ASSESSMENT OF BRAIN HAMARTOMAS IN CHILDREN WITH NEUROFIBROMATOSIS USING ^{1}H MAGNETIC RESONANCE SPECTROSCOPY

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Introduction

Neurofibromatosis (NF) type 1 with an incidence of 1 in 4000 is seen in the younger age group. Focal brain lesions commonly seen in these patients are optic gliomas, cerebral astrocytomas, aqueductal stenosis and high signal intensity lesions seen on long TR images.These lesions are usually found in the cerebellar peduncles, pons, globus pallidus and the midbrain. They are referred to in the literature as harmatomas, heterotopias or brain dysplasias. These lesions usually have no mass effect and are rarely seen on CT images. No focal neurological signs are seen as a consequence of these lesions. Spongiform myelopathy or vacuolar change of myelin is seen in these lesions on microscopy (DiPaolo 1995). MR findings are not consistent, being frequently identified as foci of hyperintensity on only T2-weighted MR images or as being hyperintensity on both T2 and T1 images with both enhancement and no signal change following gadolinium-DTPA (Castillo 1995a, Bonawitz 1998). ^{1}H MRS has been reported for seven NF type 1 patients with apparent benign hamartomas showing spectra with significant differences from gliomas (Castillo 1995b).

We have performed a preliminary study on five patients with NF type 1 to investigate the consistency of MR appearances and ^{1}H MRS spectral changes relative to normal brain

Materials and Methods

Single voxel ^{1}H spin echo acquisitions with an echo time of 135ms were made for previously identified hamartomas in five patients ranging in age from 8 - 21 years. No sedation was administered as part of this initial study. Prior to spectroscopy, routine imaging was performed comprising coronal and sagittal T1 and transverse T2/PD sequences. With the exception of one child who was having an MR examination for the first time, no Gd contrast was given For the selected hamartomas typical voxel sizes were 15x15x15mm.. Where possible, dependent upon co-operation of the child, spectroscopy was also performed for a corresponding region of normal brain in the contra-lateral hemisphere.

All spectra were processed with zero filling, gaussian filter, FFT, phase correction and smoothing. Metabolite ratios were calculated by simple peak integration. Relative metabolite concentrations between hamartomas and normal brain were calculated using non water suppressed spectra from each voxel.

Results and Discussion

Imaging findings for the five patients are given in Table 1. From the chance selection of the five patients significant differences in MR signal behaviour are seen for the hamartomas. Unusually SM showed an enhancing lesion and DP demonstrated a high signal lesion on T1 weighted images. MaA had previously presented approximately one year earlier with a hamartoma in the cerebellum. For this study no lesion was observable, however spectroscopy was performed over the region of high signal on T2 seen previously. Child LC was not able to tolerate an additional spectroscopy acquisition over a region of normal brain. Metabolite ratios are given in Figure 1.

Patient	T1 image	T2 image	Lesion position
SM	Isointense	High signal	Left basal ganglia
MiA	Isointense	High signal	Left peri-ventricular
MaA	Isointense	Isointense	Left cerebellum
DP	High signal	High signal	Right basal ganglia
LC	Isointense	High signal	Right basal ganglia

Table 1. Summary of imaging appearance.

MiA and DP show similar trends in terms of metabolite ratios, both showing a slight reduction in all ratios relative to a corresponding area of normal brain. SM and MaA show different trends, with more significant reductions in NAA/Cr and NAA/Cho but with a large significant increase in Cho/Cr. An increase in Choline is often seen in the presence of rapidly dividing cells and is increased in all primary and secondary brain tumours (Castillo 1998). Although no normal brain data is available for LC, metabolite ratios for the hamartoma appear to mirror those for SM and MaA.

Metabolite ratios for MaA indicate clear changes relative to normal brain despite no lesion being visible on imaging. Hamartomas are not generally seen in NF type 1 adults and spontaneous regression has been reported (Kim 1998).

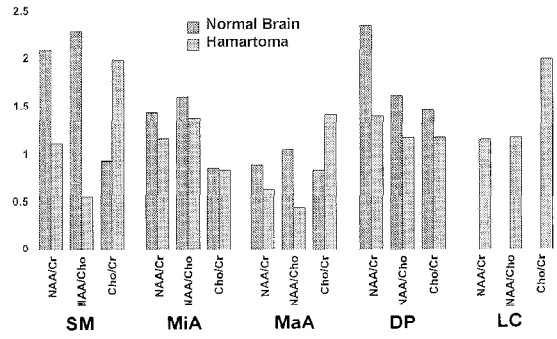

Figure 1. Metabolite ratios for normal brain and hamartomas

Metabolite concentrations relative to corresponding areas of normal brain calculated using the non water suppressed signal are given in Table 2. It was not possible to calculate ratios for LC.

Patient	Cho	Cr	NAA
SM	1.27	0.60	0.31
MiA	0.74	0.78	0.64
MaA	1.25	0.76	0.31
DP	0.94	1.17	0.69

Table 2. Metabolite concentrations: Hamartoma/Normal Brain

Significantly elevated Choline levels and decreased NAA are evident for SM and MaA. Such changes are similar to findings for astrocytomas and differ from the findings of other workers (Castillo 1995b). These significant metabolite changes were seen for a typical high signal T2 lesion (SM) and for a regressed lesion which was no longer visible on T1 or T2 weighted images(MaA).

Conclusions

Preliminary findings for a series of five NF type 1 patients has demonstrated a range of imaging and spectral appearances for hamartoma lesions. Significantly, metabolite differences between hamartomas and normal brain have been shown in contradiction to previous work. Large metabolite changes were demonstrated in two lesions which ware similar to findings in malignant tissue, one of these such hamartomas being a regressed lesion which was not visible on MR images.

Hamartomas have been considered to represent an abnormal configuration of myelin. These results suggest that this is a broad generalisation. Such lesions whilst clearly being transient, also appear to be complex and variable in their pathogenesis.

References

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