Treated pelvis: Scar versus recurrence.

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Objectives: This case-based course will allow the attendees to differentiate tumour recurrence from scar post therapy in gynecological malignancies and rectal cancer.
- Review the MR imaging protocol
- Functional imaging to differentiate scar from recurrence
- Morphological features to differentiate scar from recurrence

1. Gynecological Malignancies:

Gynecological malignancies are common accounting for 10-15% of all female malignancies [Kehoe, 2006]. Gynecological cancers are usually treated by surgery, chemotherapy and/ or radiotherapy. The management of patients with malignant gynecological disease depends upon the grade and stage of the malignancy, as well as the organ of origin.

In endometrial cancer, early stage and low grade disease is usually treated by surgery alone, whereas more advanced stages or grades are treated with a combination of surgery and radiotherapy. Patients with cervical cancer receive chemo-radiotherapy when tumours present with an advanced stage (2B or more), or exceed 4cm in maximal diameter irrespective of the stage. In ovarian cancer, chemotherapy has an important role in neoadjuvant therapy prior to surgery in nonresectable cases, and also in patients where optimal surgical resection has not been achieved.

a. Surgical Management

Hysterectomy is one of the most common abdominal procedures performed for female pelvic malignancies. The type of hysterectomy will vary depending on the type

and stage of pathology being treated. Following treatment, imaging evaluation is crucial to assess for residual or recurrent disease. The vaginal cuff is a common site of recurrence after hysterectomy, as local recurrence often takes place at the surgical resection sites [Sala et al., 2013] [Shaeffer, Randall, 2005].

The MR appearance is similar after total and radical hysterectomy. The normal vaginal cuff presents as a symmetrical or mildly asymmetrical linear structure situated posterior to the urinary bladder, typically surrounded by fat [Kasales, Langer and Arger, 1995]. The normal, smooth, low signal intensity vaginal wall is best visualized on T2-weighted MR images. In some cases, however, intermediate T2 signal intensity areas can be seen due to fibrous scar formation [Jeong et al., 2003]. The addition of fat suppression to the T2-weighted and post contrast sequences is mandatory in the treated pelvis, to improve detection of high signal-intensity recurrence from the fat surrounding the vaginal cuff. Recent studies demonstrated the added value of diffusion-weighted imaging (DWI) to distinguish high or intermediate signal fibrosis/granulation tissue on T2-weighted imaging from recurrence [Nougaret, 2013]. Areas of fibrosis typically have a low cellular density, which results in low signal intensity on high b-value DWI. In contradistinction, residual tumor areas have a relatively high cellular density and show restriction on DWI imaging. The morphology of the surgical bed can also provide clues as to the likelihood of recurrence. Scar tissue typically has a stellate appearance with concave outer margins, while recurrence presents with outer margins that are typically convex.

The best imaging modality for assessing the patient post trachelectomy is MRI. T2-weighted imaging is the sequence of choice, not only for the normal postoperative

appearances, but also for normal postoperative variants, which are important to recognize and not to confuse with disease recurrence. There are a number of normal postoperative appearances, which must be appreciated on imaging. An end-to-end anastomosis between the corpus uteri and the vaginal vault is seen in approximately 45% of cases. The formation of a neofornix of the vagina is seen in approximately 50%. This is a posterior extension of the vaginal wall forming a posterior neo-fornix at the site of the utero-vaginal anastomosis. This appearance does not change overtime and there is no abnormal soft tissue to suggest recurrence [Hricak et al., 2006]. The anastomotic sutures or the uterine cerclage suture can both give susceptibility artifacts in approximately 20% of cases. Depending on the position of the artifacts, it may be difficult to exclude recurrence on imaging alone thus clinical examination is important [Sonoda et al., 2008]. Diffuse vaginal wall thickening with abnormal increased signal intensity on T2-weighted imaging can occur in approximately 5-10% of cases. This most likely represents postoperative change which gradually resolves by one year but it can be difficult to distinguish from infiltrating vaginal recurrence and therefore a biopsy may be required [Hricak et al., 2006].

Low signal-intensity foci corresponding to metallic clips along the pelvic sidewall can be detected at the site of lymph node dissection.

b. Chemo-radiation therapy

Following treatment with radiotherapy, the signal characteristics of the primary tumour changes, and the soft tissue and fat planes within the pelvis become more indistinct. Fibrosis and contraction of the primary tumour occurs, resulting in lower T2

signal intensity and decreased volume of disease. The adjacent soft tissues also undergo a similar process of fibrotic change, therefore, appearing of low signal intensity and causing difficulty in distinguishing the pelvic anatomical planes from the primary tumour.

Distinguishing between the fat planes and the tumour post radiotherapy can be particularly challenging in patients with cervical carcinoma and parametrial invasion. It is a common pitfall on post-radiotherapy MRI that fibrosis mimics tumour recurrence in the parametrium. In these cases, intravenous contrast medium can be helpful in distinguishing between radiotherapy induced parametrial fibrosis and residual or recurrent disease [Hricak et al., 1993]. Tumour tends to enhance earlier than fibrosis and should be compared to the pre-treatment imaging appearances as recurrent tumour typically has the same dynamic contrast enhancement characteristics as the original tumour. DWI is also helpful to distinguish scar tissue from tumour recurrence, with the latter resulting in diffusion restriction [Sala et al, 2013]. Nodular changes with convex outer borders in the parametrium are suggestive of tumour recurrence.

The signal intensity of the primary tumour in patients with cervical cancer is also important. The very low signal intensity, associated with fibrotic changes on T2-weighted images, is reassuring. The signal intensity can also be compared to the adjacent pelvic sidewall muscle on T2-weighted images. Increased signal intensity compared to muscle is suspicious for recurrence [Weber et al., 1995]. The reconstitution of the normal low signal intensity cervical stroma is the most reliable indicator of a tumour-free post-radiation cervix with a 97% negative predictive value [Hricak et al., 1993]. More recently, absence of restriction on DWI is further evidence of scar tissue.

2. Rectal Cancer:

Locally advanced rectal cancer has a poor prognosis because of the high frequency of metastasis and local recurrence. The benefits of downstaging and downsizing with neoadjuvant chemoradiotherapy (CRT) include improvement in resectability, sphincter preservation, decreased rates of local recurrence, and overall survival. In several studies, CRT has resulted in 10%–20% complete tumor response rate [Madoff, 2004][Sauer et al., 2004]. After CRT with a good response, the tumor may not be visible on sagittal T2W images. The pretreatment exam and high-spatial-resolution T2W sequences along the entire length of the rectum are needed.

The reported overall accuracy of MR imaging in predicting the stage of non irradiated rectal cancer is approximately 85%, but this rate falls to 50% after treatment [Chen et al., 2005][Kuo et al, 2005]. The difficulty lies in whether tumor is still present among post therapeutic changes. Most tumors develop fibrosis, leading to a reduction in signal on T2W images and a decrease in tumor size. The main difficulty is to assess whether the low signal intensity areas represents fibrotic scar or residual tumor. Recent studies demonstrated the added value of DWI to differentiate viable tumor from fibrosis [Kim SH et al., 2009][Sun YS, 2010]. Areas of fibrosis typically have a low cellular density, which results in low signal intensity on high b-value DWI. In contradistinction, residual tumor areas have a relatively high cellular density and show high signal on DWI, which stands out against the low signal of the surrounding tissue/fibrosis [Lambregts et al., 2011][Kim Sh et al, 2011]. As such, small areas of residual tumor are better depicted on DWI. Some treated tumors develop a "colloid" response with mucin production that

results in very high signal intensity on T2W images and DWI, with no ADC restriction

(T2 shine through effect). Consequently, small residual tumor among the colloidal

changes cannot be detected. In addition, distortion due to imaging artifacts is not

infrequent with DWI, particularly around air-tissue interfaces, further complicating

interpretation.

In addition to T downstaging, an MRI tumor regression grade (MRI TRG) [Patel UB

et al., 2011] has been recently proposed derived from histopathologic grading [Dworak et

al., 1997] and seems to be a strong prognostic indicator for tumor recurrence and survival

outcomes. This new grading is based on the assumption that fibrosis results in very low

SI compared with tumor on T2W images, and mucin in very high signal intensity.

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