Recurrent cervical carcinoma: Typical and atypical MRI and CT findings

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Learning objectives

To illustrate typical and atypical MRI and CT findings in recurrent cervical carcinoma in pelvic, nodal or extrapelvic sites.

To show the clinical relevance of various type of recurrency.
Background

Definition and epidemiology

Cervical cancer is the second most common cancer worldwide, resulting in approximately 275,000 deaths yearly. In the developing world, cervical cancer is the major cause of death in women of a reproductive age.

Primary treatment for cervical cancer (surgery or radiotherapy with or without chemotherapy) has a cure rate of approximately 80% to 95% in patients diagnosed with early-stage disease (stage I or II) and approximately 60% in patients with stage III disease. Approximately 30% of women with invasive cervical cancer die of recurrent/persistent disease.

Recurrence is defined as local tumour regrowth or the development of distant metastases discovered 6 months or more after complete regression of the treated lesion.

Risk factors for recurrence of cervical carcinoma include the histologic features of the tumor, tumor size, the depth of stromal invasion, and the nodal status at presentation.

Primary treatment for clinical stage I disease involves radical hysterectomy with bilateral pelvic node dissection or radical pelvic radiation therapy with concurrent chemotherapy. Surgicopathologic factors that predict disease recurrence in stage I disease are tumour diameter, depth of stromal invasion, presence or absence of lymphvascular space invasion, presence or absence of parametrial extension at surgery or on histology, histologic variants such as small-cell cancers, presence or absence of lymph node involvement at surgery or on histology, and status of the resection margins. Patients who are deemed to be at high risk for recurrence following surgery may receive postoperative adjuvant pelvic external-beam radiation therapy with or without chemotherapy and/or brachytherapy. Primary treatment for stage II-IV disease is platinum-based chemoradiotherapy.

The majority of treated patients who develop recurrences do so in the first 2 years following primary therapy.

If primary treatment involves pelvic radiation, the distribution of recurrences depends on the original stage of disease, with a greater risk of persistent or recurrent pelvic disease in those with more advanced tumours.

The most common sites of distant recurrence are lung, para-aortic lymph nodes, abdominal cavity, and supraclavicular nodes; in excess of 90% of those who have distant recurrences will die of their disease within 5 years. After radical surgery for early-stage disease, metastases, when they occur, are typically distributed locally (i.e., vaginal apex), regionally (i.e., pelvic sidewall) or distantly (i.e., lung).
Those who survive disease recurrence are those 40% to 50% of patients with central recurrences, as these patients have effective treatment options such as pelvic radiation (in those with no prior radiation) or exenterative surgery, with the potential for cure in approximately half of these cases. Thus for every 100 patients with early-stage disease, approximately 10 to 20 patients recur; of those, approximately four to five have a central recurrence, and approximately one to two can be cured by further treatment.

Clinical presentation

Recurrent cervical cancer can have typical or atypical manifestations.

Typical manifestations include pelvic masses or adenopathy, whereas less typical manifestations include peritoneal carcinomatosis and solid organ metastases.

Treatment

Therapeutic options for recurrent tumor include surgery, radiation therapy, and chemotherapy, depending on the primary tumor therapy and the location and extent of the recurrence. Determination of the extent of recurrence with CT and MR imaging may provide clinical assistance in selection of the optimal therapy.

Localised recurrences are managed preferentially by surgery, irradiation, or a combination of the two, depending on the primary therapy. Large lesions should be excised, if feasible, with isolated pelvic recurrence of any grade being potentially curable, particularly if it occurs more than 1 or 2 years after initial therapy. In this setting, extended or radical surgery may be justified if the patient has already received prior irradiation. The results of pelvic exenteration in properly selected cases of this sort are similar to those obtained in cervical cancer and yields 5-year survival rates up to 82% with low complication rates.

With recurrent disease outside the initial treatment field, irradiation is frequently successful in providing local control and symptomatic relief.

Patients with non-localised recurrent tumours may be candidates for progestin therapy, which is continued as long as the disease is static or in remission. Maximum clinical response may not be apparent for 3 or more months after initiating therapy. Chemotherapy with cisplatinum, taxol and adriamycin has been recommended for patients with advanced or recurrent disease, non-amenable to cure by surgery and/or radiotherapy.

Surveillance and diagnosis
The concept of long-term surveillance of patients treated with curative intent is based on the premise that early detection will result in treatment that will have lower morbidity and increase survival. This assumes that surveillance has adequate sensitivity and specificity and is resource-effective, that the natural history of both the anatomic pattern and timing of disease recurrence is known, and that effective low-morbidity salvage therapy is available. Follow-up protocols after the completion of initial treatment are variable, using a number of tests at a variety of intervals with questionable outcomes.

Because the addition of radiation therapy or chemotherapy can improve the prognosis, early detection of recurrence is important. The diagnosis of local recurrence is challenging and involves clinical evaluation, imaging and histopathological examination.

Although diagnostic imaging has become more refined in differentiating post-treatment fibrosis and malignancy, it is not entirely free from false-positive and false-negative results. Imaging modalities such as transabdominal ultrasound, TVUS, CT and MRI are used in the diagnosis.

CT imaging is most commonly used for follow-up, with 93% sensitivity for the detection of recurrence. Residual tumor may be recognized on CT scans obtained with intravenous contrast material, on which it may appear as a soft-tissue mass with diminished enhancement compared with that of normal cervical tissue.

At MRI, residual tumor has high signal intensity on T2-weighted images, similar to the corresponding primary tumor.

A major limitation of these modalities is their ability to distinguish between local recurrence and post-radiation fibrosis. Weber et al and Ebner et al reported MRI to be the most accurate at differentiating between the two, with a sensitivity of 86% and a specificity of 94% in post-radiotherapy patients.

Fluorodeoxyglucose-PET and PET-CT imaging are increasingly being used for the diagnosis of recurrence, with 97.5% sensitivity and 94.0% specificity.

Definite cytological or histological diagnosis is mandatory before treatment is started.
Pelvic Recurrence

Recurrence of tumor in the pelvis is either central or at the side wall.

Central pelvic recurrence of cervical carcinoma may be located in the preserved cervix or the vaginal cuff (Fig. 1-2).

Images in the sagittal and axial planes are helpful in tumor detection, and the combination of T1- and T2-weighted images often allows tissue characterization. At MRI recurrent tumor often demonstrates heterogeneous high signal intensity on T2-weighted MR imaging. After contrast material administration, recurrent tumor is shown as a heterogeneous soft-tissue mass with variable degrees of necrosis at varying degrees of enhancement. The addition of contrast enhancement does not improve the accurate evaluation of the irradiated cervix. However, dynamic contrast-enhanced T1-weighted MR imaging is more accurate than T2-weighted MR imaging in demonstration of parametrial or pelvic sidewall recurrence and of postirradiation complications (e.g., fistula formation). In addition, serial or follow-up MR imaging is useful for distinguishing recurrent disease from radiation-induced fibrosis, as the latter is expected to remain stable or diminish in prominence over time.

Central pelvic recurrence with anterior extension may lead to ureteral obstruction (Fig. 3) by direct encasement of the ureter or by tumor infiltration of the bladder wall, which results in obstruction at the ureteral orifice. In some instances, central pelvic recurrences may extend posteriorly to involve the rectum (Fig. 4) with development of a rectovaginal fistula (Fig. 5) or extend laterally to involve the pelvic side wall. The treatment for rectovaginal fistula with recurrence is pelvic exenteration, which is required to divert the fecal stream.

At times, pelvic recurrences are identified as pelvic side wall masses that are not associated with a centrally located pelvic mass. Another manifestation of pelvic recurrence is that of tumor involving the ovaries, which may result from contiguous extension of pelvic tumor, hematogenous or lymphatic spread, or peritoneal implants.

In patients who have received radiation therapy, distinguishing radiation fibrosis from recurrent tumor can be difficult and biopsy may be necessary. Recent studies indicate that dynamic contrast-enhanced T1-weighted MR imaging may be helpful in making this important distinction, with accuracies of 82%-83%. In addition, serial or follow-up MR imaging is useful for distinguishing recurrent disease from radiation-induced fibrosis, as the latter is expected to remain stable or diminish in prominence over time.

Lymph Node Recurrence
Lymphatic involvement in cervical cancer has traditionally been separated into primary and secondary nodal groups.

The primary group (Fig. 6) consists of the paracervical, parametrial, external and internal iliac (hypogastric), and obturator nodes, whereas the secondary group includes the sacral, common iliac, inguinal, and paraaortic nodes (Fig. 7-9). In general, paracervical and parametrial lymph nodes are involved first, followed by the obturator nodes, the remaining external iliac nodes, and the internal iliac nodes.

When the secondary nodal group is involved, the prognosis worsens.

With respect to nodal disease, a somewhat orderly sequence of involvement usually occurs. In general, paracervical and parametrial lymphonodes are involved first, followed by the obturator nodes, the remaining external iliac nodes and the internal iliac nodes. The secondary group is usually subsequently involved.

Multiple extrapelvic and extraabdominal nodal sites of recurrence, including the parabronchial, supraclavicular, and axillary nodes, have been reported but are less frequently involved than the primary and secondary groups. The prevalence of recurrence at extrapelvic lymph nodes is higher in patients treated with radiation therapy or those with pelvic side wall extension than in those who undergo surgery; this is probably because this tumor stage is generally more advanced. CT is useful for detecting clinically unsuspected extrauterine metastases and lymph node metastases.

The findings of nodal metastasis range from scattered, minimally enlarged lymph nodes to large, conglomerate nodal masses at CT and MR imaging. The reported accuracy rate of CT for detecting pelvic node metastasis in patients with uterine cervical carcinoma is 73%-83%, whereas the rate for MR imaging is 76%-100%. Recently, Yang et al reported that CT and MR imaging show similar accuracy in evaluation of pelvic lymph nodes in patients with cervical carcinoma. Although CT and MR imaging cannot help distinguish reactive from neoplastic lymph nodes, they are useful for detecting enlarged nodes. Determination of metastatic infiltration of lymph nodes with CT and MR imaging is based on their size. Although the size criterion for metastatic lymph nodes is currently debatable, most authors agree that nodes greater than 1 cm in short-axis diameter are considered to represent metastatic lymph node involvement with accuracy rates of 75%-88%. Central lymph node necrosis is a helpful finding for differentiating metastatic nodes from nonmetastatic and hyperplastic nodes. When central necrosis is detected in a lymph node, the positive predictive value for malignancy is 100%.

**Distant Metastases**

Distant metastases from cervical carcinoma are usually due to recurrent disease and are seen in the abdomen, thorax, and bone, in decreasing order of frequency. After the pelvis and lymph nodes, the solid organs of the abdomen are the most frequent sites of involvement of recurrent cervical carcinoma.
Abdominal metastasis occurs in the peritoneal cavity and solid organs such as the liver and adrenal gland.

**Solid organs of the abdomen**

After the pelvis and lymphnodes, the solid organs of the abdomen are the most frequent sites of involvement by recurrent cervical carcinoma.

The abdominal solid organ most commonly involved is the liver. CT and MR imaging permit detection of small liver metastases. Hepatic metastasis of cervical carcinoma usually appears as multiple focal masses with variable enhancement. Therefore, the CT and MR imaging findings of hepatic metastasis in recurrent cervical carcinoma are indistinguishable from those of involvement by other primary malignancies.

Involvement of another abdominal solid organ, such as the adrenal gland (Fig. 10), spleen, kidney, pancreas, or gastrointestinal tract, is rare and in almost all cases occurs as widespread metastasis involving other organs as well.

**Peritoneal, omental and mesenteric recurrences** (Fig. 11-12)

Although imaging of peritoneum, omentum and mesentery is often performed with CT, MR imaging has been advocated as an accurate means of detecting peritoneal disease. In particular, gadolinium-enhanced fat-saturated T1-weighted MRI has proved useful in the detection of peritoneal disease.

The CT and MR imaging findings of metastases to the peritoneal cavity include ascites, implants scalloping the liver contour, peritoneal thickening with nodularity, and serosal soft-tissue masses that cause extrinsic compression of the bowel. Although ascites is a non-specific finding, it often occurs in association with peritoneal carcinomatosis, and its presence should prompt a meticulous search for recurrent disease involving the peritoneum.

**Gastrointestinal tract recurrence**

The rectum is frequently involved by recurrent cervical carcinoma, usually as a result of contiguous extension of tumor from the preserved cervix or vaginal cuff (Fig. 4). Invasion of the rectum usually occurs at the rectosigmoid junction and is evidenced by mass effect, speculation, and luminal narrowing.

The colon and the small bowel may be involved by recurrent tumor in many different ways, including contiguous extension from the pelvis and intraperitoneal seeding, resulting in obstruction of large or small intestine (Fig. 12) that can be demonstrated with barium examination, CT, and MRI. Other manifestations of recurrent disease involving the
gastrointestinal tract include fistula formation (Fig. 13) and focal bowel wall thickening and tethering of bowel loops due to tumor implants in the mesentery.

**Chest recurrence**

Lung metastases from recurrent cervical carcinoma are reported to occur in 33%-38% of autopic series. Lung metastases may be present for a significant period of time before becoming symptomatic. Lung metastases occur with equal frequency in patients with adenocarcinoma and squamous cell carcinoma and may be either solitary, or, most commonly, multiple. Chest radiography is commonly used to screen for recurrent disease; however, CT permits visualization of small nodules that may not be detected with conventional chest radiography (Fig. 14-15).

Other sites of recurrent tumor in the chest include, less commonly, the pleura, bronchus, pericardium, and chest wall (Fig 16-17). Pleural involvement may be detected as pleural thickening and nodularity.

Mediastinal or hilar adenopathy and pleural lesions or effusions are present in approximately one-third of patients with metastatic disease to the chest.

Rare findings include endobronchial obstruction and lymphangitic carcinomatosis.

Metastatic cervical carcinoma of the pericardium usually manifests as nodular soft-tissue thickening of the pericardium at CT or MRI.

**Osseous recurrence**

The prevalence of osseous metastases in the setting of recurrent cervical carcinoma ranges from 15% to 29% as reported in multiple autopsy series and is associated with advanced disease and a poor prognosis.

Bone involvement may occur secondary to direct extension from adjacent lymph nodes, by lymphatic or hematogenous spread (Fig. 18), or from a pelvic recurrence (Fig. 19) and most commonly involves the lumbar spine, followed by the pelvis, ribs, and extremities.

Accurate detection of bone metastasis is important for staging and proper management, such as the use of bisphosphonates. In the past, patients who had suspected metastasis usually were worked up with x-ray, computed tomography (CT), ultrasonography, and whole-body bone scintigraphy.

In the modern era, magnetic resonance (MR) imaging and positron emission tomography (PET) or integrated PET/CT using 18F-fluorodeoxyglucose (18FFDG) increasingly are used. Both MR and PET are considered to have high sensitivity for detecting bone marrow or osteolytic bone metastasis. Because hematogenous bone metastasis is considered to start in the bone marrow, and the majority of metastatic bone lesions in cervical cancer
seem to be of an osteolytic nature, both MR imaging and PET may facilitate the detection of bone metastasis.

Bone metastases may appear as destructive lesions associated with soft-tissue masses of variable size. Gadolinium-enhanced fat-suppressed T1-weighted imaging is particularly useful in the detection of bone metastases, which are depicted as foci of enhancement within the marrow space.

A recent study from Liu FY et al (Cancer 2009) demonstrated the relative superiority of 18F-FDG-PET over CT and MR imaging for detecting hematogenous bone metastasis in patients with advanced cervical cancer.

Hematogenous bone metastasis in cervical cancer is associated with the extent of lymph node metastases rather than the FIGO stage. Early identification and proper management of lymph node metastasis may be important for decreasing the rate of distant hematogenous recurrence in patients with invasive cervical cancer.

**Other sites of recurrence**

Other relatively uncommon sites of recurrent cervical carcinoma have been reported, including the skin and the subcutaneous tissues, that have been demonstrated in up to 10% of patients with recurrent cervical carcinoma. In general, the remaining sites that include brain, meninges, heart, and breast, show evidence of metastases in no more than 3% of patients.
Fig. 0: Central recurrence at vaginal cuff and upper vagina. The T2w-FSE images along sagittal (a), coronal (b) and axial (c,d) planes before (a,b) and after (c,d) chemo-radiation therapy show large tumoral recurrence on vaginal vault and in the upper two thirds of vagina (arrows)

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**Fig. 0:** Pelvic recurrence. The T2w-FSE images along sagittal (a), axial (b) and coronal (c) planes show heterogeneous soft-tissue mass with central necrosis and large fistulas (arrowhead).

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Fig. 0: Lateral pelvic wall recurrence with ureteral obstruction. The coronal (a) and axial (b) FSE T2-weighted images show an irregular solid mass (arrows) with infiltrating borders in the lateral right pelvic wall, encasing and obstructing the omolaterale ureter and causing right hydronephrosis (c,d).

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**Fig. 0:** Central recurrence with vesical and rectal infiltration. The sagittal (a) and axial (b) T2-weighted images show a large central recurrence at vaginal cuff with anterior and posterior extension and infiltration of bladder and rectal wall.

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Fig. 0: Large central and side-wall local recurrence with recto-vaginal fistula. The axial T2-weighted image (a) shows irregular infiltrating solid tissue (arrow) on the right pelvic sidewall, with ureteral obstruction. The more caudad T2-weighted axial view (b) and the T2-weighted sagittal view (c) depict large recto-vaginal fistula (arrows), confirmed by vaginal opacification at rectal enema with hydrosoluble iodinate contrast agent (arrow in d).

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**Fig. 0:** Pelvic lymphnodal recurrence. The sagittal (a), coronal (b) and axial (c) T2-weighted images and the axial post-contrast T1-weighted fat-suppressed image clearly depict a large pelvic external iliac lymphnodal recurrence.

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**Fig. 0:** Inguinal and para-aortic recurrence. The axial contrast-enhanced CT images show a subcutaneous recurrence in the left inguinal canal (arrow in a) and lymphnodal recurrence at lombo-aortic level (arrowhead in b).

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**Fig. 0:** Lymphnodal and pelvic recurrence. The axial contrast-enhanced CT images show a large para-aortic lymphnodal mass (arrow in a) and a pelvic side-wall infiltrative recurrence of disease (arrow in b)

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**Fig. 0:** Para-aortic and pelvic lymphnodal recurrence. The axial b-SSFP (a) and T2-weighted FSE images show large lumbo-aortic lymphnodal recurrence (arrow in a) and right obturatory lymphnodal recurrence (arrow in b)

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**Fig. 0:** Adrenal recurrence. The MRI axial T2-weighted (a) and T1-weighted post-contrast (b) images show enlarged and irregular adrenal glands, with inhomogeneous enhancement after contrast agent administration, due to hematogenous recurrence of cervical carcinoma. the patient had also lung and pelvic recurrence.
Fig. 0: Peritoneal and mesenteric recurrence. The axial contrast-enhanced CT images show two large nodular masses due to intraperitoneal diffusion of abdominal recurrence of cervical carcinoma (arrows in a and b).

Fig. 0: Peritoneal carcinomatosis with intestinal obstruction. The antero-posterior abdominal radiography (a) shows multiple large intestinal endoluminal air-fluid levels and
hyperdistension of small bowel loops, secondary to peritoneal carcinomatosis, clearly depicted in the axial CT image (arrow in b)

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**Fig. 0:** Pelvic recurrence with intestinal fistula. The axial (a) and sagittal (b) T2-weighted images show a large infiltrating pelvic recurrence with a large fistula with an ileal loop (arrows).

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Fig. 0: Lung metastases. In the chest x-ray images (a,b) two nodular lung opacities are displayed (arrows in b). The axial CT images (c,d) better depict multiple soft tissue attenuation parenchymal nodules in both lungs, due to hematogenous metastases from recurrent cervical carcinoma.

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**Fig. 0:** Lung metastases. The two axial CT images show multiple nodular parenchymal opacities due to recurrence of cervical carcinoma.

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Fig. 0: Pelvic, chest wall, lung and mediastinal recurrence. The axial CT images (a,b) show a large infiltrative mass in the anterior right chest wall infiltrating lung parenchyma and anterior mediastinum (arrows). The sagittal (c) and axial (d) MRI T2-weighted images clearly depict a pelvic recurrence on the vaginal cuff (arrows).

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**Fig. 0:** Chest wall and pleural recurrence. The axial MRI b-SSFP image (a) and CT image (b) show a recurrence in posterior right chest wall (arrows). The axial CT images (c,d) depict a subpleural anterior recurrence in the right lung (arrows).

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Fig. 0: Osseous recurrence. The axial T1-weighted (a), fat-suppressed T2-weighted (c) and fat-suppressed T1-weighted after c.a. administration (d) and the coronal T2-weighted image (b) show a round solid metastasis in left acetabulum.

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**Fig. 0:** Pelvic recurrence with bone infiltration. The T2w-FSE images along sagittal (a), coronal (b) and axial (c,d) planes show large tumoral pelvic recurrence with infiltration of the sacrum, the right iliac wing and the right sacral plexus (arrows)

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Conclusion

Local and systemic recurrences are still a problem plaguing patients with cervical cancer. Because the addition of radiation therapy or chemotherapy can improve the prognosis of these patients, early detection of recurrence is important.

Familiarity with the imaging features of recurrent cervical carcinoma will facilitate prompt and accurate diagnosis and treatment.
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