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SHORT COMMUNICATION

Diffusion-weighted imaging in ectopic pregnancy: ring of restriction sign

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Objective: To demonstrate the diffusion-weighted imaging (DWI) findings of ectopic pregnancy (EP) and introduce the “ring of restriction” sign by discussing possible causes.

Methods: Between January 2014 and January 2017, patients with EP and examined by MRI on a 3T scanner were retrospectively evaluated. MRI and DWI findings were recorded.

Results: A total of 40 patients were diagnosed with EP at our university hospital, 8 of whom (20%) were evaluated by MRI and DWI. All of them were haemodynamically and clinically stable and could be imaged adequately. Locations were ovary ($n = 3$, 37.5%), tuba

($n = 2$, 25%), Caesarean section scar ($n = 2$, 25%) and parauterine ($n = 1$, 12.5%). In all eight EPs, the gestational sac diameter was compatible with 7–9 weeks. With DWI, the gestational sac was seen as a thick-walled cyst-like structure. The thick wall showed diffusion restrictions in all patients (ring of restriction sign).

Conclusions: DWI through its cellular and molecular evidence may contribute diagnosis of EP.

Advances in knowledge: Being aware of the EP wall shows diffusion restriction (ring of restriction) avoids interpretation errors especially in appropriate clinical setting with no need for contrast material.

INTRODUCTION

Ectopic pregnancy (EP) is the implantation of a developing blastocyst at a site other than the uterine endometrium. The classic triad of EP symptoms includes abdominal or pelvic pain, vaginal bleeding and a tender adnexal mass that classically emerges 6 to 8 weeks after the last menstruation.¹ The rapid and correct diagnosis of this life-threatening condition is of great importance.

EP's main risk factors are a prior history of EP, pelvic inflammatory disease and gynaecologic and other abdominal surgeries, history of infertility, placenta previa, intra-uterine device, *in vitro* fertilization, congenital uterine anomalies, endometriosis, smoking, exposure to diethylstilboestrol.² Its incidence is expected to be rising currently.

The majority of EP cases (95%) are tubal in location, occurring most commonly in the ampullary portion.² The finding of an adnexal mass that is distinct from the ovary is a typical finding of a tubal EP with all imaging modalities.³ Other cases in which EP is encountered are the abdominal cavity, uterine cervix, ovaries, interstitium, intraligamentous,

heterotopic pregnancy, Caesarean section scar, pregnancy after supracervical hysterectomy.

Sensitive human chorionic gonadotropin measurement devices and the common use of ultrasonography (US) and laparoscopy have led to early and accurate diagnoses. US features in a classical tubal EP encompass a live extra-uterine pregnancy, tubal ring, heterogeneous adnexal mass, haematosalpinx, and a “ring of fire” on a colour Doppler.⁴ The ring of fire is accepted as a measure of the hyper-vascularity of the ectopic gestational sac; its primary value is in discovering an obscure EP, especially one covered by a haematoma.⁴ It has been suggested that the enhancing ring in adnexa on CT images was correlated with the “ring of fire” sign on US of tubal pregnancy, as the endometrium may contain a thin-walled decidual cyst or a pseudogestational sac.^{2,5} MRI findings of tubal EP include haematosalpinx, a haemorrhagic or heterogeneous mass, bloody ascites, tubal dilatation and wall enhancement.⁶ The wall of the gestational sac is characteristically iso-intense on both T_1 - and T_2 weighted images.⁷ This thick wall is enhanced after the administration of contrast material.^{7,8} MRI offers the benefits of multiplanar imaging, a relatively unlimited field of view compared with US, lack of

Table 1. Features of the patients

Patient number	Age	Predisposing factor	Localization	Gestational sac diameter (mm)	Gestational age (week)
1	29	Smoking	Right ovary	14	7
2	31	–	Left tuba	15	7
3	36	Prior Caesarean section	Caesarean section scar	18	7
4	32	Endometriosis, prior laparoscopy	Right ovary	14	7
5	41	<i>In vitro</i> fertilization	Left ovary	13	7
6	37	Prior Caesarean section, smoking	Caesarean section scar	12	7
7	33	–	Right tuba	22	8
8	30	Prior pelvic inflammatory disease	Parauterine	29	9

ionizing radiation and greater soft-tissue contrast and tissue characterization options.⁹

In this paper, we present imaging findings of EP with special emphasis to “ring of restriction” sign on diffusion-weighted imaging (DWI) and discuss possible causes of “ring of restriction”.

METHODS AND MATERIALS

After intuitional ethical committee approval gynaecology and radiology archives were evaluated retrospectively. Between January 2014 and January 2017, a total of 40 patients were diagnosed with EP at our university hospital, 8 of whom (20%) were evaluated by both conventional MRI and DWI. Patients were examined by a 3-Tesla scanner (Achieva 3.0T, Philips Healthcare, Cleveland, OH). The obtained sequences were coronal and transverse T_2 turbo spin echo, transverse dual gradient echo, transverse single shot turbo spin echo with relatively short and

longer TE, transverse T_2 spair, DWI. DWI parameters were TR 3400 ms, TE 60 ms, frequency and phase matrix 144×256 , field of view 310–350 with rectangular FOV of 80%, EPI factor 109, sensitivity encoding factor (SENSE) 2, half scan factor 60%, b values of 50 and 800.

RESULTS

All of the 8 patients (all female, mean age 34; 29- to 41-year-old) were haemodynamically and clinically stable. Patients could not be imaged satisfactorily by US due to limited field of view or non-specific imagind findings. MRI could reveal the patients adequately. Patients' profile can be seen in [Table 1](#). Locations of EP were ovary ($n = 3$, 37.5%), tubal ($n = 2$, 25%), Caesarean section scar ($n = 2$, 25%) and parauterine ($n = 1$, 12.5%). In all eight EPs, the gestational sac diameter was compatible with 7–9 weeks (mean 17 ± 5 mm). With DWI, the gestational sac was seen as a thick-walled cyst-like structure. The thick wall showed diffusion restrictions in all patients ([Figures 1–3](#)). We named this

Figure 1. (a–c) EP at the site of Caesarean section scar (a) transverse fat-saturated T_2 TSE, (b) DWI and (c) ADC map show a thick-walled cyst with “ring of restriction” sign. ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; EP, ectopic pregnancy; TSE, turbo spin echo.

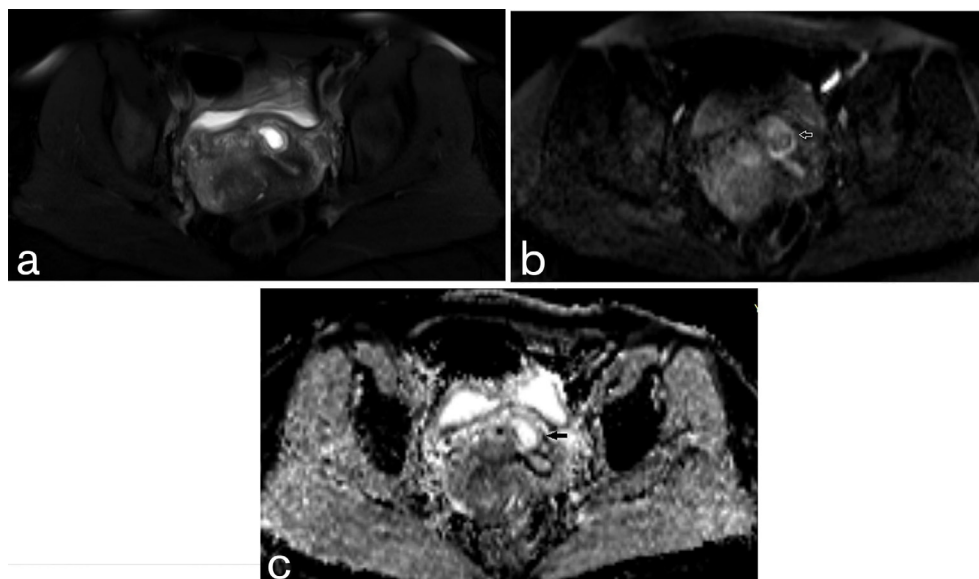
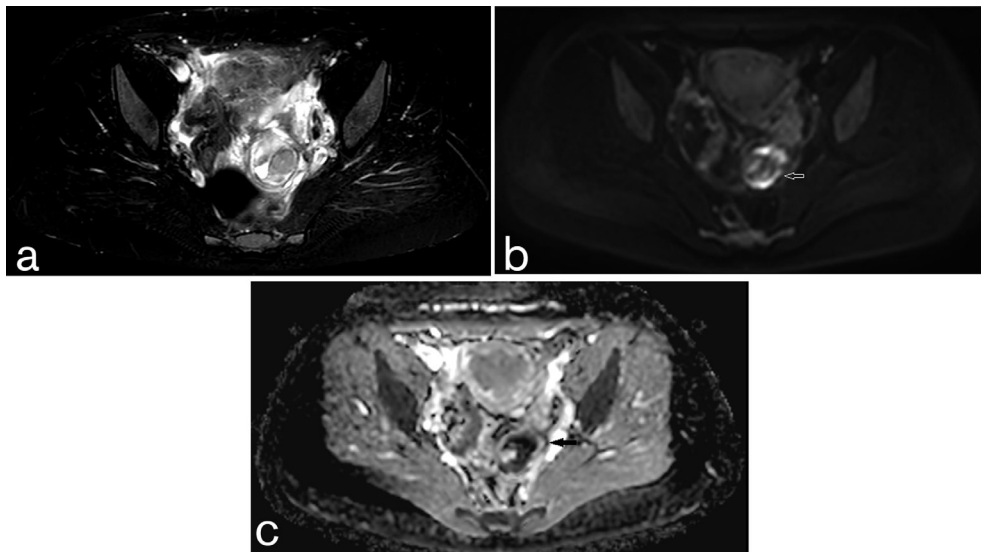


Figure 2. (a-c) EP at parauterin region (a) transverse fat-saturated T_2 TSE, (b) DWI and (c) ADC map show an enhancing thick-walled cyst with “ring of restriction”. ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; EP, ectopic pregnancy; TSE, turbo spin echo.



relatively early finding as “ring of restriction” similar to “ring of fire” described by the other modalities.

Patients were treated conservatively.

DISCUSSION

DWI provides information at the molecular level of tissues and pathological processes. This method principally measures the diffusion of water molecules through the extracellular matrix of the tissue concerned. Dense cellular structures, aggressive tumours, high cellular proliferation rate, large nucleus size, intracellular macromolecules, high nucleus-cytoplasm ratio and the limited size of the extracellular matrix may all lead to diffusion restriction.¹⁰⁻¹² Additionally, DWI requires no contrast agents. A study on conventional MRI and DWI findings of non-neoplastic

diseases of the Fallopian tube concluded that MRI is the method of choice for studying adnexal pelvic masses, while qualitative and quantitative functional imaging with DWI can be of help in the characterization of tubal diseases.¹³ However, this paper covers only tubal EP and gives entire diffusion restriction of the lesion. In our study group diffusion restriction has been encountered at the wall of the EP. Additionally, in another study on findings and clinical utility of MRI for EP have mentioned ring or dot like hyperintensity on DWI similar to our results.¹⁴

The wall of the gestational sac contains trophoblasts. Higher cellularity of trophoblasts due to high ratio of cellular proliferation, additional vascular-fibroblastic proliferation, macromolecules within the cytoplasm and extracellular matrix may all contribute to the diffusion restriction of the lesion. The large,

Figure 3. (a-c) EP at the right tuba (a) coronal fat saturated T_2 TSE, (b) DWI and (c) ADC map show a thick-walled cyst with “ring of restriction”. ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; EP, ectopic pregnancy; TSE, turbo spin echo.

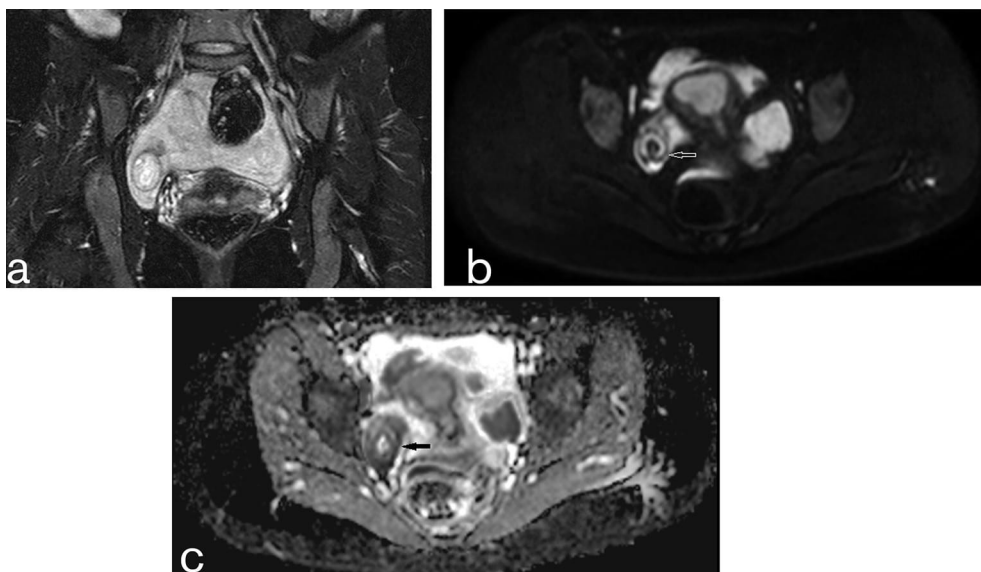
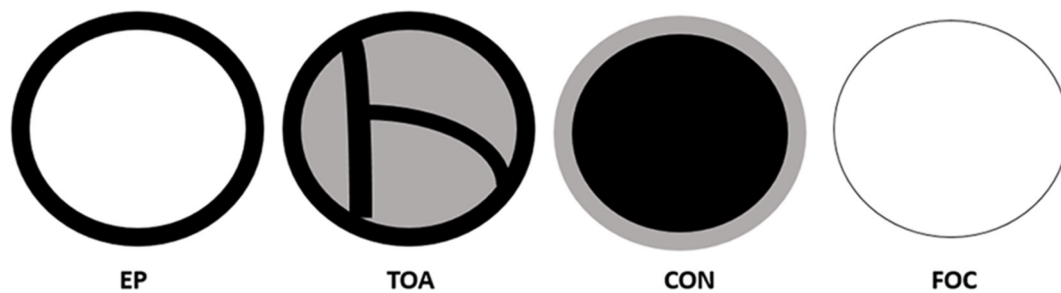


Figure 4. Representative figure demonstrating ADC map findings of cystic adnexal masses. While EP shows “ring of restriction”, TOA displays diffusion restriction in their walls, septa and purulent content, CON in their cystic components and FOC shows no diffusion restriction. CON, cystic ovarian neoplasm; EP, ectopic pregnancy; FOC, functional ovarian cyst; TOA, tubo-ovarian abscess.



round-to-oval-shaped nuclei were of different size, hyperchromatic and featured prominent nuclear membranes. Glycosaminoglycans are produced in cytotrophoblasts and released extracellularly.¹⁵ In addition, fibronectin is a high-molecular weight glycoprotein of the extracellular matrix of trophoblastic activity.¹⁶ Fibronectin plays a major role in cell adhesion, growth, migration and differentiation.¹⁶ Another set of macromolecules, laminins, are high-molecular weight proteins of the extracellular matrix. Laminins affect cell differentiation, migration and adhesion.¹⁷

Up to the present study, all US, colour Doppler US, CT and MRI findings of EP have been primarily based on anatomical considerations and increased vascularity.^{1-6,14} However, DWI in our paper may show cellular, macromolecular and extracellular EP features, in addition to anatomical considerations and increased vascularity.

The differential diagnosis of an adnexal mass with peripheral enhancement includes tubo-ovarian abscess, cystic ovarian neoplasm and a functional ovarian cyst, including a corpus luteum cyst. Tubo-ovarian abscesses are expected to show diffusion restriction in their walls, septa and purulent content.¹³ Cystic ovarian neoplasms have been reported to have low ADC values in their cystic components.¹⁸ A functional ovarian cyst shows no diffusion restriction. Thus, DWI may serve as a discrimination tool (Figure 4).

As a conclusion, the EP gestational sac demonstrates diffusion restriction in its wall, which may be attributed to its cellular possessions, vascular-fibroblastic proliferation, macromolecules within the cytoplasm and the extracellular matrix. Studies conducted with larger population and supported by histopathology are required. DWI may be of value in helping to discriminate EP from other cystic lesions in this region.

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