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·临床病例讨论·

胃癌子宫转移2例并文献复习

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[摘　要] 本文探讨胃癌子宫转移患者的临床病理特点、诊断及鉴别诊断。例1，患者女，40岁，以阴道少许出血就诊。病理显示在子宫内膜表浅间质内可见小灶分布的肿瘤细胞，大小形态较一致，细胞轻-中度异型性，细胞质嗜酸，部分细胞可见核仁，核分裂象罕见，部分区域累及子宫内膜腺体。免疫组织化学显示瘤细胞表达CEA、MUC6、MUC5AC、CK18、CK7、CK20、CDX2等消化系统来源标志物，不表达ER、PR及PAX8，D-240染色显示淋巴管癌栓。随后，该患者行胃镜检查，病理活检示胃低分化腺癌，形态与子宫内膜转移癌相似。例2，患者女，47岁，同样以阴道流血就诊，有胃癌病史。活检发现宫颈间质内见腺样排列或散在单个分布的癌细胞，免疫组织化学表达CK、CK20、CDX2等消化道来源标志物。胃癌子宫转移罕见，部分病例可无胃癌病史以阴道出血为首发症状就诊，极易误诊和漏诊，需仔细观察寻找证据，并加行免疫组织化学鉴别诊断。

[关键词] 胃癌；子宫转移；临床病理特征；免疫表型；鉴别诊断

Gastric cancer metastatic to uterus: A report of 2 cases and literature review

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Abstract In this paper, the clinicopathological features, diagnosis and differential diagnosis of two cases of metastatic gastric cancer to the uterus were discussed. Case 1 is a 40-year-old female who was hospitalized with light vaginal bleeding. The pathology showed the tumor cells were located in the superficial endometrial stroma, with focal distribution. The tumor cells had similar size and shape, mild-moderate atypia, and acidophilic cytoplasm. Nucleolus could be seen in some cells. Mitotic activity was rare. In some areas, endometrial glands were involved. Immunohistochemistry showed that the tumor cells were positive to CEA, MUC6, MUC5AC, CK18, CK7, CK20, CDX2 and other original markers of digestive system, while negative to ER, PR and PAX8. D-240 staining showed lymph vessel tumor emboli. After endoscopic examination and biopsy, poorly differentiated gastric adenocarcinoma was confirmed. Case 2 is a 47-year-old female with vaginal bleeding too. Unlike case 1, she had a history of gastric cancer. The biopsy revealed adenoid or scattered tumor cells in the interstitium of the cervix. Immunohistochemistry showed that the cells were positive to CK, CK20, CDX2, and other original markers of

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the digestive system. The case of gastric cancer metastatic to uterus is rare. In some cases, the patients present with vaginal bleeding but without a history of gastric cancer are easily misdiagnosed or never diagnosed. To avoid misdiagnosis, it is important for us to be fully aware of this carcinoma and apply immunohistochemistry to differential diagnosis.

Keywords gastric cancer; uterine metastasis; clinicopathological features; immunophenotype; differential diagnosis

来自生殖系统以外的恶性肿瘤转移到子宫非常少见。没有原发癌病史，以子宫内膜转移为首发症状就诊的更为罕见，因此给诊断增加了相当的难度。我们报告2例胃癌子宫转移的病例(其中转移到子宫内膜的1例无原发癌病史)，并复习相关文献，分析其临床病理学特征、免疫组织化学表型、诊断及鉴别诊断，以避免临床上误诊、漏诊。

1 临床资料

1.1 例1

例1，患者女，40岁，因无明显诱因出现阴道出血就诊，出血持续1 d，量少。2个月前曾无诱因出现恶心、偶有呕吐(少许胃内容物)，无明显腹胀、腹痛等症状。当地医院查^{14}C尿素呼气试验幽门螺旋杆菌阳性，胃镜活检示慢性非萎缩性炎。血HCG、CA-125、CEA、CA19-9均持续增高。阴道B超示：内膜厚约1.4 cm，宫腔内未见明显孕囊回声。双侧卵巢未见明确异常回声。遂行刮宫检查。

肉眼观：灰红色子宫内膜组织一堆，大小2.5 cm×1.8 cm×0.8 cm，切面局灶呈灰白、灰黄色，质中、稍软。

组织学：子宫内膜呈分泌期样改变，子宫内膜表浅间质中可见多小灶散在分布的腺样及团巢状肿瘤细胞。瘤细胞中等大小，形态较一致，细胞质嗜酸性，部分细胞可见核仁，核分裂象罕见，可见凋亡。瘤细胞多数在间质生长，局灶累及内膜腺体。未见明显间质反应。可见个别淋巴管癌栓(图1)。

免疫组织化学：瘤细胞表达CEA、CK18、MUC6、MUC5AC、CK7、CK20、CDX2(图2)，不表达ER、PR、PAX8、p16、VIM、p63、Syn、CD10、GATA3，D-240染色示个别淋巴管癌栓。

病理诊断：子宫内膜转移癌，免疫组织化学提示消化道来源可能性大。

后续检查：该患者行PET-CT示胃壁弥漫增厚并放射性摄取稍增高，以胃角、胃底明显，最大标准化摄取值(SUVmax)为2.7，胃壁浆膜毛糙。考虑胃癌伴腹膜及淋巴结转移、双侧肾上腺转移、右侧胸膜转移、骨及骨髓转移可能性大；子宫及双侧附件代谢活性未见明确异常(图3)。再次行胃镜检查(间隔1个月余，图4)示胃底穹窿部片状黏膜充血、粗糙伴糜烂，胃角、胃窦黏膜粗糙，倾向胃癌，病理活检示弥漫成片的肿瘤细胞浸润，瘤细胞中等大小，细胞质嗜酸性，可见小核仁，形态与子宫内膜转移癌相似(图5)，并见多发淋巴管癌栓。免疫组织化学示：CEA、MUC5AC、MUC6、CDX2阳性(图6)，MUC2、ER、PAX8阴性，提示为胃型。免疫表型与形态均与子宫内膜转移癌相似，提示二者同源，胃为原发病灶。

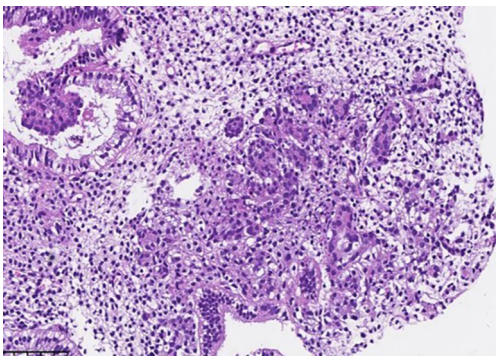

图1 例1：子宫内膜活检示肿瘤细胞呈团巢样浸润，伴细胞异型(HE，×100)

Figure 1 Case 1: endometrial biopsy shows a mass nest-like infiltration of tumor cells with mild atypia (HE, ×100)

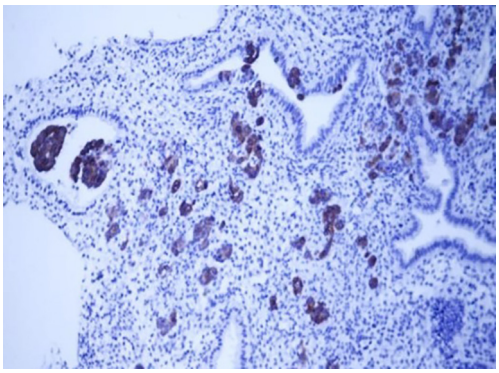

图 2 例 1：瘤细胞表达 CK20(IHC，×100)

Figure 2 Case 1: CK20 are positive in tumor cells (IHC, ×100)

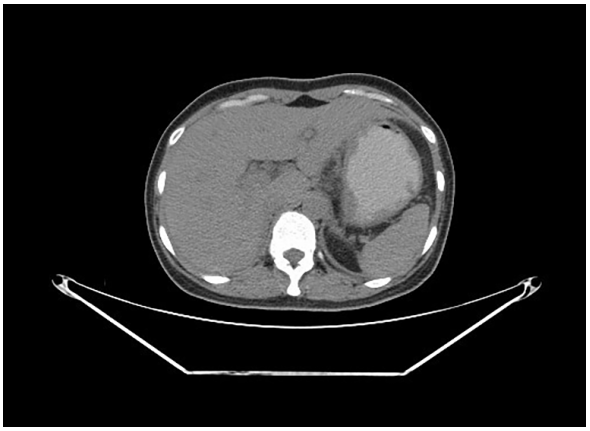

图3 例1：PET-CT检查

Figure 3 Case 1: PET-CT examination

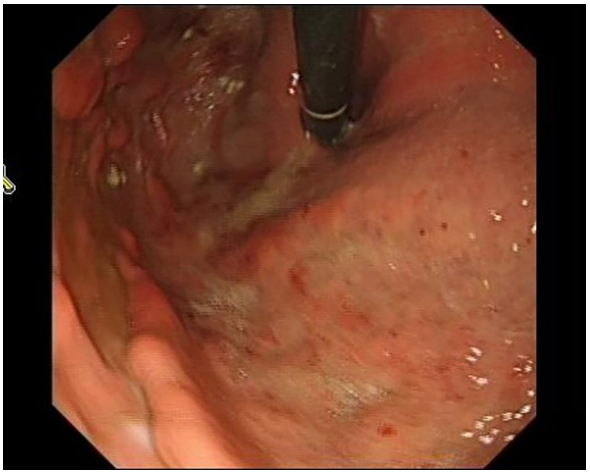

图 4 例 1：胃镜检查

Figure 4 Case 1: endoscopic examinations

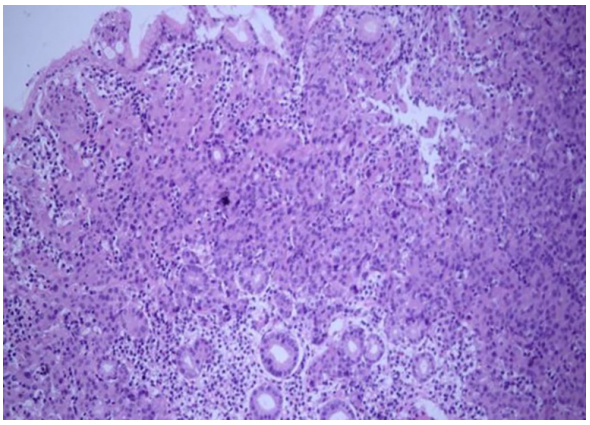

图 5 例 1：胃活检见弥漫浸润的癌细胞 (HE，×100)

Figure 5 Case 1: gastric biopsy shows diffuse infiltrating cancer cells (HE, × 100)

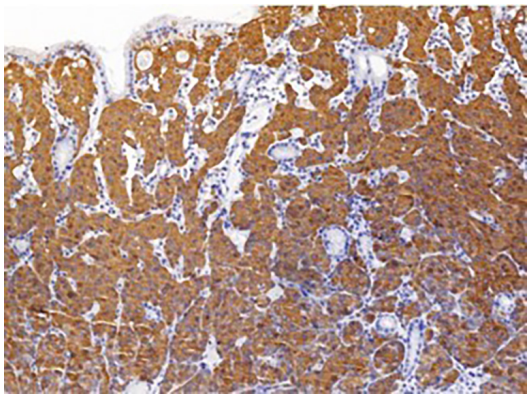

图 6 例 1：癌细胞 CK20 阳性 (IHC，×100)

Figure 6 Case 1: CK20 are positive in cancer cells (IHC, × 100)

1.2 例2

例2，患者女，47岁，有胃低分化腺癌病史2年，肿瘤最大径8 cm，侵及浆膜外，1、3、5、6、8组淋巴结可见转移。术后行SOX方案化疗，评价为病情稳定(stable disease，SD)。因阴道出血1周就诊。

肉眼观：灰白色宫颈活检组织1块，大小约0.7 cm×0.5 cm×0.3 cm，质中。

组织学：宫颈间质中可见单个散在或呈腺样排列的癌细胞，细胞异型明显，局灶可见黏液分泌(图7)，未见周围宫颈腺上皮非典型改变。

免疫组织化学：瘤细胞表达CK、CK20、CEA、CDX2(图8)，不表达p16和Pax8。

病理诊断：宫颈转移癌，结合病史及免疫组织化学考虑为胃癌转移。

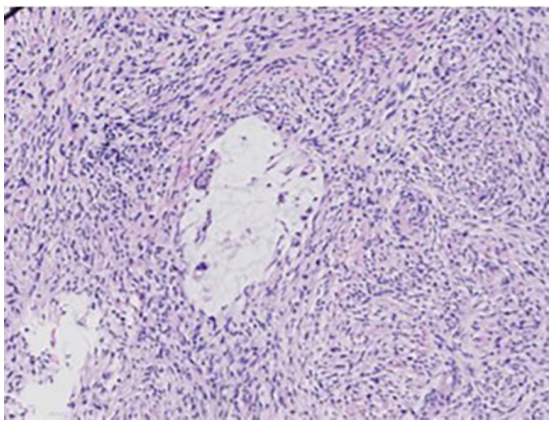

图7 例2：宫颈活检示瘤细胞呈腺样或单个散在(HE，×100)

Figure 7 Case 2: cervical biopsy shows adenoid or scattered tumor cells (HE, × 100)

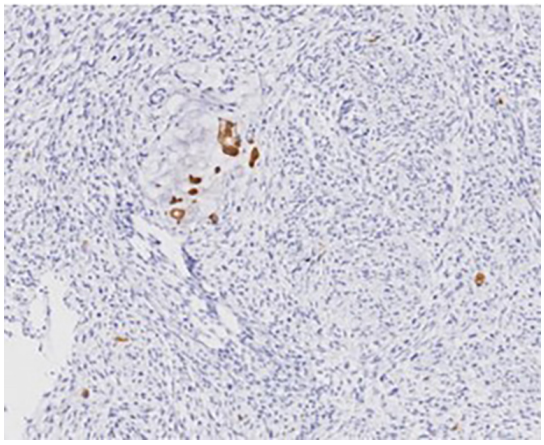

图8 例2：瘤细胞表达CK20(IHC，×100)

Figure 8 Case 2: CK20 are positive in tumor cells (IHC, × 100)

2 讨论

生殖系统以外的恶性肿瘤转移到子宫非常少见[1]，极易引起误诊。

首例第1例生殖系统外肿瘤转移到子宫的病例是Legg于1878年报告的恶性黑色素瘤转移[2]。其后有学者[3-5]相继报道了生殖系统外肿瘤转移到子宫的病例。这些转移癌以源自乳腺最为多见，其次为胃癌、小肠癌、恶性黑色素瘤、肺癌等[6]。在生殖系统外肿瘤转移到子宫的病例中，宫颈少于宫体，仅占总数的20%[7]。

大多数病例同时伴有卵巢受累。Weingold等[4]报道的病例基本伴有卵巢受累，实际上，卵巢是生殖系统外肿瘤转移最好发的部位(Krukenberg tumor)。胃癌转移到卵巢与淋巴结转移密切相关[8]。超过6个淋巴结转移的胃癌更容易发生卵巢转移[9]。但胃癌子宫转移的机制尚不清楚。目前认为大多数子宫转移灶是继发于卵巢转移灶，后者经局部淋巴结传播所致[10]。研究[5]表明：绝大多数病例(96.2%)有子宫肌层受累，约1/3的病例(32.7%)同时有肌层和子宫内膜受累，仅子宫内膜受累很少见(3.8%)，提示淋巴和血管播散及通过Fallopian管自卵巢直接管内播散可能是转移至子宫的机制；同时该团队回顾一些尸检病例发现为数不少(35%)的病例转到子宫却不伴有卵巢转移。因此也有观点[11]认为：血行转移也在其中起重要作用，因为胃癌子宫转移但未累及卵巢，且同时有肺远处转移。

例1患者为刮宫活检，B超和PET-CT均未发现卵巢异常。但无论是子宫内膜标本还是胃活检标本，都发现淋巴管癌栓，同时虽然没有发现血管侵犯，但PET-CT提示伴有远处转移，因此淋巴和血行转移可能都起重要作用。

多数病例有原发癌的病史。例2有胃癌病史，宫颈活检可见少量异型腺体伴黏液分泌。主要与原发于宫颈的胃型腺癌相鉴别。胃型宫颈腺癌是最常见的非HPV感染相关腺癌，形态学改变可轻微，容易漏诊。癌细胞胞质丰富，常呈透明或淡嗜酸性，细胞间界限较清晰[12]，多呈大小不等的腺管状，腺腔扩张或成角，可伴程度不一的间质促纤维反应；免疫组织化学p16多为阴性，表达MUC6、CK20和CDX2。例2未见宫颈腺体癌前病变，且有临床病史，诊断相对容易。

但Mazur等[13]研究发现：约1/5转移到女性生殖道的患者之前没有发现原发癌灶，这些病例大多数为胃肠道，还有部分病例一直没有发现原发灶。研究[5,14]显示：分别有3例(n=11)、5例(n=20)没有原发病史而以子宫转移为首发症状就诊，如异常出血。同时很多患者会出现血清CA125升高，因此为诊断带来很多挑战[9]。

临床上对本病的确诊需要依靠病理。在镜下可观察到肿瘤细胞呈灶性分布，缺乏坏死，找不到伴随的子宫内膜癌前改变，提示转移癌的可能[14]。

例1患者没有胃癌病史，形态上也有特殊之处：1)转移的癌细胞位置较表浅，呈小灶状散在分布，于子宫内膜腺体间生长；2)没有明显的间质反应，上皮与间质比例没有明显异常；3)部分区域可见子宫内膜腺上皮部分被肿瘤细胞取代，或位于腺腔内，易造成子宫内膜原发病变的假象，极易误诊及漏诊。但包埋全部组织，仔细寻找，可以发现2处淋巴管癌栓，提示为转移癌。追问病史，患者此前有恶心呕吐等症状，但当地医院行胃镜检查未见肿瘤。提示当遇到类似形态时，应当想到转移的可能，需要多取材、仔细寻找转移的证据，并加行免疫组织化学染色，避免漏诊。同时提醒临床复查胃镜，必要时加行其他检查。

参考文献

1. Pasini A, Mandelli P, Belloni C. Endometrial metastases from gastric adenocarcinoma: a case report[J]. Tumori, 1995, 81(5): 383-386.
2. Legg JW. Melanotic sarcoma of the eyeball, secondary growths in the organs of the chest and belly, particularly in the liver[J]. Trans Pathol SocLond, 1878, 29: 225-230.
3. Charache H. Metastatic carcinoma in the uterus[J]. Am J Surg, 1941,

53: 152-157.

4. Weingold A, Boltouch SM. Extargenital metastases to the uterus[J]. Am J Obstet Gynecol, 1978, 22: 503-506.
5. Kumar NB, Hart WR. Metastases to the uterine corpus from extragenital cancers. A clinicopathologic study of 63 cases[J]. Cancer, 1982, 50: 2163-2169.
6. Scopa CD, Aletra C, Lifschitz-Mercer B, et al. Metastases of breast carcinoma to the uterus. Report of two cases, one harboring a primary endometrioid carcinoma, with review of the literature[J]. Gynecol Oncol, 2005, 96: 543-547.
7. Piura B, Yanai-Inbar I, Rabinovich A, et al. Abnormal uterine bleeding as a presenting sign of metastases to the uterine corpus, cervix and vagina in a breast cancer patient on tamoxifen therapy[J]. Eur J Obstet Gynecol Reprod Biol, 1999, 83: 57-61.
8. Kim NK, Kim HK, Park BJ, et al. Risk factors for ovarian metastasis following curative resection of gastric adenocarcinoma[J]. Cancer, 1999, 85: 1490-1499.
9. Feng Q, Pei W, Zheng ZX, et al. Clinicopathologic characteristics and prognostic factors of 63 gastric cancer patients with metachronous ovarian metastasis[J]. Cancer Biol Med, 2013, 10: 86-91.
10. Stemmermann GN. Extrapelvic carcinoma metastatic to the uterus[J]. Am J Obstet Gynecol, 1961, 82: 1261-1266.
11. Daphne T, Martin B, Ian H, et al. Gastroc adenocarcinoma presenting as uterine metastasis - A case report[J]. Gynecologic Oncol, 2005, 97: 932-934.
12. Kojima A, Mikami Y, Sudo T, et al. Gastric morphology and immunophenotype predict poor outcome in mucinous adenocarcinoma of the uterine cervix[J]. Am J Surg Pathol, 2007, 31(5): 664-672.
13. Mazur M, Hsueh S, Gersell D. Metastases to the female genital tract. Analysis of 325 cases[J]. Cancer, 1984, 53: 1978-1984.
14. Kumar A, Schneider V. Metastases to the uterus from extrapelvic primary tumours[J]. Int J Gynecol Pathol, 1983, 2(2): 134-140.

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