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PET/CT Scan in Gynecological Cancers

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Cervical cancer

Introduction

Cervical cancer is the third frequent neoplasm among females (1). Around 75% of the cases have squamous cell carcinoma, the others are adenocarcinoma. Cervical cancer generally spreads progressively from local adjacent structures and regional lymph nodes to the pelvic, para-aortic, and supraclavicular lymph nodes. Dissemination to distant organs occurs late during disease (2). At the time of initial diagnosis, the most important prognostic parameters include tumor size, parametrial invasion, and lymph node involvement (3, 4).

[^{18}F]FDG PET/CT in Cervical Cancer

Cervical cancer is staged by the FIGO criteria, which shows a difference between clinical and surgical staging, of 25% to 90% in more advanced tumors (5). This approach does not include many important prognostic factors (such as tumor size, grade, local or retroperitoneal lymph node involvement) that can result in a different prognosis and require different clinical management. Approximately one-third of patients with locally advanced cervical cancer have metastasis to the para-aortic lymph nodes, which influences treatment choice. Therefore, surgical staging is recommended in patients with advanced disease but, not recommended in patients with early-stage, as it is often associated with severe morbidity and complications (4).

The NCCN guidelines recommend [^{18}F]FDG PET/CT for:

1. Pretreatment assessment in patients with stage IB2 (clinically visible lesion greater than 4 cm not invading beyond the uterus) or higher.
2. Para-aortic lymph node disease is found at surgical staging.
3. Invasive cervical cancer is found incidentally at hysterectomy for another reason.
4. Conventional imaging equivocal or negative.
5. 3–6 months after chemoradiation for locally advanced cervical cancer (6).

[^{18}F]FDG PET/CT is not recommended for routine surveillance without clinical suspicion or histologically proven local recurrence.

Key Learning Points

- [^{18}F]FDG PET/CT is recommended for disease staging because of its high sensitivity in detecting lymph node metastases, particularly in extra-pelvic sites (7).
- [^{18}F]FDG PET/CT is also indicated for restaging the disease and for evaluation of treatment response.
- Incomplete metabolic response at [^{18}F]FDG PET is associated with poor prognosis (3).

Staging of Cervical Cancer

FIGO Stage		Stage description
I		The cancer cells have grown from the surface of the cervix into deeper tissues of the cervix. Cancer has not spread to nearby lymph nodes. Cancer has not spread to distant sites.
	IA	There is a very small amount of cancer, and it can be seen only under a microscope. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IA1	The area of cancer can only be seen with a microscope and is less than 3 mm (about 1/8-inch) deep. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IA2	The area of cancer can only be seen with a microscope and is between 3 mm and 5 mm (about 1/5-inch) deep. It not has not spread to nearby lymph nodes. It has not spread to distant sites.
	IB	This includes stage I cancer that has spread deeper than 5 mm (about 1/5 inch) but is still limited to the cervix. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IB1	The cancer is deeper than 5 mm (about 1/5-inch) but not more than 2 cm (about 4/5-inch) in size. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IB2	The cancer is at least 2 cm in size but not larger than 4 cm. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IB3	The cancer is at least 4 cm in size and limited to the cervix. It has not spread to nearby lymph nodes. It has not spread to distant sites.
II		The cancer has grown beyond the cervix and uterus, but hasn't spread to the walls of the pelvis or the lower part of the vagina. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIA	The cancer has grown beyond the cervix and uterus but has not spread into the tissues next to the cervix (called the parametria). It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIA1	The cancer is not larger than 4 cm (about 1 3/5 inches). It not has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIA2	The cancer is 4 cm or larger. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIB	The cancer has grown beyond the cervix and uterus and has spread into the tissues next to the cervix (the parametria). It has not spread to nearby lymph nodes. It has not spread to distant sites.
III		The cancer has spread to the lower part of the vagina or the walls of the pelvis. The cancer may be blocking the ureters (tubes that carry urine from the kidneys to the bladder). It might or might not have not spread to nearby lymph nodes. It has not spread to distant sites.
	IIIA	The cancer has spread to the lower part of the vagina but not the walls of the pelvis. It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIIB	The cancer has grown into the walls of the pelvis and/or is blocking one or both ureters causing kidney problems (called hydronephrosis). It has not spread to nearby lymph nodes. It has not spread to distant sites.
	IIIC	The cancer can be any size. Imaging tests or a biopsy show the cancer has spread to nearby pelvic lymph nodes (IIIC1) or para-aortic lymph nodes (IIIC2). It has not spread to distant sites.
IV		The cancer has grown into the bladder or rectum or to far away organs like the lungs or bones.
	IVA	The cancer has spread to the bladder or rectum or it is growing out of the pelvis.
	IVB	The cancer has spread to distant organs outside the pelvic area, such as distant lymph nodes, lungs or bones.

Endometrial Cancer

Introduction

Endometrial cancer is the sixth most common malignancy among women (8). It's risk factors include: obesity, high fat consumption, long-lasting endogenous or exogenous hyperestrogenism (nulliparity, anovulation, premature menarche and late menopause, polycystic ovary syndrome, tamoxifen therapy), arterial hypertension, diabetes mellitus, and genetic predisposition.

Although the routine screening test does not exist, but most cases are diagnosed early (vaginal bleeding). This leads to high survival rates. The two major histological types of endometrial carcinoma are estrogen-dependent endometrioid carcinomas (Type 1), that constitute 80% of endometrial carcinomas and is detected earlier also it has better prognosis and is usually well-differentiated and can be associated with endometrial hyperplasia but estrogen-independent non-endometrioid carcinomas (Type 2) are considered serous carcinomas, while clear cell carcinomas constitute a rare and heterogeneous group of tumors with intermediate features between Type 1 and Type 2.

High-grade endometrial carcinomas (grade 3 endometrioid, serous and clear cell adenocarcinomas) have poor prognosis and respond to adjuvant therapy differently (8). Since standard treatment is hysterectomy with bilateral salpingo-oophorectomy, these tumors have always been classified according to the FIGO classification which is based on intraoperative findings; this classification does not include imaging parameters for staging. In contrast, the NCCN guidelines recommend [^{18}F]FDG PET/CT imaging for evaluation of extrauterine disease in high-risk patients with endometrial cancer, with the purpose of better patient selection and surgical planning.

[^{18}F]FDG PET/CT in Endometrial Cancer:

[^{18}F]FDG PET/CT has 82% sensitivity and 90% specificity for detecting the primary lesion.Suboptimal sensitivity in detecting the primary lesion can be related to interference in the interpretation of images induced by metabolic changes associated with the ovulatory and menstrual phase in premenopausal women.

High specificity justifies the use of [^{18}F]FDG PET/CT for initial staging of patients with the main purpose of sparing unnecessary lymphadenectomy (minimizing morbidity and complications of this surgical procedure) to patients who will not benefit from lymphadenectomy because they already have advanced disease.

In patients with early-stage endometrial cancer, [^{18}F]FDG PET/CT is indicated when histology of the primary tumor present high-risk characteristics. The high diagnostic performance of [^{18}F]FDG PET/CT in the detection of locoregional and distant metastasis appears to be influenced by the site of recurrence; in fact, the diagnostic performance of [^{18}F] FDG PET/CT is higher for pelvic lymph node metastasis than for para-aortic lymph node metastasis (9).

Key Learning Points

- Endometrial cancer can be staged with [^{18}F]FDG PET/CT, which has sufficient diagnostic accuracy for detecting the primary lesion, and especially distant metastasis.
- Patients who have negative PET scan for lymph node metastasis can be considered for a less invasive surgery.
- [^{18}F]FDG PET/CT is useful for assessment of response to therapy.

Staging of endometrial cancer

Stage	Stage grouping	FIGO Stage	Stage description*
I	T1 N0 M0		The cancer is growing inside the uterus. It may also be growing into the glands of the cervix, but not into the supporting connective tissue of the cervix (T1). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IA	T1a N0 M0	IA	The cancer is in the endometrium (inner lining of the uterus) and may have grown less than halfway through the underlying muscle layer of the uterus (the myometrium) (T1a). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IB	T1b N0 M0	IB	The cancer has grown from the endometrium into the myometrium. It has grown more than halfway through the myometrium, but has not spread beyond the body of the uterus (T1b). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
II	T2 N0 M0	II	The cancer has spread from the body of the uterus and is growing into the supporting connective tissue of the cervix (called the cervical stroma). But it has not spread outside the uterus (T2). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
III	T3 N0 M0	III	The cancer has spread outside the uterus, but has not spread to the inner lining of the rectum or urinary bladder (T3). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIIA	T3a N0 M0	IIIA	The cancer has spread to the outer surface of the uterus (called the serosa) and/or to the fallopian tubes or ovaries (the adnexa) (T3a). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIIB	T3b N0 M0	IIIB	The cancer has spread to the vagina or to the tissues around the uterus (the parametrium) (T3b). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIIC1	T1-T3 N1, N1mi or N1a M0	IIIC1	The cancer is growing in the body of the uterus. It may have spread to some nearby tissues, but is not growing into the inside of the bladder or rectum (T1 to T3). It has also spread to pelvic lymph nodes (N1, N1mi, or N1a), but not to lymph nodes around the aorta or distant sites (M0).
IIIC2	T1-T3 N2, N2mi or N2a M0	IIIC2	The cancer is growing in the body of the uterus. It may have spread to some nearby tissues, but is not growing into the inside of the bladder or rectum (T1 to T3). It has also spread to lymph nodes around the aorta (para-aortic lymph nodes) (N2, N2mi, or N2a), but not to distant sites (M0).
IVA	T4 Any N M0		The cancer has spread to the inner lining of the rectum or urinary bladder (called the mucosa) (T4). It may or may not have spread to nearby lymph nodes (Any N), but has not spread to distant sites (M0).
IVB	Any T Any N M1	IVB	The cancer has spread to inguinal (groin) lymph nodes, the upper abdomen, the omentum, or to organs away from the uterus, such as the lungs, liver, or bones (M1). The cancer can be any size (Any T) and it might or might not have spread to other lymph nodes (Any N).

Ovarian Cancer

Introduction

Ovarian cancer is one of the three most common gynecologic malignancies and the most lethal. 90% of ovarian cancers are of epithelial origin and include serous, mucinous, and endometrioid histological subtypes.
Ovarian cancer spreads to the inguinal, pelvic, and para-aortic lymph nodes, followed by involvement of mediastinal lymph nodes. Distant metastasis occurs mainly to the pleura, liver, lungs, spleen, and bone marrow. Because early ovarian cancer is clinically silent, it often presents in an advanced stage (4).
Follow-up with CA-125 has 94% sensitivity and 82% specificity. That declined to 60% in premenopause because other conditions (such as endometriosis, cystadenoma, pelvic inflammatory disease, and peritoneal dissemination of non-ovarian cancers) can also induce elevated serum levels of CA-125 (10). In combination with imaging, the evaluation of the serum levels of CA-125 actually plays an important role in assessing disease progression and response to treatment.

[^{18}F]FDG PET/CT in Epithelial Ovarian Cancer

[^{18}F]FDG PET/CT has been demonstrated to be superior to transvaginal US, CT, and MRI for staging and presurgical evaluation of disease in patients with epithelial ovarian cancer. False-positive results of [^{18}F]FDG PET/CT are reduced when scan is scheduled in days at some distance from ovulation or menstrual cycle (7).
[^{18}F]FDG PET/ CT is more accurate than the other imaging modalities for identifying metastasis in regional & retroperitoneal lymph nodes (including normal-sized lymph nodes), as well as in distant metastases. Peritoneal metastases detection with [^{18}F]FDG PET/CT is more sensitive than CT, especially for lesions located in the right upper abdomen and small intestinal mesentery.
In the initial staging, the SUVmax of the primary cancer derived from [^{18}F]FDG PET/CT is associated with FIGO stage and histology and is a predictor of overall survival (OS) and disease-free survival (DFS). Pretreatment metabolic volume (MTV) and total lesion glycolysis (TLG), measured with [^{18}F]FDG PET/CT, are inversely correlated with the progression-free interval.
[^{18}F]FDG PET/CT accurately differentiates responders from non-responders after neoadjuvant therapy.
The superiority of [^{18}F]FDG PET/CT compared to other imaging modalities is particularly obvious in the identifying residual viable tumor after treatment and early detection of recurrent ovarian cancer in asymptomatic patients with increased serum markers.

[^{18}F]FDG PET/CT, can change the therapeutic strategy in more than 60% of the patients with ovarian cancer, particularly in patients with gross lesions as candidates for cytoreductive surgery (11).

[^{18}F]FDG PET/CT-guided intensity-modulated radiotherapy (IMRT) improves tumor response and 3-year overall survival compared with CT-guided IMRT.

Key Learning Points

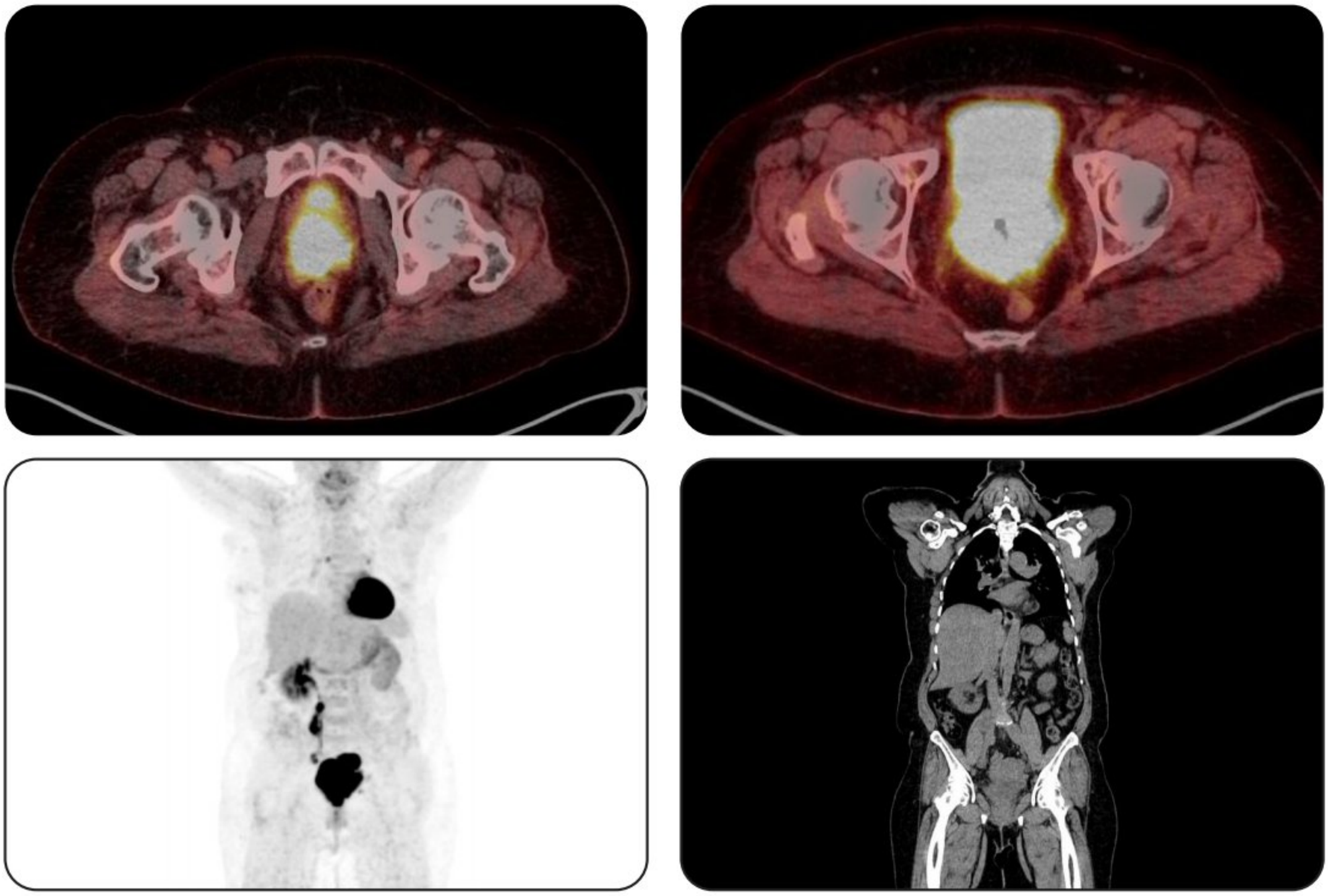
- [^{18}F]FDG PET/CT is a diagnostic modality for initial staging in patients with epithelial ovarian cancer.
- Primary tumor SUVmax at diagnosis is a strong prognostic indicator.
- [^{18}F]FDG PET/CT is an optimal diagnostic imaging modality for identifying non-responder patients and the site of relapse in cases of elevated serum markers and for defining optimal radiotherapy plans (12).

Staging of Ovarian Carcinoma

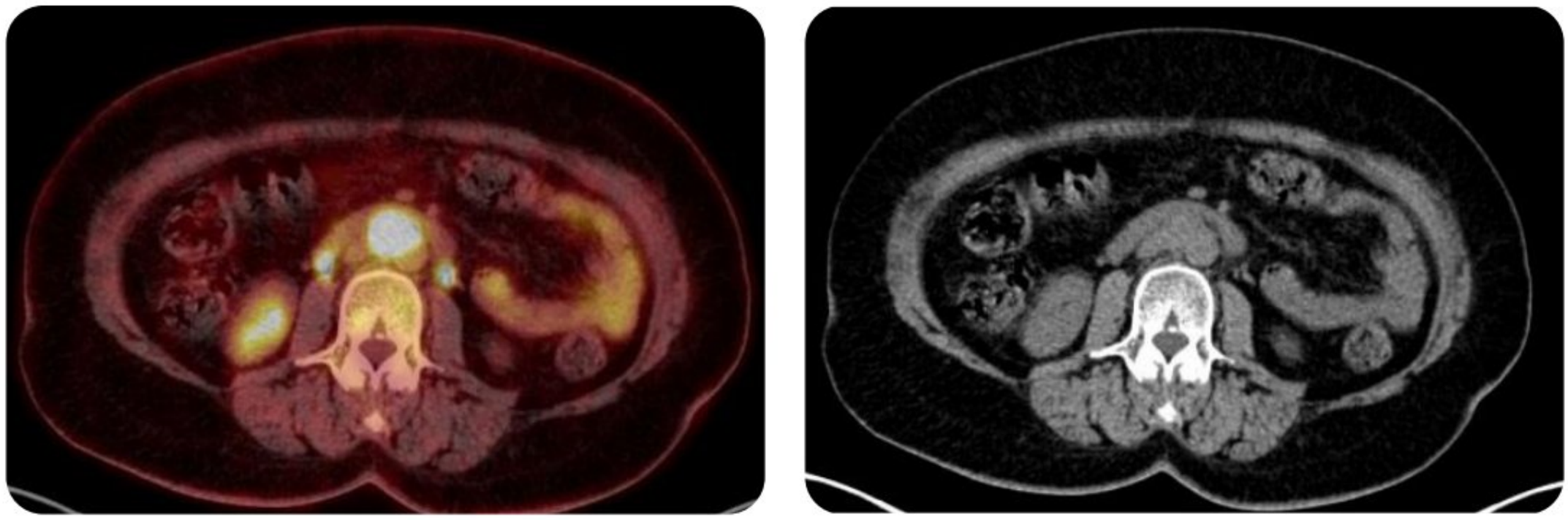
AJCC Stage	Stage grouping	FIGO Stage	Stage description*
I	T1 N0 M0	I	The cancer is only in the ovary (or ovaries) or fallopian tube(s) (T1). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IA	T1a N0 M0	IA	The cancer is in one ovary, and the tumor is confined to the inside of the ovary; or the cancer is in one fallopian tube, and is only inside the fallopian tube. There is no cancer on the outer surfaces of the ovary or fallopian tube. No cancer cells are found in the fluid (ascites) or washings from the abdomen and pelvis (T1a). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IB	T1b N0 M0	IB	The cancer is in both ovaries or fallopian tubes but not on their outer surfaces. No cancer cells are found in the fluid (ascites) or washings from the abdomen and pelvis (T1b). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IC	T1c N0 M0	IC	The cancer is in one or both ovaries or fallopian tubes and any of the following are present: • The tissue (capsule) surrounding the tumor broke during surgery, which could allow cancer cells to leak into the abdomen and pelvis (called surgical spill). This is stage IC1. • Cancer is on the outer surface of at least one of the ovaries or fallopian tubes or the capsule (tissue surrounding the tumor) has ruptured (burst) before surgery (which could allow cancer cells to spill into the abdomen and pelvis). This is stage IC2. • Cancer cells are found in the fluid (ascites) or washings from the abdomen and pel-vis. This is stage IC3. It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
II	T2 N0 M0	II	The cancer is in one or both ovaries or fallopian tubes and has spread to other organs (such as the uterus, bladder, the sigmoid colon, or the rectum) within the pelvis or there is primary peritoneal cancer (T2). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIA	T2a N0 M0	IIA	The cancer has spread to or has invaded (grown into) the uterus or the fallopian tubes, or the ovaries. (T2a). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIB	T2b N0 M0	IIB	The cancer is on the outer surface of or has grown into other nearby pelvic organs such as the bladder, the sigmoid colon, or the rectum (T2b). It has not spread to nearby lymph nodes (N0) or to distant sites (M0).
IIIA1	T1 or T2 N1 M0	IIIA1	The cancer is in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer (T1) and it may have spread or grown into nearby organs in the pelvis (T2). It has spread to the retroperitoneal (pelvic and/or para-aortic) lymph nodes only. It has not spread to distant sites (M0).
IIIA2	T3a N0 or N1 M0	IIIA2	The cancer is in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. During surgery, no cancer is visible in the abdomen (outside of the pelvis) to the naked eye, but tiny deposits of cancer are found in the lining of the abdomen when it is examined in the lab (T3a). The cancer might or might not have spread to retroperitoneal lymph nodes (N0 or N1), but it has not spread to distant sites (M0).
IIIB	T3b N0 or N1 M0	IIIB	There is cancer in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. The deposits of cancer are large enough for the surgeon to see, but are no bigger than 2 cm (about 34/ inch) across. (T3b). It may or may not have spread to the retroperitoneal lymph nodes (N0 or N1), but it has not spread to the inside of the liver or spleen or to distant sites (M0).
IIIC	T3c N0 or N1 M0	IIIC	The cancer is in one or both ovaries or fallopian tubes, or there is primary peritoneal cancer and it has spread or grown into organs outside the pelvis. The deposits of cancer are larger than 2 cm (about 34/ inch) across and may be on the outside (the capsule) of the liver or spleen (T3c). It may or may not have spread to the retroperitoneal lymph nodes (N0 or N1), but it has not spread to the inside of the liver or spleen or to distant sites (M0).
IVA	Any T Any N M1a	IVA	Cancer cells are found in the fluid around the lungs (called a malignant pleural effusion) with no other areas of cancer spread such as the liver, spleen, intestine, or lymph nodes outside the abdomen (M1a).
IVB	Any T Any N M1b	IVB	The cancer has spread to the inside of the spleen or liver, to lymph nodes other than the retroperitoneal lymph nodes, and/or to other organs or tissues outside the peritoneal cavity such as the lungs and bones (M1b).

Case Presentations

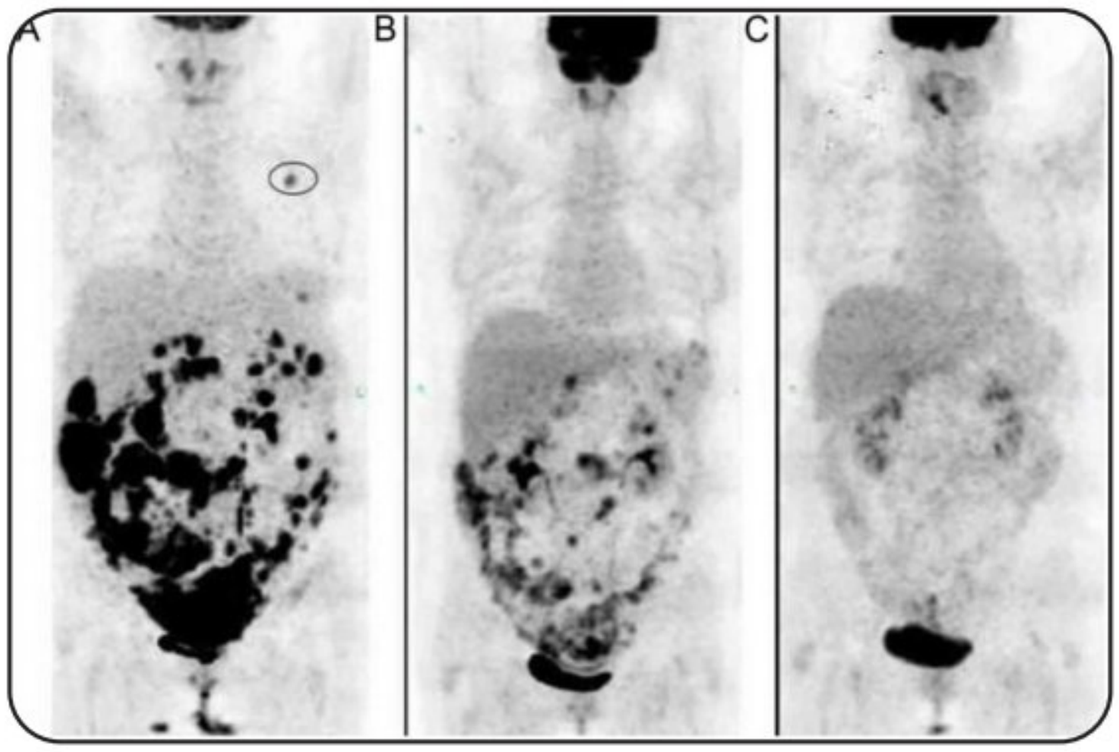
Case 1: PET/CT image shows a primary [18F]FDG avid tumor in the uterine cervix and uterus with invasion to the posterior bladder wall in a patient with newly diagnose cervical cancer refer for staging.



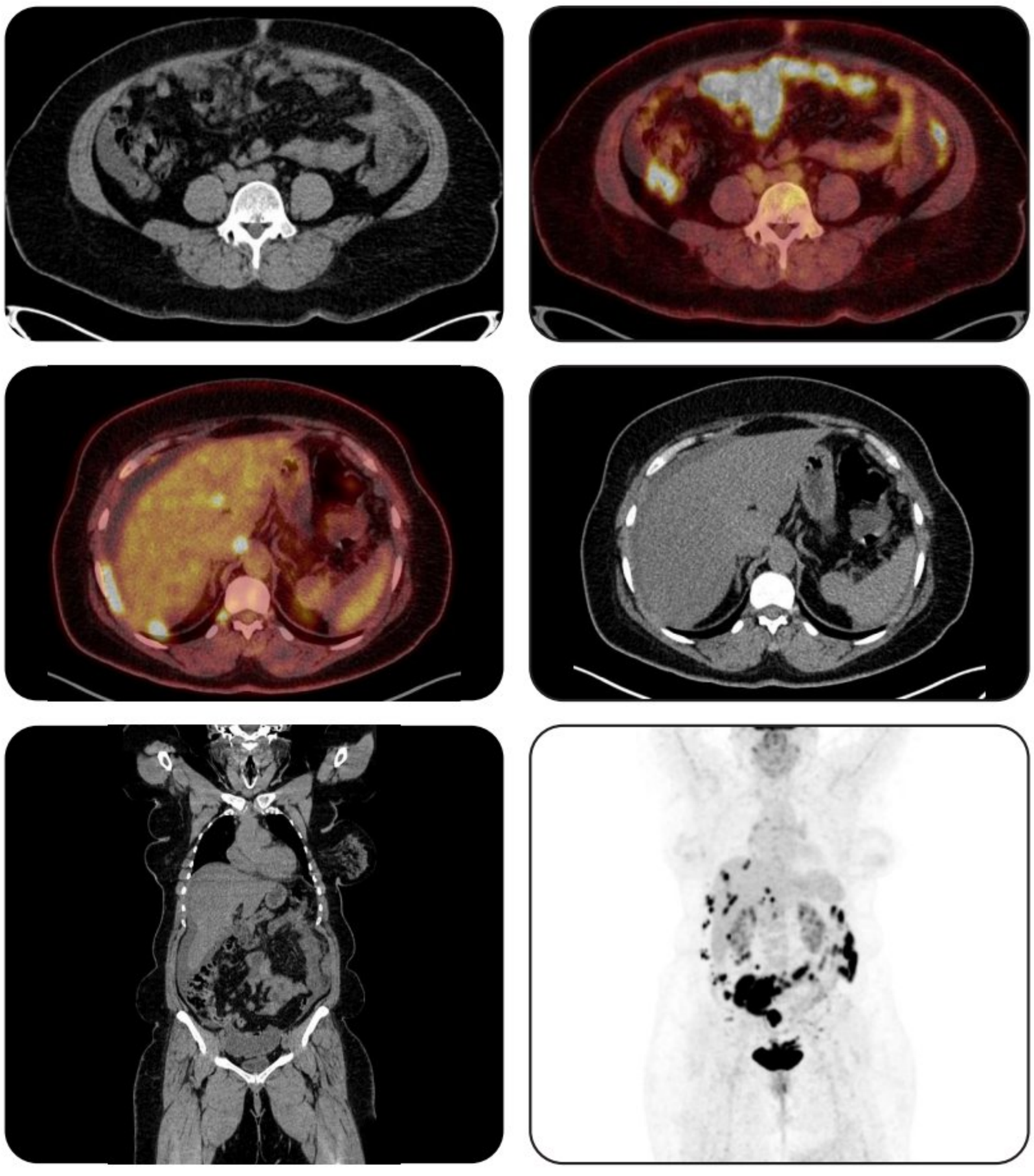
Case 2: The patient is referred for restaging of endometrial adenocarcinoma two years after TAH-BSO follow by chemotherapy with an intensely [^{18}F]FDG avid aortocaval metastatic lymph node.



Case 3: PET/CT scans of a patient with ovarian cancer, was referring for response to treatment (A) prior to treatment, and fallow the (B) second and (C) third treatment. The results revealed that the metabolism of the lesions had disappeared.



Case 4: Omentum and liver capsule metastases in a patient with ovarian cancer; status post TAH-BSO 4 years ago follow by chemotherapy, referred for restaging.



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