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Original article

Conventional magnetic resonance imaging in the differentiation between high and low-grade brain tumours in paediatric patients

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ABSTRACT

Objective: It has been described that hyperintensity in diffusion-weighted imaging (DWI) correlates with high-grade tumours, and high signal-intensity in T2-weighted (T2w) images identifies low-grade tumours. We aimed to investigate the potential of routine conventional MRI sequences, such as DWI and T2-w, to pre-operatively distinguish between low-grade and high-grade brain tumours in paediatric patients.
Material and methods: Two raters, blinded to the histological diagnosis, rated the aspect and signal intensity of MR images (T2w and DWI) from 37 children with newly diagnosed brain tumours. Histological diagnoses included 18 low-grade and 19 high-grade brain tumours.
Results: The inter-rater agreement was 81–95%. High-grade tumours were never hypointense on DWI and low-grade tumours were usually hyperintense on T2w. Specificity was 100% for low-grade tumours and 90% for high-grade tumours. About 95% of the high-grade tumours and about 70% of the low-grade tumours were correctly diagnosed.
Conclusion: The combination of general morphological aspect of the tumours and signals on T2-w and DWI yield a high accuracy of pre-operative differentiation between low-grade and high-grade paediatric tumours.

1. Introduction

Paediatric neuro-oncologic imaging can be challenging, primarily because paediatric tumours of the central nervous system are relatively uncommon and histology is diverse. Conventional MRI has become an essential modality in the diagnosis and evaluation of intracranial tumours in children: although it lacks specificity for tumours and can lead to ambiguous results, it helps to characterise tumour aggressiveness and hence, tumour grade. Diagnosis of high-grade brain tumours in adults is suggested by mass effect and necrosis, contrast enhancement and oedema. In children, the value of these parameters, particularly of enhancement, is limited because low-grade tumours such as pilocytic

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astrocytomas also typically enhance. Unlike adult grade IV brain tumours, malignant paediatric brain tumours are less necrotic, but are highly cellular with high nuclear-to-cytoplasmic ratios.

The signal intensities of T2-weighted (T2-w) and of diffusion-weighted imaging (DWI) are indirect markers of tumour cellularity. Highly cellular tumours are typically iso- to hypointense in T2w and hyperintense on DWI.[1] In children with cerebellar tumours, T2-w signal intensity helps to identify "low-grade" and predict histopathology[1,2] but it is unclear to which extent the conventional MRI, and particularly T2w and DWI, provide reliable information on cellularity, a marker of tumour grade.

Our aim was to evaluate whether the MRI aspect and features alone (i.e. conventional MRI, T2w, DWI, without quantitative measurements) could distinguish low-grade from high-grade paediatric tumours of the CNS.

2. Material and methods

2.1. Subjects

We retrospectively queried MRI reports from June 2008 to January 2013 in our department with the keywords "brain tumour in children" and selected all patients with confirmed histopathological diagnosis (according to World Health Organization (WHO) 2007),[3] MR images (T2w, DWI and apparent diffusion coefficient (ADC) maps) before any treatment and lesions bigger than 1 cm. Only 37 children (1/4 of all paediatric tumour reports in the given period) met all these criteria; in the other patients MRI was performed only after treatment and/or the first examination was carried out elsewhere and did not include DWI and/or ADC maps.

2.2. Imaging studies

MR imaging of the brain was performed on a 3 T whole body system (Magnetom Verio, Siemens Medical Solutions, Erlangen, Germany) with an 8-channel phased array head coil. The protocol included axial T2-w images, fluid attenuated inversion recovery (FLAIR), T2*-w images and T1-w images before and after administration of the intravenous contrast agent. Further axial echo planar diffusion-weighted images (DWI) were performed in all patients (TR/TE 4900/88; 130 × 130 matrix; 220 × 220 mm field of view) using *b*-values of 0, 500, and 1000 s/mm^2 and identical orientation for all axial images. Diffusion gradients were applied in the z, y and x directions. ADC maps (mm^2/sec) were automatically calculated by the built-in software of the scanner.

2.3. Analysis

Two senior neuroradiologists, one of whom is also a paediatric radiologist, blinded for histopathological diagnosis, analysed the general aspect, as well as other tumoural characteristics, such as the presence of bleeding and cysts, T2w and DWI signal intensities.

The analysis of the general aspect was based on the synopsis of the location, the size and extent of the tumour, tumour margins as well as the type of enhancement after application of the contrast agent and signal changes on all available sequences. We also recorded the presence of mass effect, peritumoural oedema, contrast enhancement, cysts, necrosis, calcification and haemorrhage.

On both T2w and DWI we determined signal intensities in the solid tumour component (identified on axial contrast enhanced T1-w images or on T2-w images when contrast enhancement lacked) relative to the normal cerebral cortex and classified them as: hypointense, isointense and hyperintense on both, DWI and T2-w images. To rule out "T2-shine-through" effect, ADC values were also evaluated.

2.4. Statistics

For each variable we computed the inter-rater reliability as the percent agreement and Cohen's Kappa κ (an index of agreement between 2 raters or tests corrected for chance agreement). We used the guidelines from Landis and Koch 1977[4] to judge the κ: <0 poor; 0–0.20 slight; 0.21–0.40 fair; 0.41–0.60 moderate; 0.61–0.81 substantial and 0.81–1.0 almost perfect. For the variables with κ >0.6 we also computed their sensitivity and specificity relative to histological grade as gold standard. Mismatch or "unclear" ratings were marked as misclassified. We used the freely available software R Statistics 2.15.1 for all analysis (http://www.R-project.org/) together with functions from the packages "irr" and "caret" (R Core Team 2012, Kuhn 2008).[5,6]

3. Results

A total of 37 children with newly diagnosed brain tumours were evaluated retrospectively. Diagnoses included 18 children with low-grade brain tumours (10 WHO I astrocytomas, 4 WHO II astrocytomas, 1 pilomyxoid astrocytoma, 1 craniopharyngiomas, 1 ganglioglioma and 1 astroblastoma) and 19 children with high-grade brain tumours (7 medulloblastomas, 4 WHO III ependymomas, 1 PNET, 1 malignant rhabdoid tumour, 1 malignant germ cell tumour, 3 WHO III astrocytoma, 1 WHO IV astrocytoma, 1 rhabdomyosarcoma metastasis).

According to the World Health Organization (WHO),[3] histologically diagnosed WHO III and IV tumours were defined as high-grade and WHO I and II tumours were defined as low-grade.

3.1. Inter-rater reliability

For the variables below there was substantial to almost perfect agreement (κ 0.67–1, percent agreement 81%–100%; see Table 1).

3.2. Comparison to histological grading as gold standard

Considering the general aspect, malign or benign, 90%–100% (sensitivity, depending on rater) of the high-grade paediatric brain tumours were correctly identified as malign while only 67%–72% of low-grades were correctly identified as benign.