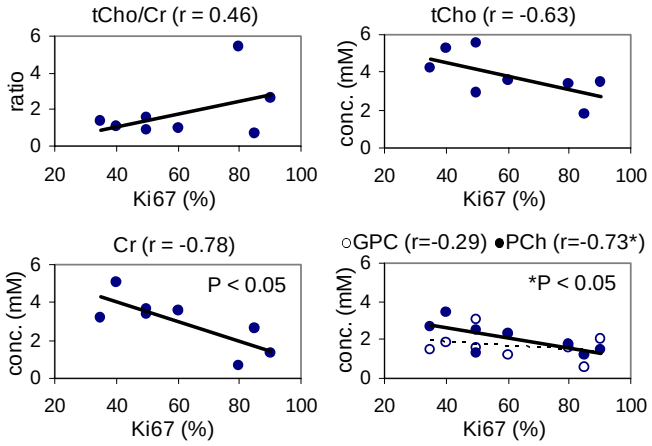


Fig 3. Correlations between metabolite concentrations and Ki 67 index



Correlations between metabolite concentration and Ki 67 are presented in fig 3. There is a non-significant correlation between total choline (tCho) / Cr ratio and Ki 67 index. However, the increasing trend of this ratio with Ki 67 is due to a significant decrease in creatine concentration rather than increased total choline. An estimate of the separate glycerphosphocholine (GPC) and phosphocholine (PCh) concentration may be obtained from the region 3.5 to 4.0 ppm and shows that the negative trend of total choline with Ki 67 is due to a significant negative correlation of PCh.

CONCLUSIONS

Significant differences exist between ^{1}H MRS metabolite concentrations of the primary tumour in childhood medulloblastoma differs between those with metastatic disease and those with localised tumours implying that metastatic tumours are biologically distinct from localised tumours. Localised tumours have a higher proliferation rate which may be explained by rapid growth leading to early detection prior to metastatic change. The non-significant trend to high tCho / Cr ratio in tumours with a high Ki 67 proliferation index is due to low Cr rather than high tCho. All medulloblastomas grow rapidly and low Cr, a combination of creatine and phosphocreatine, may indicate a depleted energy status for the cell.

REFERENCES

[1] Girard N, Wang ZJ, Erbetta A, Sutton LN, Phillips PC, Rorke LB, Zimmerman RA. Prognostic value of proton MR spectroscopy of cerebral hemisphere tumors in children. Neuroradiology 40(2):121-125, 1999.