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Report

Magnetic Resonance Imaging Features of Invasive Mole Clinically Treated as Choriocarcinoma

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Recently, the incidence of gestational trophoblastic disease, which comprises a spectrum of trophoblastic tumors that includes hydatidiform mole (partial and complete), invasive mole, and choriocarcinoma, has been decreasing worldwide; in particular, invasive mole and choriocarcinoma are now rare in Japan. We describe the case of a 49-year-old Japanese woman with a histologically confirmed invasive mole who was clinically treated for choriocarcinoma and underwent total hysterectomy. Preoperative magnetic resonance imaging revealed an intramyometrial hypervascular tumor in the enlarged uterine body that included multiple cystic lesions that represented hydropic villi and that invaded into the parametrium. These features were consistent with invasive mole. Although patients with gestational trophoblastic disease are primarily treated by chemotherapy following a clinical diagnosis based on clinical scoring systems, magnetic resonance imaging, which often reflects histological characteristics of the disease, can be feasible for correct diagnosis and appropriate treatment.

Key words: gestational trophoblastic disease, invasive mole, magnetic resonance imaging, uterus

Introduction

Invasive mole or choriocarcinoma as malignant forms of gestational trophoblastic disease (GTD) are uncommon. Such tumors are primarily treated by chemotherapy in accordance with clinical scoring systems and seldom diagnosed pathologically. We present a rare case of histologically diagnosed invasive mole that was clinically classified as high-risk GTD or clinical choriocarcinoma; although magnetic resonance (MR) imaging features were consistent with invasive mole, the patient underwent total hysterectomy. We correlate radiologic and pathologic findings in this case.

Case Report

A 49-year-old Japanese woman, gravida 3, para 2, whose last pregnancy was terminated by artificial abortion at age 28 was referred to a local hospital with a 2-month history of atypical genital bleeding. The uterine contents were evacuated and histologically confirmed to be necrotic decidua. Tranvaginal ultrasonography revealed a cystic lesion in the uterine cervix. She was referred to our institution for suspicion of cervical pregnancy. On initial pelvic examination, the uterus was enlarged to fist size and palpated myomatous-hard with tenderness. Laboratory tests showed elevated levels of asparatate aminotransferase (AST; 45 IU/L), alanine aminotransferase (ALT; 66 IU/L), and lactate dehydrogenase (LDH; 342 IU/L). All tumor markers were within normal ranges, except serum β-human chorionic gonadotropin (β-hCG; 1,000 ng/mL) and urine hCG (230,083 IU/L). Tranvaginal ultrasonography demonstrated a heterogeneous mass with multiple small anechoic areas in the enlarged uterus and a

cystic lesion in the uterine cervix. On Doppler sonography, the former mass showed hypervascularity. The following day, she was admitted to the obstetrics and gynecology department with the presumptive diagnosis of GTD.

MR imaging revealed an ill-defined mass, approximately 8 cm in maximal diameter, located predominantly in the myometrium of the right lateral wall of the enlarged uterine body and extending to the right parametrium. T_2-weighted imaging showed the mass as an area of heterogeneous high intensity with partially disrupted junctional zone and multiple small cystic lesions; on T_1-weighted imaging, areas of high intensity represented hemorrhage. Flow signal voids were prominent in and around the mass (Fig. 1, 2). Marked enhancement was visualized in the early phase of contrast-enhanced dynamic study (Fig. 3, 4). These findings were likely to be consistent with GTD, especially invasive mole. In addition, a cystic lesion in the uterine cervix indicated a nabothian cyst. No metastasis was identified even on later computed tomographic examination.

According to the 2002 revised International Federation of Gynecologists and Obstetricians (FIGO) scoring system, the patient's tumor was classified as a high-risk GTD (score 9). Furthermore, according to the choriocarcinoma diagnostic scoring system widely used in Japan, it was also diagnosed as clinical choriocarcinoma (score 11). She underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy one month after admission. At laparotomy, the tumor in the enlarged right lateral wall of the uterine body was very rich in blood vessels, and extension to the right parametrium caused right hydroureter. The tumor was incompletely resected to preserve the right ureter. Grossly, the mass comprised hydropic villi, necrotic tissue, and hemorrhage (Fig. 5). Microscopically, cytotrophoblasts and syncytiotrophoblasts with marked atypia proliferated around the hydropic villi (Fig. 6). Consequently, the definitive diagnosis was invasive mole. She underwent multi-agent chemotherapy for residual tumor after surgery.

Discussion

GTD comprises a spectrum of trophoblastic tumors including hydatidiform mole (partial, complete and invasive mole) and choriocarcinoma. Their prevalence varies considerably with geography, with the highest rates of disease in Southeast Asian nations and low to intermediate risk in North American and European countries[1)2)]. This variation may be due to socio-economic/dietary and environmental factors, and improvement in these factors has been credited with globally decreasing the incidence of GTD[3)4)]. In Japan, invasive moles and choriocarcinomas, in particular, have become rare.

GTD is suspected in patients with genital bleeding and a clinically enlarged uterus and is usually diagnosed on the basis of persistently high hCG values. Furthermore, ultrasonography is utilized as the first imaging modality for diagnostic evaluation. Uterine masses with or without cystic lesions and increased vascularity with pathologic resistive and pulsatility indices are the main sonographic features in patients with GTD[5)~7)]. However, ultrasonography is operator dependent and only poorly reproducible and, so, seems to be less than optimal for evaluating tumor size and extent of infiltration, which is important for tumor staging and adequate therapy[7)].

MR imaging allows high contrast resolution and reproducibility to most accurately assess histological characteristics, size, and infiltration of tumor in neoplastic diseases of the pelvis. The following MR imaging features regarding GTD have been reported. On T_2-weighted imaging, GTD tumors typically have a heterogeneous high intensity with an indistinct boundary between the endometrium and myometrium, and diffusely increased myometrial intensity reflects diffuse myometrial involvement by tumor[1)2)7)~11)]. On T_1-weighted imaging, tumors may include areas of high intensity that represent hemorrhage, which is quite variable on both T_1 and T_2-weighted images depending on its age[1)2)7)~11)]. Features indicating tumor hypervascularity are tortuous flow voids consistent with vessels that pass through the tumor and within the adjacent myometrium, parametrium, and adnexae[1)7)10)11)]. Internal iliac and uterine vessel engorgement, especially with respect to the external iliac vessels, is

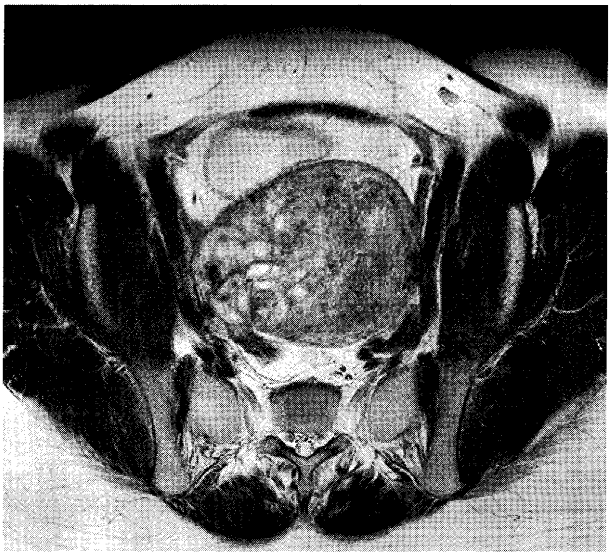

Fig. 1 T_2-weighted axial image reveals an ill-defined intramyometrial mass of heterogeneous high intensity that includes multiple small cystic lesions in the right lateral wall of the uterine body
The mass protrudes into the right parametrium.

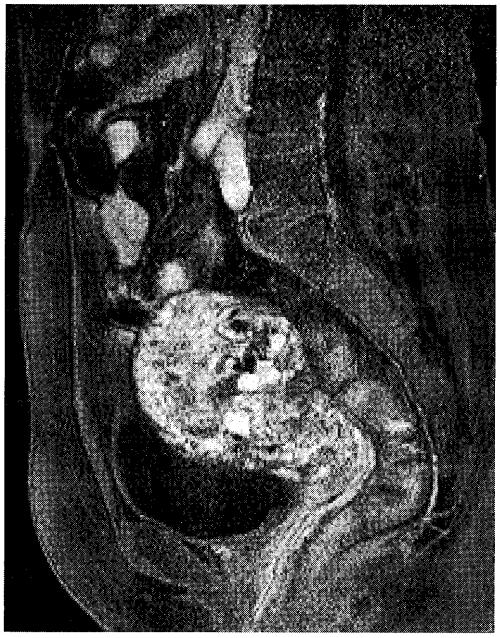

Fig. 3 The early phase of contrast-enhanced dynamic sagittal image reveals heterogeneous marked enhancement in the mass

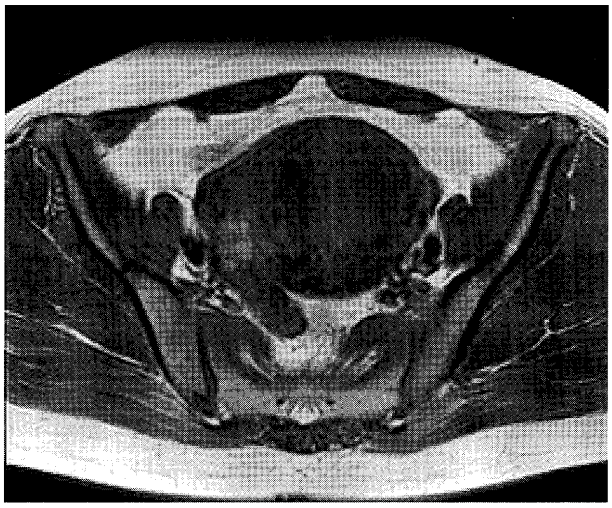

Fig. 2 T_1-weighted axial image reveals areas of high intensity that represent hemorrhage within the mass
Note flow signal voids in the posterior wall of the uterine body.

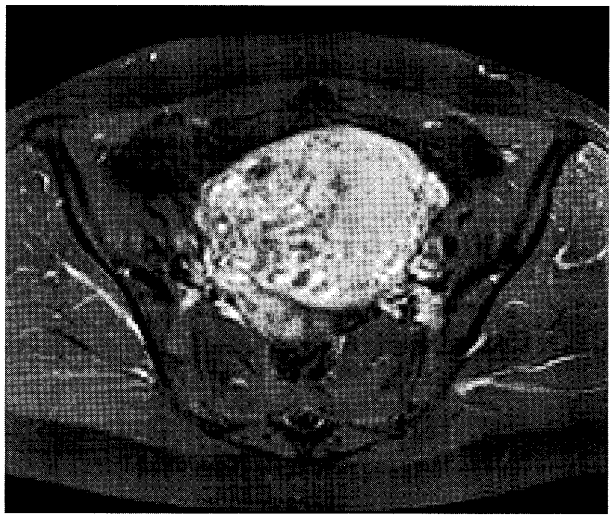

Fig. 4 Post-contrast-enhanced T_1-weighted axial image with fat suppression reveals the heterogeneously enhanced mass, which includes multiple small cystic lesions

also a feature[1)10)]. On contrast-enhanced dynamic MR imaging, tumors show marked enhancement in the early dynamic phase[1)7)10)]. Furthermore, the uterus is diffusely enlarged, and multi-loculated cystic lesions, known as theca-lutein cysts of the ovary, may be revealed in both enlarged ovaries, reflecting elevated hCG levels[7)8)10)12)].

Invasive mole and choriocarcinoma, as malignant forms of GTD, invade into the myometrium, distorting the uterine zonal structures, and may involve the parametrium; on T_2-weighted imaging, they can be readily visualized as enlarged masses of high intensity within the parametrium and beyond the uterine cavity, whereas hydatidiform moles are localized within the endometrium[1)2)7)~10)]. Generally, invasive moles are locally invasive; in contrast, chorio-

Fig. 5 Gross specimen shows an intramyometrial tumor consisting of hydropic villi accompanied by necrosis and hemorrhage in the uterine body that extends beyond the serosa

Fig. 6 Photomicrograph (hematoxylin-eosin stain) shows proliferated trophoblasts with atypia around the hydropic villi

carcinomas often develop hematogeneous metastases to the lungs, vagina, vulva, kidneys, liver, ovaries, brain, bowel, and other organs[1)8)]. However, differential diagnosis between invasive moles and choriocarcinomas is sometimes difficult, especially in the absence of metastatic lesions. Absence of chorionic villi on histology is an important diagnostic feature of choriocarcinoma, whereas diagnostic imaging of hydatidiform mole and invasive mole can show multiple cystic lesions that represent hydropic villi[2)8)10)11)]. Magnetic resonance imaging features of the present tumor are thought to be consistent with an invasive mole as described above, especially because the mass included multiple small cystic lesions that represented hydropic villi and protruded invasively into the right parametrium. These findings were also histologically confirmed by radiologic and pathologic correlation.

In the many patients in whom the diagnosis of invasive mole or choriocarcinoma remains unclear, hysterectomy is rarely justified or necessary, and chemotherapy is the preferred treatment. The FIGO scoring system revised in 2002 is used in many institutions to stratify patients with malignant GTD into 2 therapeutic groups. Those with a low FIGO score (≤ 6) who are treated as having an invasive mole with an almost 100% cure rate have a low risk of developing disease resistant to single drug therapy (methotrexate or actinomycin D), whereas those with a high score (>6) who are treated as having a choriocarcinoma with an 80 to 90% cure rate require multi-agent combination therapy[1)13)]. Our patient was classified into the high-risk group and diagnosed with clinical choriocarcinoma according to the choriocarcinoma diagnostic scoring system widely used in Japan, which categorizes disease of patients with a low score (≤ 4) as clinical invasive mole and disease with a high score (>4) as clinical choriocarcinoma with an accuracy of better than 90%[14)]. Nevertheless, our patient's MR imaging features reflected the histological diagnosis of invasive mole following hysterectomy. Almost all patients with invasive mole can be successfully treated by single-agent chemotherapy. In contrast, multi-agent chemotherapy is primarily used for the treatment of choriocarcinoma, and EMA / CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine) has been the most preferred treatment choice with the response rates from 70% to 90% in patients with choriocarcinoma[15)]. Severe myelosuppression and secondary tumor development, such as primary leukemia, colon and breast cancer, and malignant melanoma, are especially hazardous in this treatment. MR imaging can provide information for correct diagnosis, thereby reducing unnecessary adverse events from aggressive treatment for patients with choriocarcinoma, whereas it is generally known to be useful, especially in assessing myometrial and parametrial tumor extension and tumor vascularity, and an accurate tool in tumor staging. Hereafter, the frequency of this discrepancy between radiologic and pa-

thologic diagnosis should be clarified by accumulation of such cases. Thus, the feasibility of MR imaging in accurate diagnosis and proper patient management is mandatory to investigate for improving the quality of patients' life by reducing unnecessary aggressive treatment.

In conclusion, our patient was clinically treated as having choriocarcinoma according to both the new FIGO scoring system and the choriocarcinoma diagnostic scoring system, but her MR imaging features were consistent with invasive mole, which was confirmed histologically following hysterectomy. Even in such a rare case, MR imaging can be useful for correctly diagnosing and adequately treating GTD.

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臨床的絨毛癌として治療された侵入奇胎のMRI所見

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絨毛性疾患は世界的に減少しており，特に侵入奇胎と絨毛癌は今日の日本において稀である．今回我々は，臨床的絨毛癌と診断され，子宮全摘術が施行されたが，組織学的に侵入奇胎と診断された症例を経験したので，そのMRI所見を中心に報告する．

症例は49歳女性．妊娠3回，分娩2回．最終妊娠は人工妊娠中絶が施行された．不正性器出血を主訴に近医受診し，子宮内膜掻爬が施行されたが，組織学的に変性脱落膜のみであった．経腟超音波検査にて子宮頸部に嚢胞性病変を認め，子宮外妊娠が疑われ，当院産婦人科に紹介受診となり，血清β-hCGが1,000 ng/mL，尿中hCGも230,083 IU/Lと高値であった．FIGOスコアでhigh risk GTD（9点），絨毛癌診断スコアで臨床的絨毛癌（11点）と診断され，子宮全摘術が施行されたが，組織学的に侵入奇胎と確定された．

術前MRIでは腫大した子宮体部筋層内に不整形腫瘤を認めた．腫瘤はT2強調像で不均一な高信号を示し，内部にT1強調像で出血を示唆する高信号域を有し，造影早期相で濃染され，腫瘤周囲にはflow voidが目立ち，富血管性腫瘍の特徴を示した．子宮傍組織への浸潤所見と腫瘤内には多数の嚢胞性病変を認め，組織学的には水腫様に腫大した絨毛組織に相当し，通常絨毛癌では認められない．また，遠隔転移も認めず，以上のMRI所見は侵入奇胎に合致していた．

MRIは組織コントラストが高く，病変の組織学的特徴の評価に有用である．侵入奇胎や絨毛癌はFIGOスコアや日本独自の絨毛癌診断スコアをもとに臨床的に診断され，主に化学療法で治療されるが，両者の治療方針は異なり，その鑑別は非常に重要である．MRIを併用することにより，両者を鑑別でき，適切な治療に導くことが可能になると考えられた．