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INTRODUCTION

Radiation therapy is an important treatment modality that has improved survival among children with brain malignancies. However, radiation therapy administered to the brain, even at relatively low doses, can generate a spectrum of adverse acute, early delayed and late effects. Radiation-induced injury is associated with demyelination, necrosis, and vascular abnormalities. While early effects can be transient, late effects have been associated with a range of clinical brain toxicities, including neurocognitive deficits, which can have long-term implications for learning and memory. Diffusion tensor imaging (DTI) is a non-invasive method that has provided unique information on radiation-induced white matter pathology. It has also been shown to be useful in providing information on normal maturation of white matter tracts as well as cortical and deep gray matter nuclei. A recent DTI study evaluating the maturation of white matter tracts and deep gray matter nuclei among children and adolescents demonstrates that FA and ADC changes can be quite profound throughout childhood and adolescence. The aim of this prospective study was to evaluate FA and ADC values in specific gray matter regions among children who have received brain radiation.

METHODS

Five pediatric patients (all boys, age range 12.5-14.9 years) who received radiation to the brain were examined. The diagnoses included acute T-cell lymphoma, astrocytoma (pineal region), medulloblastoma (posterior fossa), malignant glioneuroma (frontal lobe), and craniopharyngioma (suprasellar). The control group was comprised of 5 healthy children (4 girls, ranging in age from 13.3-14.4 years, and one boy, age 14.6). All subjects were evaluated with a battery of neuropsychological tests. The patients were examined 27 months following completion of RT. MRI data were acquired with a single-shot spin echo planar sequence with 15 non-collinear diffusion gradient directions (b=1000 s/mm²) and two b=0 s/mm² images. The following parameters were used: 24 axial slices, 96*96 acquisition matrix, FOV 240 mm², 5 mm slice thickness, no gap. FA, ADC, and color maps were calculated from raw data using the in-house developed software ‘DTI Studio’. Each region of interest (thalamus (1), globus pallidus (2), putamen (3), caudate head (4), and parahippocampal region (5)) was drawn on the color maps two times and the measurements were averaged. GLM ANOVA was applied for statistical evaluations, using the SPSS software. Statistical significance was set to p<0.05.

RESULTS

The overall analysis revealed a statistically significant difference in ADC between patients and controls (group x region: p = 0.044) (fig. 1). The mean ADC value (calculated from all regions in both hemispheres) was 8.9% higher in patients compared with controls. In individual regions, mean ADC was 10.4% higher in the parahippocampal region in patients (p=0.007). There were no statistically significant differences in mean FA between the controls and the patients in any of the regions, although there was a trend towards a relative increase in FA among the patients (p = 0.081) (fig. 2). For both ADC and FA, there was a trend to wider range of values within regions among patients when compared to controls. Compared to healthy children, patients tended to have a better performance on the memory test (Woodcock-Johnson Memory Test of Words; p<0.08 for both raw and standard scores).

DISCUSSION

Recent literature has shown that mean diffusivity of these gray matter regions decreases over time, correlating with what is believed to be normal developmental maturation of these structures. In our study, a significant increase in the mean ADC value calculated from five separate regions comprising deep gray matter and parahippocampal gray matter was detected between patients and age-matched controls, despite no visible pathology on conventional MR imaging. This suggests that radiation may cause damage to deep gray matter, which could lead to a failure of these structures to mature normally. No statistically significant difference in FA was observed, however. This may be secondary to the non-uniform directionality of fibers in gray matter, unlike large white matter tracts. In addition, the wider range of FA values among patients may be reflective of differences in radiation dose to these regions, and thus differences in the degree of potential damage.

Abnormal ADC values were observed among patients who exhibited no concurrent clinical signs of memory impairment on neuropsychological testing. This suggests that this modality may identify injury to brain structures known to be integral to learning and memory earlier than clinical testing can detect such damage.

The differences in diffusivity were observed at 27 months following radiation therapy. While some of these differences may be secondary to radiation therapy, it will be important to determine if these differences were present prior to the start of radiation therapy to determine if they are also potentially attributable to the patients’ malignancy, or other treatment parameters, such as chemotherapy and surgery. In summary, the results presented here are highly suggestive that DTI is able to detect delayed changes in deep gray matter integrity associated with RT. This has potentially broad implications for the development of deep gray matter among pediatric patients who receive RT for brain malignancy. The results also suggest that these changes may be apparent on DTI before they become clinically relevant.

REFERENCES