Primary Endometrial vs Endocervical uterine cancer: Can MRI readily predict tumor origin?

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Learning objectives

To review the value of MRI in determining the site of uterine cancer origin (cervix versus endometrial cavity) in cases with indeterminate clinical and histological findings and present our experience with 10 cases.

Background

Endometrial cancer is, most of the times, easily differentiated from endocervical carcinoma by both physical examination and histology.

However, in a small number of patients, there is substantial overlap between the two histologies and conventional biopsy results may be indeterminate. Overall incidence of this small but important subset of cases, is practically unknown, with a 3.25% reported at a single institution study [1].

The use of specific immunohistochemical markers, like vimentin, estrogen receptors (ER), carcinoembryonic antigen (CEA) and p16 may be of value in such cases [2]. In contrast to low grade endometrial adenocarcinomas, endocervical adenocarcinomas are positive for p16 and CEA and negative or only focally positive for ER and vimentin. Reported accuracy of such immunohistochemical stains ranges from 65-80% [3].

In cases of large high grade or undifferentiated adenocarcinomas, especially when biopsy or curetted tissue samples are small, diagnosis may be difficult, even when specific immunohistochemical stains are used [4].

Diagnosis of cervical versus endometrial carcinoma is critical because it may alter treatment planning. Cervical carcinomas are usually treated with radical hysterectomy (early stage) or primary chemoradiation (advanced stage). Surgery (simple hysterectomy or sometimes modified radical hysterectomy with pelvic lymphadenectomy, when tumour extends to the cervical stroma), is the treatment of choice for endometrial carcinomas.

MRI may aid determination of tumour origin by evaluating its morphology and perfusion characteristics. It can also provide important information regarding the extent of the disease with prognostic and therapeutic implications.
Findings and procedure details

In our department, during a 5-year period, 10 women with uterine cancer of uncertain origin were referred for MRI evaluation. A dedicated MR protocol was applied to all patients. All MRIs were interpreted by two radiologists with experience in gynecologic imaging and consensus was reached.

8/10 patients were finally treated with radical hysterectomy, while two received chemoradiation. 6/8 patients had cervical cancer while 2/8 patients had endometrial cancer in final surgicopathological examination.

In the 2 patients who did not have surgery, diagnosis was based on immunohistochemistry findings; in one patient, curetted tissue sample was positive for vimentin, p16 and ER receptors and therefore endometrial cancer was diagnosed; in the other, staining was positive for CEA and HPV, but negative for vimentin or ER and findings were, therefore, more consistent with endocervical carcinoma. Both patients were treated with chemoradiation.

MRI correctly predicted the site of tumor origin in 9/10 patients. In one patient, although the bulk of the tumour was centred at the cervix, final histology was consistent with high grade endometriod adenocarcinoma (Fig. 1-3).

Parametrial invasion was noted almost exclusively in patients with cervical carcinoma (5/6) and in only one patient with endometrial cancer.

We found the following signs helpful in determining site of origin:

- Defining the epicenter of the uterine mass (cervix vs uterine cavity) (Fig. 4,7).
- Early arterial enhancement is more frequent with cervical tumors while endometrial cancers tend to be more hypovascular, with delayed enhancement (Fig. 2,5,8).
- Parametrial invasion and distended endometrial cavity due to obstruction favors cervical cancer (Fig. 6,7).
- Presence of tumor within the endometrial cavity favors endometrial cancer (Fig. 9,10).
T2-weighted and dynamic contrast-enhanced T1-weighted images seem to have the most impact in diagnosis.

DWI may play an important role, since endometrial carcinomas usually present with lower ADC values than cervical cancer, but further data need to be collected [5].

Currently, MRI is used for cervical or endometrial cancer staging, since prognostic factors like myometrial involvement, extension to cervix, parametrical infiltration or lymph node status can be reliably evaluated. Reported overall MRI accuracy in staging is 85%-93% for endometrial cancer [6] and 75%-96% for cervical cancer [7]. Reported sensitivity and specificity values of MRI in the detection of cervical involvement from endometrial cancer are 72% and 93%, respectively [8].

MRI accuracy in determining the site of origin of uterine cancer is high (up to 85%), although available data is limited [9].

However, some authors found the value of MRI limited in predicting tumor origin in histologically indeterminate cases; the same authors also reported low MRI sensitivity (21%) in the detection of stage II endometrial cancer [10].

Vargas et al concluded that "when a radiologist attributed a tumour's origin to either the uterine corpus or cervix on the basis of MR images, the odds of the tumor originating from that site were about six times greater than they would have been if no other information about the tumor were available" [1].

Images for this section:
Fig. 1: A 57-year-old woman, with poorly differentiated uterine adenocarcinoma of indeterminate origin. Sagittal T2-W image shows a quite large mass filling the endometrial
cavity and the cervical canal (white arrow). Although, the bulk of the tumor is located in the cervix, histopathologic examination of the surgical specimen revealed high grade endometrial adenocarcinoma.
Fig. 2: Sagittal dynamic contrast-enhanced (DCE) image, in early arterial phase of the same patient as in Figure 1, shows a hypovascular tumor (long arrow), which is suggestive of endometrial origin. Note the intense, early enhancement of the normal myometrium (short arrow).

Fig. 3: Axial T2-W image of the same patient as in Figure 1 shows a large tumor in the cervix with thinning of cervical stroma (black arrows) but no parametrial involvement.
Fig. 4: A 48-year-old patient with pre-op biopsy positive for endometrial carcinoma, who was finally treated with hysterectomy. Final histology was consistent with a high grade adenosquamous cervical carcinoma. Sagittal T2-W image clearly shows a large cervical mass with extension to the uterine corpus (white arrows).
Fig. 5: Sagittal DCE image of the same patient as in Figure 4. Note early arterial enhancement of the cancerous mass (white arrow), an imaging feature which favors cervical cancer.

Fig. 6: Axial T2-W image of the same patient as in Figure 4, reveals bilateral parametrial tissue infiltration (black arrows). Parametrial involvement is a usual finding in cervical cancer, but it is rather uncommon in endometrial carcinomas.
Fig. 7: Sagittal T2-W image shows a large uterine mass, which is centered at the endocervix (white arrows). The endometrial cavity is distended due to cervical obstruction. A poorly differentiated carcinoma of the endocervix was found on surgery.
**Fig. 8:** Sagittal DCE image of the same patient as in Figure 7. The tumor demonstrates early arterial enhancement (white arrow), which is indicative of cervical origin.
Fig. 9: A 64-year-old woman presenting with abdominal distension and vaginal bleeding. Axial oblique T2-W image shows an enlarged uterus with a diffusely abnormal myometrium and a large tumor within the endometrial and cervical canal. There was extension of the tumor to the left adnexa (not shown). Note the air-fluid level in the endometrial cavity, which is highly suggestive of pyometra (asterisk). Immunohistochemistry was positive for vimentin and estrogen receptors (ER), findings more compatible with endometrial cancer.
**Fig. 10:** Sagittal ADC image of the same patient as in Figure 9. The whole uterus demonstrates restricted diffusion (arrows), but the bulk of the tumor is clearly located within the endometrial cavity.
Conclusion

The role of MRI in the staging of uterine cancer is well established. Although diagnosis of cervical and endometrial cancer is based on tumor biopsy, in cases of unclear findings, MRI may help determine tumor origin.

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