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Qualitative and quantitative analysis of diffusion-weighted imaging of gestational trophoblastic disease: Can it predict progression of molar pregnancy to persistent form of disease?

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ABSTRACT

Purpose: To describe the diffusion-weighted imaging (DWI) appearance of gestational trophoblastic disease (GTD) and to determine its apparent diffusion coefficient (ADC) values. To evaluate the feasibility of DWI to predict progression of hydatidiform mole (HM) to persistent disease.
Methods: During a period of 6 months, women with preliminary diagnosis of GTD, based on ultrasound and ßhCG levels, underwent 1.5T MRI (T2 high-resolution and DWI; b values 50, 400, 800; sagittal and perpendicular to the endometrium; and T1, T2 Turbo Spin Echo [TSE] axial images). Patients were followed for 6–12 months to monitor progression to persistent form of the disease. ADC values and image characteristics were compared between HM and persistent neoplasia and between GTD and non-molar pregnancy using Mann–Whitney *U* and Fisher's exact tests, respectively.
Results: Among the 23 studied patients, 19 (83%) were classified as molar and 4 (17%) as non-molar, based on pathology reports. After 6–12 months of follow-up, 5 (26%) cases progressed to persistent disease and 14 (74%) cases were benign HM. There was no significant difference between ADC values for HM ($1.93 \pm 0.33 \times 10^{-3}$ mm^2/s) and persistent neoplasia ($2.03 \pm 0.28 \times 10^{-3}$ mm^2/s) (P = 0.69). The ADC of non-molar pregnancies was ($0.96 \pm 0.46 \times 10^{-3}$ mm^2/s), which was significantly different from GTD ($1.96 \pm 0.32 \times 10^{-3}$ mm^2/s) (P = 0.001). Heterogeneous snowstorm appearance, focal intratumoral hemorrhage, myometrial contraction, and prominent myometrial vascularity were more common in GTD compared to non-molar pregnancy (P < 0.05).
Conclusion: Heterogeneous snowstorm appearance, focal intratumoral hemorrhage, myometrial contraction, and prominent myometrial vascularity are among the imaging characteristics of GTD. We cannot use ADC values to predict progression to persistent disease.

1. Introduction

Gestational trophoblastic diseases (GTD) include a spectrum of pregnancy-related diseases caused by abnormal proliferation of the placenta. The spectrum includes both benign hydatidiform mole (HM) and invasive/malignant gestational trophoblastic neoplasia (GTN). GTNs are characterized by a propensity for local invasion and distant metastases. These neoplasms usually follow a molar pregnancy, but can also occur after a normal pregnancy or abortion [1,2].

The incidence of GTD varies widely in different geographical regions. The incidence of HM in North America, Australia, and Europe is 0.57–1.1 per 1000 pregnancies. In South East Asia and Japan, the incidence is as high as 2 per 1000 pregnancies, and 8 per 1000 pregnancies in Thailand. Epidemiological studies in Iran have reported an incidence of 5.4 per 1000 pregnancies for HM [1,3,4].

The potential diagnosis of HM is often made by ultrasound, but histological examination of evacuated material is essential to confirm the diagnosis. Based on accepted guidelines, close follow-up with serum βhCG monitoring every 1–2 weeks after evacuation of HM is essential to detect invasive mole or choriocarcinoma [1,2]. The diagnosis of GTN is made on the basis of an elevated serum βhCG plateau or a rising titer over a period of several weeks. If three consecutive tests show normal levels, subsequently, the βhCG level

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should be determined every 3 months for 6 months [1,2,5]. This method, which requires weekly follow-up, is currently the only way to detect persistent disease and a definite diagnosis of GTN cannot be made before a significant time has elapsed.

The initial diagnosis of GTD is usually made before the classic symptoms occur, attributable mainly to the widespread use of routine pregnancy ultrasound studies [2,6–8]. A few decades ago, this diagnosis was made using transabdominal hysterography or angiography [9,10]. CT scans and MRIs have also been employed to evaluate GTD [7]. With its superior contrast resolution, MRI has been used to estimate the depth and extent of myometrial and parametrial invasion [8,11].

Diffusion-weighted imaging (DWI) has now been integrated into routine abdominal imaging, particularly in oncology. Specifically, DWI has been used in endometrial and cervical cancers to determine the differential diagnosis, the depth of invasion, and the tumor response to therapy [12–18].

Conventional MRI has been evaluated for diagnosing and determining the depth of myometrial invasion and the extent of parametrial invasion in GTD. However, unlike endometrial and cervical cancers, to the best of our knowledge, DWI findings have not been evaluated in GTD. The primary aim of this study was to determine whether DWI and ADC values (as an indicator of microstructure and cellularity) can predict later progression of HM to GTN. If prediction was feasible, we would be able to eliminate the time and cost of the current method of weekly βhCG monitoring. In addition, we would be able to manage the patient before CT scans or MRIs of the chest, brain, and abdomen and pelvis to particularize the extent of disease. We also aimed to describe the DWI appearance of GTD and to measure ADC values of the tumor.

2. Patients and methods

2.1. Patient population

The institutional ethical committee approved the study, and written, informed consent was obtained from all patients. The study was performed in two teaching hospitals affiliated with Shiraz University of Medical Sciences, namely, Zeinabieh Hospital, which is a fetal-maternal hospital, and Shahid Faghihi Hospital, which is a general hospital. Between November 2011 and May 2012, all pregnant women with early pregnancy bleeding, increased serum βhCG levels, and ultrasound findings suggestive of molar pregnancy were included in the study. Patients who were considered hemodynamically unstable, those with general contraindications to MRI, and patients who did not provide consent were excluded from the study.

2.2. Imaging protocol

All patients underwent pelvic MRI at Shahid Faghihi Hospital using a 1.5T system (Avanto, Siemens Medical Solutions, Erlangen, Germany) equipped with an 8-channel body coil on the same day of preliminary diagnosis. The patients underwent TSE T1- and T2-weighted axial images of the pelvis. High-resolution T2-weighted images of the uterus were also obtained both axial and perpendicular to the endometrial lining (in sagittal images).

Echo-planar DWI was obtained both axially and perpendicular to the endometrial lining (in sagittal images) with the following parameters: TR/TE = 2600/95 ms [b = 50,400 and 800 s/mm^2]; bandwidth 1042 Hz/pixel; section thickness 5 mm; intersection gap 1 mm; field of view (197–244x 242–300); matrix (117x 192); number of signal averages 4; and fat saturation as a fat suppression technique. ADC maps were obtained using the software of the MRI unit on a voxel-by-voxel basis using the slope of logarithmic decay for signal intensity in DWI images (b values of 50, 400, and 800 s/mm^2) against the b value. Average time of the whole exam was 11 min.

2.3. Final diagnosis

The uterus was then evacuated in all patients by suction curettage. Those cases with spontaneous, missed abortion, in which the possibility of molar pregnancy was considered initially, based on clinical, ultrasound findings, and lab data, but in whom pathological findings showed normal villi, were classified as non-molar pregnancies.

Patients with molar pregnancy were followed for 6–12 months. Based on weekly serum βhCG levels, their disease was classified as persistent or non-persistent disease at the end of the follow-up period.

2.4. Qualitative image analysis

Images were evaluated, in consensus, by two radiologists with five years experience in body MRI. Image interpretation was conducted on an Infinitt (3, 1, 1, 0, 4) Picture Archiving and Communication System (PACS) workstation. Both readers were aware of the preliminary diagnosis of molar pregnancy, but neither pathology reports, nor final follow-up results were known at the time of image evaluation.

T1- and T2-weighted images were evaluated subjectively for the presence or absence of the snowstorm appearance and transient myometrial contractions. Focal myometrial thickenings that were not visible on ultrasound images were called transient contractions. In addition, the endometrial outline (sharp versus irregular) and the endometrial-myometrial junction (partly-seen versus well-seen) were assessed onT2-weighted images. The form and outline of the endometrial cavity and hemorrhage (focal round or oval versus crescent bleeding) were assessed on T1 and DWI images. Engorged and dilated vessels were also evaluated in the myometrium and subjectively classified as prominent versus non-prominent; this was done separately on T2-weighted and DWI images.

2.5. Quantitative image analysis

All measurements, as well as the subjective image interpretations, were performed on an Infinitt PACS station. The regions of interest (ROI) were first drawn on the T2-weighted MR images with the subjectively largest visible tumor surface in the sagittal plane, as well as in the plane perpendicular to the endometrial lining. The ROIs were then copied to the ADC maps. The automatically measured average signal intensity was recorded as the ADC value. We did not exclude obvious hemorrhagic parts; therefore, for calculation of the ADC values, the whole endometrial content was included in the manually drawn irregular ROI.

2.6. Statistical analysis

Data were analyzed using SPSS software, version 17. Descriptive statistics were assessed. For comparison of ADC values between invasive and non-invasive trophoblastic disease and non-molar pregnancy, the Mann–Whitney *U* test was used. To evaluate the accuracy of ADC values for the differentiation of molar and non-molar pregnancies, ROC curves were used. To compare qualitative values, Fisher's exact test was used.

3. Results

Over a period of 6months, 23 patients with early pregnancy bleeding, typical ultrasound, and a preliminary diagnosis of GTD