Early Detection of Tumor Aggression and Prediction of Progression in Children with Diffuse Pontine Tumors: A Longitudinal In Vivo ^{1}H MRSI Study

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Introduction

Brain stem tumors account for 10 to 20% of all CNS tumors in the pediatric age group (1). Among them, diffuse pontine tumor is perhaps the most dreaded diagnosis in pediatric neurooncology due to their historically grave prognosis despite aggressive treatment (2). One single voxel ^{1}H MRS study (3) of pediatric diffuse pontine masses shows characteristic increase in choline compounds (Cho) and decrease in N-acetylaspartate (NAA) levels. A relationship between high Cho/NAA ratio and short duration of survival was demonstrated in a heterogeneous group of pediatric brain tumors (4). In this longitudinal study, in addition to the routine brain MRI protocol, pediatric patients with diffuse pontine tumors underwent MRSI examinations pre- and post-radiation/chemotherapy treatments. The goal was to determine if proton MRS measurements provide early detection of the aggressive nature of the tumor and early prediction of the cancer progression, and consequently, if proton MRS can play an important role in future clinical management of these types of patients.

Methods

Two pediatric patients (7 yr male and 10 yr female) who were diagnosed with diffuse pontine tumors underwent MRI/MRS examinations prior to radiation/chemotherapy treatment (baseline), approximately 5 weeks (follow-up 1), and 13 weeks (follow-up 2) following the completion of the treatment.

MRI/MRS scanning sessions were performed using a 1.5T GE Excite scanner with the quadrature head coil as the transceiver. Multi-slice axial FLAIR images were used as scouts for placement of the volume of interest for the 3D MRSI acquisition, which encompassed the lesion (hyperintense areas on FLAIR images), as well as some normal-appearing brain tissue areas (see white box in Fig. 1 left panel). The MRSI data were acquired using a PRESS sequence with TE=144 ms, TR=1000 ms, 8 cm FOV, 1 cm slice thickness, and 3D phase encoding (8 x 8 x 8) (part of encoding matrix shown in green in Fig. 1 left panel), resulting in 1 cc nominal voxel size. Post-contrast T_1-weighted axial images were collected following the MRS acquisition. The 3D MRSI data were processed using GE's FuncTool software, with interpolation in the superior-inferior direction to overlay the spectra onto the thinner (3 mm) FLAIR images. Peak area ratios of Cho/NAA and Cho/Cr (total creatine) were analyzed at baseline, follow-up 1 and follow-up 2 for the voxels located in the same anatomical regions. Our home-built image processing software was used to trace and measure contrast enhancement volume (CEV) in the post-contrast T_1-weighted images.

Results

The right panel of Fig. 1 shows the proton spectra of the male patient obtained at baseline from a voxel located in the lesion ROI (upper right) and a voxel located in the normal-appearing ROI (NAROI) (lower right). The spectral patterns were similar for both patients. Figs. 2 and 3 depict, over the time course of this longitudinal study, the changes of Cho/NAA, Cho/Cr in the same lesion and NAROI voxels and the changes of CEV for the female and the male patients, respectively. There was no visible contrast enhancement in the lesions for both patients at the baseline. However, both baseline ratios of Cho/NAA and Cho/Cr in both lesions were significantly elevated compared to those in the NAROIs, suggesting the aggressive nature of the tumors, which were not implicated by clinical examinations at this stage. For example, the male patient had very atypical symptoms (mainly headaches without neurological findings) at presentation for a radiologically typical diffuse pontine tumor.

Cho/Cr and Cho/NAA were further elevated to various degrees in different regions of both lesions at follow-ups 1 and 2, indicating cancer progression despite radiation/chemotherapy treatment and signs of excellent clinical improvement for both patients at follow-up 1. Both patients showed clinical deteriorations at follow-up 2 and the female patient deceased shortly after follow-up 2. The Cho/NAA and Cho/Cr ratios in the NAROIs remained relatively unchanged over the time course of follow-up. MRI contrast enhancement appeared at follow-up 1 and the CEV was further increased at follow-up 2 for both patients. However, since radiation necrosis cannot be readily differentiated from tumor progression based on contrast enhancement and the Cho/NAA and Cho/Cr elevations were well beyond the areas of contrast enhancement, the MRS data were critical in showing disease progression and predicting clinical deterioration, particularly at follow-up 1 when both patients' symptoms had dramatically improved.

Discussion

Although the results are preliminary and patient number is limited, this longitudinal study suggests that compared to conventional post-contrast MRI, proton MRS can provide earlier detection of tumor aggressiveness in children with diffuse pontine tumors, and that proton MRS also serve as a better indicator in early prediction of cancer progression. Inclusion of proton MRS in radiological examinations may be of critical importance in clinical management of pediatric patients with diffuse pontine tumors, who usually have very poor prognosis and short survival duration. Early detection of viable tumor and prediction of cancer progression may lead to alteration of therapy regiment at an earlier stage to possibly treat the cancer more effectively, thus prolonging the duration of survival.

References

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Fig. 1

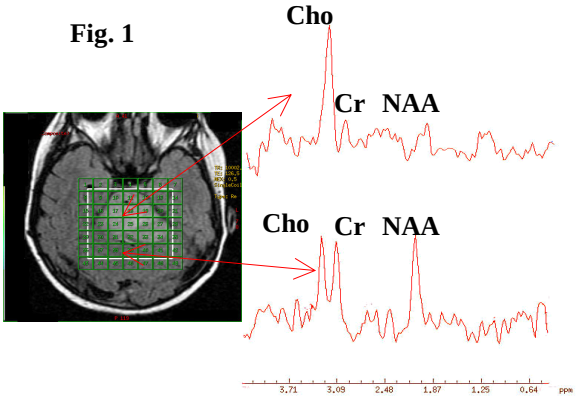

Fig. 2

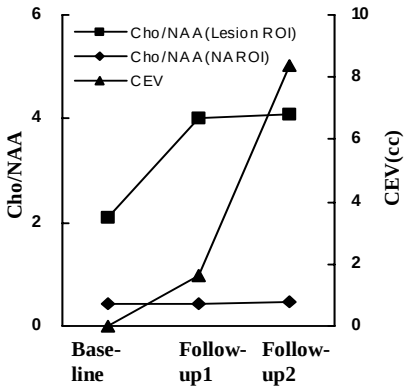

Fig. 3