

Research Letter

## Exaggerated placenta site in placenta previa: an imaging differential diagnosis of placenta accreta, placental site trophoblastic tumor and molar pregnancy

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A 34-year-old primigravida was referred to our tertiary hospital for further management, because of intrauterine fetal demise and suspected placenta previa accreta, with focal uteroplacental hypervascularization despite three doses of methotrexate (MTX) treatment at 24 weeks of gestation. Serum  $\beta$ -hCG level decreased from 9000 IU/mL to 3000 IU/mL after the 2<sup>nd</sup> MTX treatment. The patient had a history of endometriosis and adenomyosis, for which she underwent a laparoscopic surgery and conceived naturally soon after the procedure. Genetic amniocentesis was performed at 16 weeks of gestation, because of advanced maternal age, and revealed a normal 46,XX karyotype.

A sagittal transabdominal ultrasound (US) image shows a demised fetus and bulky placenta, with multicystic sonolucent spaces in the lower half of enlarged placenta parenchyma (Fig. 1). A sagittal transabdominal power Doppler US image shows hypervascularity, with low resistance turbulent flow surrounding the echogenic uterine lesion (Fig. 2). T2 weighted magnetic resonance imaging (MRI) (Fig. 3) showed accumulated flow voids just under the central part of the placenta. The myometrium beneath the abnormal retroplacental vascular area showed a well defined area with high to intermediate heterogeneous signal intensity on T2-weighted MRI.

Prophylactic transcatheter arterial embolization (TAE) of bilateral uterine arteries was performed, which showed uterine

hypervascularity (Fig. 4). The demised fetus was extracted through fundal hysterotomy. Manual removal of the placenta was uneventful. However, a raised nodular mass measuring 3 cm in length at the posterior wall of the uterus was identified. The resected specimen was sent for histopathology examination. The nodular mass was composed of proliferations of medium to large sized mononuclear and multinucleated intermediate trophoblasts and cytotrophoblasts, with cells of lesion permeating throughout the myometrium and intravascular spread (Fig. 5). There was an absence of mitotic figures and a low Ki-67 labeling index (<5%), thus exaggerated placenta site (EPS) was diagnosed. Postoperatively, serial US showed unremarkable finding at 7 months follow up period.

EPS and placenta site trophoblastic tumor (PSTT) originated from implantation site intermediate trophoblasts (IT). EPS differs from PSTT, in that it has no confluent growth, no mitosis and is mixed with deciduas and villous [1]. The serum  $\beta$ -hCG level in PSTT or EPS is not correlated with tumor burden or malignant behavior [2]. A decreased Ki-67 labeling index reflects the non-neoplastic feature of IT. The Ki-67 index in IT of the EPS site was near zero, but in the molar implantation sites of molar pregnancy, the Ki-67 index was  $5.2\% \pm 4.0\%$ . In contrast, the Ki-67 index in IT of the PSTT was  $14\% \pm 6.9\%$  and in the choriocarcinoma was  $69\% \pm 20\%$  [3].

It often accompanies proliferation of IT in placenta accreta [4]. Our case is diagnosed as EPS without evidence of placenta accreta according to the absence of infiltrating chorionic villi destruction in the myometrium and we easily separated the placenta during surgery.

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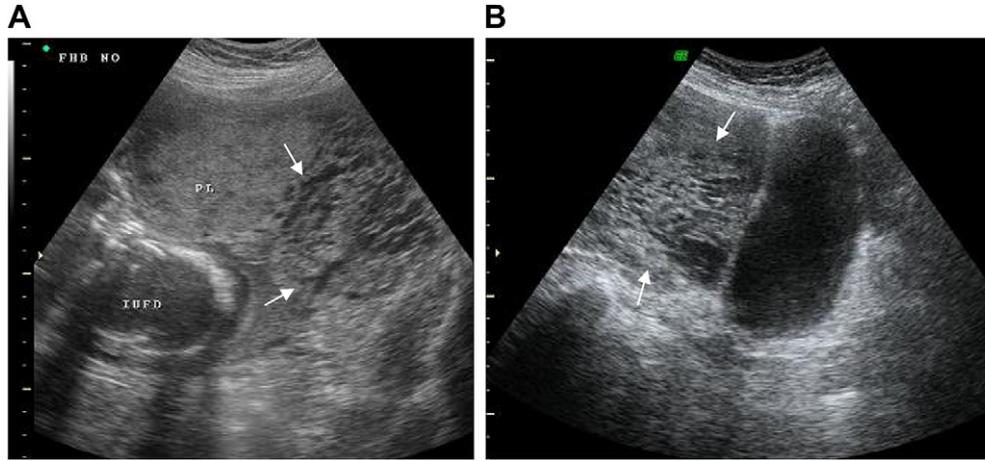


Fig. 1. (A) sagittal transabdominal ultrasound (US) image shows a demised fetus and bulky placenta, with multicystic sonolucent spaces in the lower half of the enlarged placenta parenchyma; and (B) note the “honeycomb appearance” of cystic molar changes (arrows) were clearly seen in the lower half of placenta (arrows) adjacent to bladder.

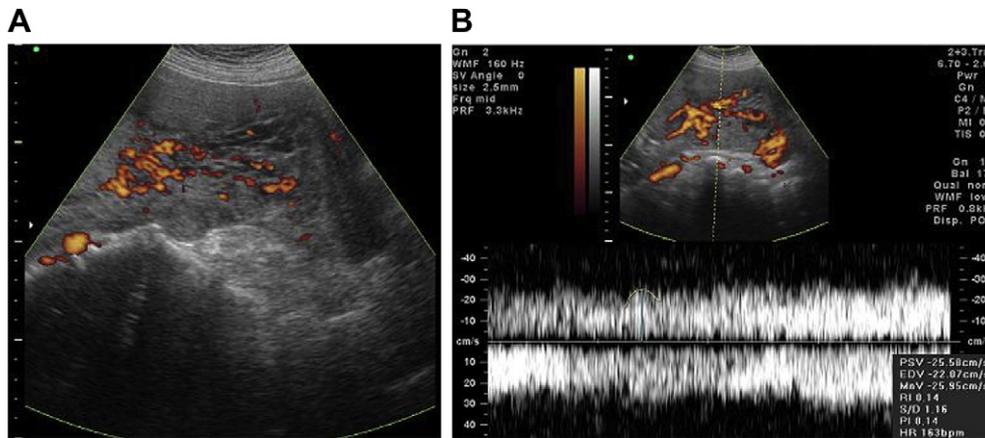


Fig. 2. (A) Sagittal transabdominal power Doppler US image shows hypervascularity with (B) low resistance turbulent flow surrounding the echogenic uterine lesion.

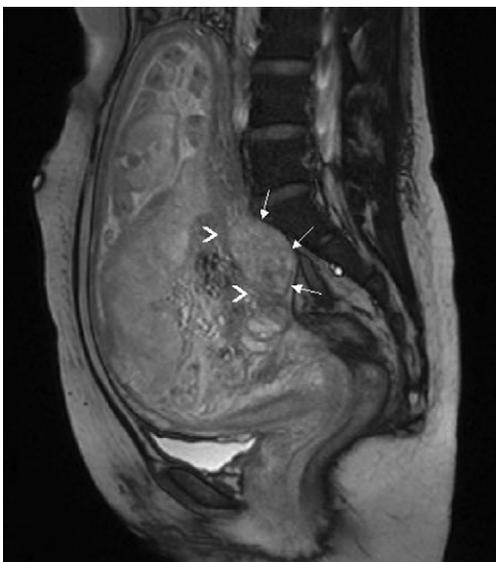


Fig. 3. Sagittal T2-weighted MRI image shows the posterior uterine wall, a well defined heterogeneous high to intermediate signal intensity mass (arrow). Flow void area located between placenta and the uterine mass, with continuous hypointense inner layer of the myometrium (arrowheads).

Characteristic gray scale US imaging of the EPS and PSTT showed ill-defined margins of mass lesions from the surrounding myometrium [5–7]. Intraplacental multiple irregular lacunae with a “moth-eaten” appearance and a low resistance turbulent flow, is a characteristic US sign of placenta accreta/increta/percreta [8,9], but this sonographic sign is not present in the EPS or PSTT. In addition, myometrial thickness is <1 mm, or loss of the visualization of the myometrium in placenta accreta/increta/percreta. However, in EPS and PSTT, lesions may present as thickened myometrium by gray-scale US examination [5–7]. The MRI image of the EPS showed a continuous inner layer of myometrium over the hypervascularized area, which would loss in placenta accreta (Fig. 3).

A PSTT appears, sonographically, as small heterogeneous echogenic uterine lesions surrounded by numerous intramyometrial vascular signals, with fluid-filled cysts representing hemorrhagic areas [10]. It can also appear on a US scan as a solid tumor invading the myometrial wall [9]. Both PSTT and EPS are isointense on the T1-weighted image. On the T2-weighted image, the heterogeneity of both cases is much different. In EPS cases, the mass is heterogeneous, with high

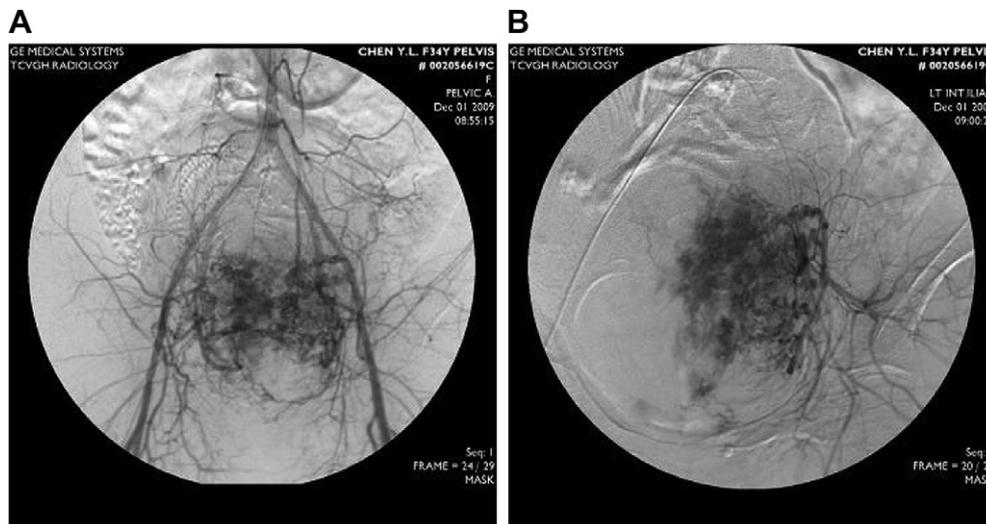


Fig. 4. Pelvic arteriography shows dilatation and tortuosity of the bilateral uterine arteries and prominent stains over the lower segment of uterus: (A) posterior to anterior view (PA) view; and (B) left lateral view.

to intermediate signal intensity. In PSTT cases, there is flow void area within the mass, except the high to intermediate signal intensity of the solid part [5,6].

A partial hydatidiform mole involves the combination of a fetus with localized placental molar degeneration. Classically, a partial mole presents on US examination as an enlarged placenta containing multicystic avascular sonolucent spaces with a “Swiss cheese appearance”, with normal or high uterine arterial resistance to flow [10]. A pregnancy with hydropic changed placenta and a demised fetus may resemble a partial molar pregnancy, and the low HCG level may exclude the diagnosis. We cannot differentiate our case from

a partial molar pregnancy or coexistent mole and fetus, sonographically.

Our case demonstrated characteristic sonographic features of EPS during pregnancy, and added an imaging differential diagnosis to partial molar pregnancy, placenta accreta and PSTT.

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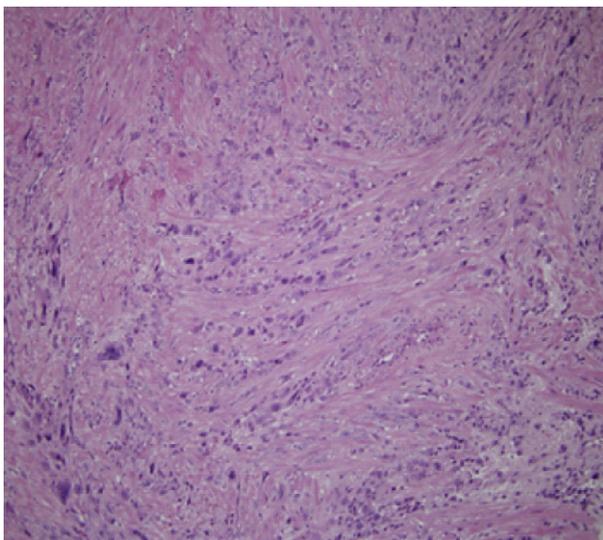


Fig. 5. Proliferation of medium to large-sized mononuclear and multinucleated cytotrophoblasts and intermediate trophoblasts is noted in the whole layer of the myometrium. (hematoxylin-eosin stain,  $\times 100$ ).