Krukenburg Tumors Arising from Rare Primary Sites: Role of ^{18}F-Fluorodeoxyglucose-Positron Emission Tomography/Computed Tomography in Management and Outcome

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Abstract

Krukenberg tumors described by Friedrich Ernst Krukenberg are still fascinating for their mysterious origin. It is known to be a rare entity and commonly originates from adenocarcinoma of stomach. We present three interestingly rare cases of this entity, revealed by ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography (F-18 FDG-PET/CT) scan and discuss how F-18 FDG-PET/CT can prognosticate, alter the course of treatment in such patients. Ovarian metastatic deposits were detected in patients with renal cell, duodenal, and gall bladder carcinoma. Three visits were possible in patient with duodenal cancer (favorable response to therapy), two visits in renal cell cancer (progressive disease pattern) and only single visit for gall bladder cancer. Potentials of F-18 FDG-PET/CT scan for Krukenberg disease is still in exploratory phase, but it's applications in diagnosis, disease monitoring, therapeutic response monitoring, and prognosticating are unparalleled with other imaging modalities.

Keywords: *Krunkenburg tumor in ^{18}F-FDG PET/CT, PET/CT in monitoring follow-up of krunkenburg tumor, unusual primary sites for krunkenburg tumor*

Introduction

Krukenberg tumors (KTs) described by Friedrich Ernst Krukenberg is still a mystery to be solved. KTs are commonly associated with adenocarcinoma of stomach and rarely seen with other gastrointestinal or non-gastrointestinal tumors. We present three rare primaries of this rare entity detected on ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography (F-18 FDG-PET/CT). Ovarian masses were detected in patients with renal cell, duodenal, and gall bladder carcinoma, respectively. Three visits were possible in patient with duodenal cancer, two visits in renal cell cancer and only single visit for gall bladder cancer. Potentials of FDG-PET/CT scan for Krukenberg disease is still in exploratory phase, but its applications in diagnosis, disease monitoring, therapeutic response monitoring, prognosticating are unparalleled with other imaging modalities. Treating KT is a Herculean task, and it is still uncertain whether surgical resection of ovarian metastases and/or primary tumor could improve the overall outcome, as we know that in itself KT is an indicator of dismal prognosis. Controversies still exist about treatment of KT, but metastasectomy and intraperitoneal chemotherapy have gained popularity. Hence, we bring upon a few cases to explain the current scenario of KT in an imaging perspective.

Case Reports

Case 1

A perimenopausal lady presented with pain abdomen for 2 months, underwent upper GI endoscopy, which revealed ulcerative growth in the D2 segment of the duodenum, biopsy from this lesion revealed papillary adenomatous carcinoma. She underwent Whipple's procedure and received seven cycles of 5-fluorouracil-based chemotherapy. F-18 FDG-PET/CT was performed, which revealed multiple mesenteric deposits, retroperitoneal lymph nodes, and bilateral adnexal deposits [Figures 1 and 2]. The patient received two more cycles of similar chemotherapy and F-18 FDG-PET/CT was repeated, which revealed large solid-cystic right pelvic mass. Considering progression of the disease, chemotherapy

How to cite this article: Rangan K, Ora M, Israrahmed A, Gambhir S. Krukenburg tumors arising from rare primary sites: Role of ^{18}F-fluorodeoxyglucose-positron emission tomography/computed tomography in management and outcome. Indian J Nucl Med 2019;34:302-6.

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Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.IJNM_86_19

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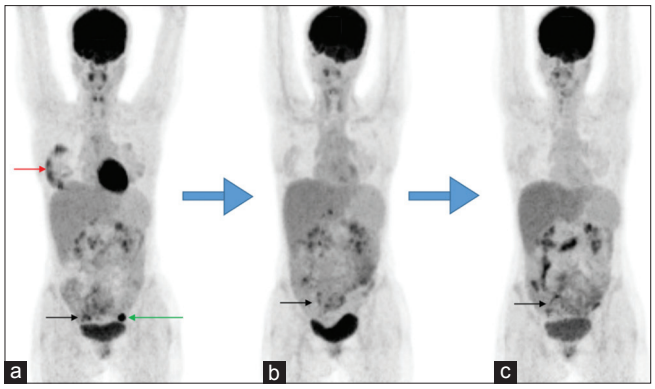

Figure 1: Maximum intensity projection images of the three subsequent scans (a) Baseline Maximum intensity projection, black arrow indicating an abnormal fluorodeoxyglucose avidity in the right side of the pelvis (red arrow-normal physiological breast uptake, Green arrow-fluorodeoxyglucose avidity in the left ovary corresponding to corpus luteal cyst) (b) After two cycles of chemotherapy, all the lesions were increasing in size (c) After changing the chemotherapy regimen, two more cycles were given, upon which patient had a partial response to treatment

was upgraded to oxaliplatin-based regimen. The patient received sic cycles of oxaliplatin-based chemotherapy and F-18 FDG-PET/CT was repeated. The third scan revealed overall decrease in size and avidity of the mass, leading to favorable response to therapy. The patient is on regular follow-up with no complaints.

Case 2

The patient presented with pain abdomen, ultrasonography abdomen revealed cholelithiasis, for which the patient underwent cholecystectomy. After 2 months, the patient developed swelling at the scar site, Biopsy from the scar site revealed metastatic adenocarcinoma. Whole-body 18-F FGD-PET/CT was done to evaluate disease status, which revealed mass in the gall bladder fossa, with multiple peritoneal deposits, anterior abdominal wall deposit, and bilateral adnexal masses [Figure 3]. The patient was started on gemcitabine and cisplatin-based chemotherapy. Unfortunately, the patient was lost to follow-up.

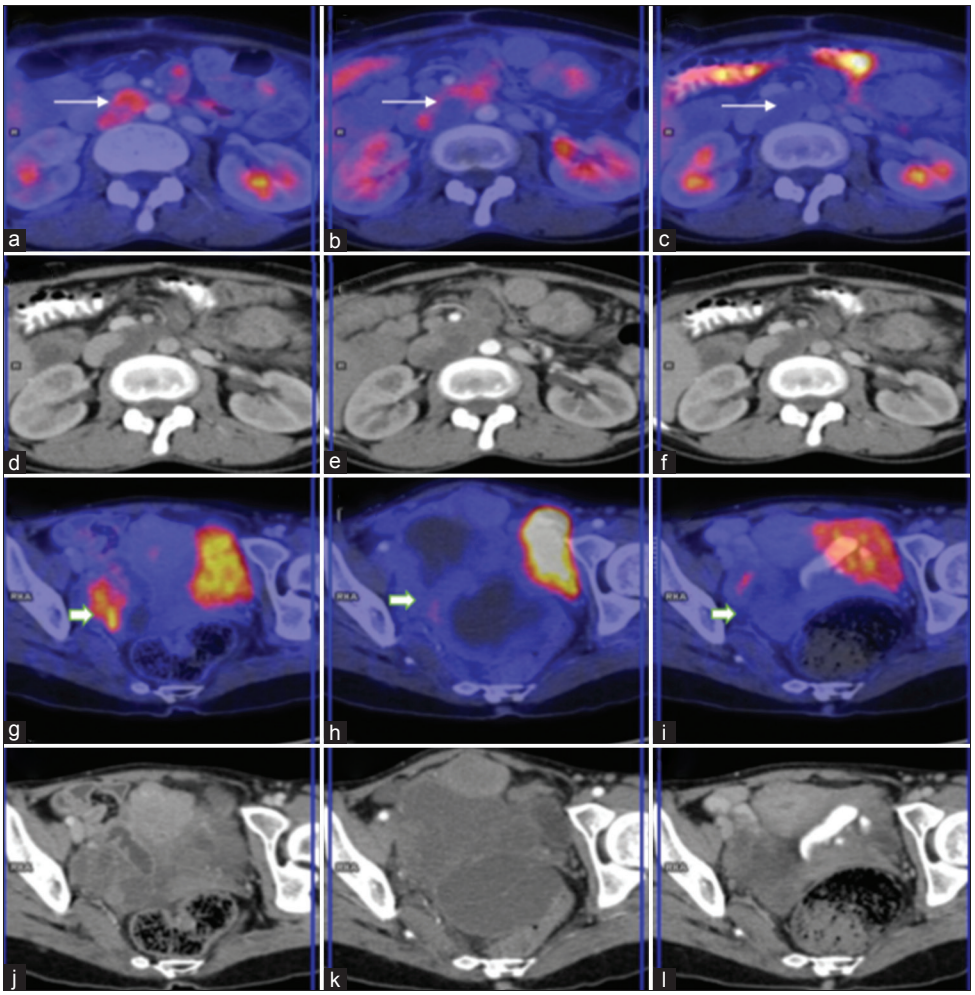

Figure 2: (a-f) Transaxial positron emission tomography-computed tomography with corresponding computed tomography images reveal heterogeneously avid aortocaval lymph node (a and d), which increases in size after two cycles of chemotherapy (b and e) and after changing the chemotherapy regimen, there is partial response (c and f). (g-l) Transaxial-fused positron emission tomography-computed tomography with corresponding computed tomography images reveal peripherally enhancing, fluorodeoxyglucose avid solid-cystic lesion in the right adnexa (g and j), which increases in size after two cycles of chemotherapy (h and k) and after changing the chemotherapy regimen there is partial response (i and l)

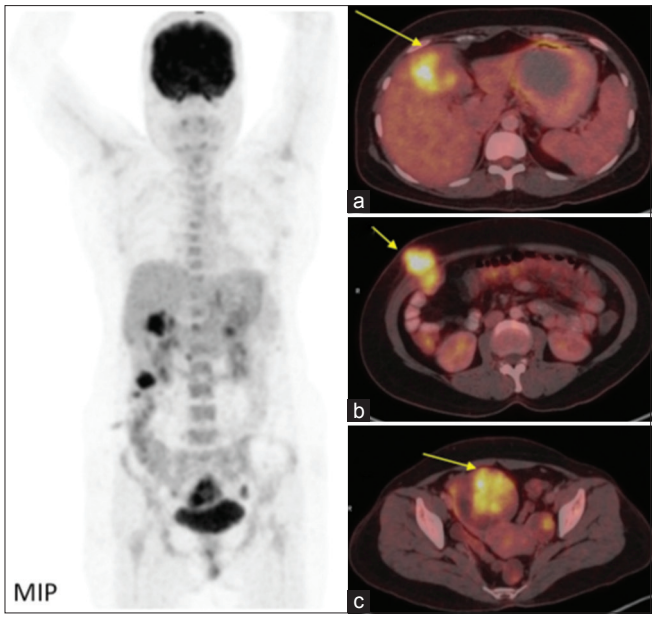

Figure 3: MIP-Maximum intensity projection image with abnormal uptakes in the abdomen. (a-c) are transaxial fused positron emission tomography-computed tomography images, revealing (a) heterogenous fluorodeoxyglucose avid mass lesion in the gall bladder fossa, with local infiltration (b) fluorodeoxyglucose avid soft-tissue dense mass lesion in the anterior abdominal wall, at the port site (c) Heterogeneously fluorodeoxyglucose avid solid-cystic lesion in both the both adnexa (bilateral ovarian metastases, right >left)

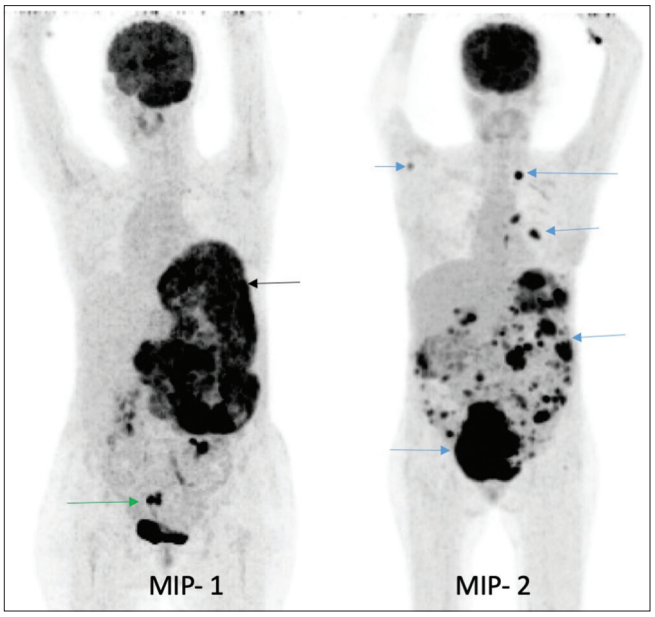

Figure 4: MIP 1-Maximum intensity projection images (Baseline fluorodeoxyglucose positron emission tomography-computed tomography) - large tracer avid mass lesion in the left side of the abdomen (black arrow) and a small focus of fluorodeoxyglucose avidity in the right side of the pelvis (green arrow), MIP 2-Maximum intensity projection images (follow-up after left radical nephrectomy), multiple tracer avid lesions (blue arrows) are noted in the head of right humerus, left supraclavicular lymph node, multiple lung nodules, multiple omental, multiple peritoneal deposits, and an enlarged pelvic mass lesion. Overall, there is progression of the disease

Case 3

The patient presented as mass in abdomen, CT scan revealed locally advanced left renal mass with inferior vena cava (IVC) thrombus. Tumor was infiltrating spleen, distal pancreas, diaphragm, and transverse mesocolon. PET/CT was done, which also revealed similar findings, with an additional finding of an enhancing nodular lesion in the right adnexa. Exploratory laparotomy with distal pancreatectomy, left radical nephrectomy, *en-bloc* splenectomy, and resection of IVC thrombus was done. The patient was on clinical follow-up, underwent repeat PET/CT after 5 months, which revealed progression of the disease with multiple retroperitoneal lymph nodes, peritoneal deposits, hepatic surface deposits, bilateral ovarian mass, and bilateral lung nodules [Figures 4 and 5].

Discussion

KTs have multiple definitions, which has always been a mystery to be solved. Krukenberg attributed few typical features to a primary ovarian tumor, defining it "fibrosarcoma mucocellulare carcinomatodes."[1-3] Many authors still continue to use the term KTs in spite of the relatively well-defined diagnostic criteria. This is because the standard definition of KTs is not universally accepted. Multiple hypotheses for the pattern of spread have been elaborately explained in the literature, among them the "seed-and-soil" hypothesis by Paget has been well appreciated, wherein particular tumor type a has predilection for specific secondary sites, independent of anatomical or vascular factors.[4] Furthermore, retrograde lymphatic spread, peritoneal spread, and hematogenous spread are believed to be different routes of dissemination.[5-7]

KTs involves both the ovaries in most of the cases; however, it is not always true. The most common site of primary malignancy is adenocarcinoma of stomach (~76%), followed by colorectal region (11%), breast (4%), biliary tract and gall bladder (3%), and rest of the rare sites (~15%).[4,8,9] Presentation of the KTs can be along with the primary tumor (synchronous presentation) or after removal of the primary disease (metachronous presentation).[10,11] Conventional imaging modality such as ultrasound, CT, and magnetic resonance imaging (MRI) have been used since decades for diagnosis of KTs. Ultrasound reveals homogeneously hyperechoic and reveal the "lead vessel sign," consisting of a large lead vessel penetrating the tumor from the periphery and then branching in a tree pattern.[12] CT shows lobulated, mostly solid tumors with homogeneous enhancement of the solid portion, and MRI shows a solid component with an hypointense signal density at T2-weighting. Although sonography is the preferred method in the initial evaluation of ovarian masses and is superior to CT in differentiating a solid mass from a cystic one, CT is popularly used for the evaluation of the extent of the ovarian tumor as well as in evaluating recurrence and the response following treatment.

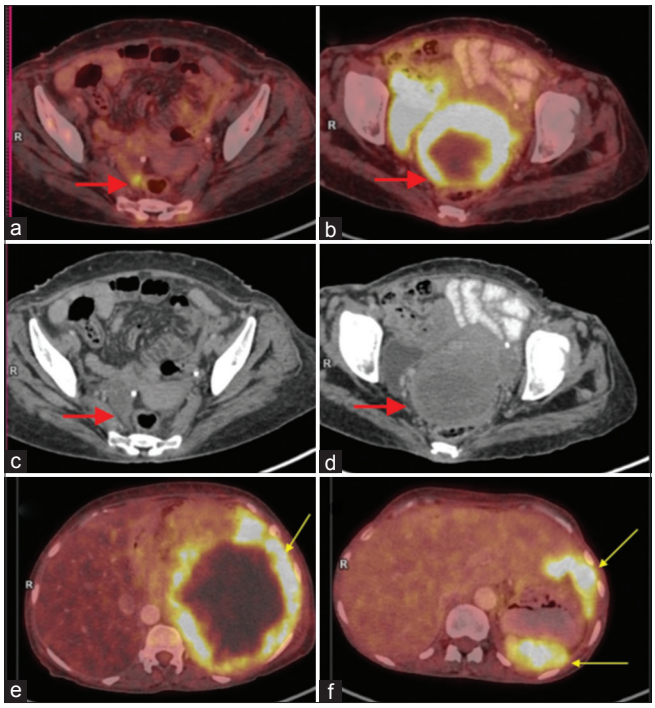

Figure 5: (a and c) (Baseline, transaxial fluorodeoxyglucose positron emission tomography-computed tomography with corresponding computed tomography images) reveal peripherally enhancing fluorodeoxyglucose avid solid-cystic lesion in the right adnexa. (b and d) (Follow-up, transaxial fluorodeoxyglucose-positron emission tomography/computed tomography with corresponding computed tomography image) reveal previously said solid-cystic mass has increased in size (4.2 cm × 5.6 cm), with central necrosis and peripheral fluorodeoxyglucose avidity (e) transaxial fluorodeoxyglucose-positron emission tomography/computed tomography image (baseline scan)-large peripherally fluorodeoxyglucose avid left primary renal mass with central necrosis (f) Transaxial fluorodeoxyglucose-positron emission tomography/computed tomography image (follow up)-after left radical nephrectomy, scan revealed multiple omental and peritoneal deposits

However, it has been generally regarded that the ultrasound and CT findings of KTs are indistinguishable from those of primary ovarian carcinomas.[13-16]

F-18 FDG-PET/CT has been gaining popularity in evaluation of the disease burden in high-risk tumors. It is an established fact that cystic neoplasm has low uptake pattern in FDG-PET/CT, but there is always been a heterogeneous uptake pattern in KTs due to its mixed solid-cystic nature. PET/CT has been explored in the field of diagnosis, disease monitoring, therapeutic response monitoring, and prognosticating KTs.

Gall bladder cancer has high fatality rate. Ovarian metastasis from gall bladder mimics primary neoplasm and have very few literature searches. We have described a young female, who has been operated for cholelithiasis and presented with scar site mass. FDG-PET/CT revealed a scar site mass lesion, residual disease in the gallbladder (GB) fossa, multiple peritoneal and ovarian metastasis. FDG-PET/CT not only demonstrated local recurrence but also other metastatic sites as well. The potential use of PET/CT in disease monitoring and therapy response evaluation can be achieved in such patients. F-18 FDG-PET/CT has been found useful in avoiding unnecessary exploration, providing restaging information after cholecystectomy, and aiding in determination of prognosis of GB adenocarcinoma.[17]

Renal cell cancer very rarely spread to the ovary as metastasis. Regardless of the imaging appearance, metastatic disease to the ovaries should be considered for any ovarian mass in a patient renal cell carcinoma (RCC).[18] Increased serum levels of CA-125, cytokeratin 7, α-fetoprotein, and human chorionic gonadotropin can help establish a diagnosis of a primary ovarian malignancy. Cytokeratin 7 and CA-125 are expressed in ovarian cancers but not in RCC.[18] Baseline FDG-PET/CT demonstrates high-risk features, such as renal vein tumor thrombosis, peritoneal deposits, and suspicious ovarian lesion. PET/CT helped in providing prognostication of these patients in a single scan. After receiving chemotherapy, PET/CT has role in therapy monitoring, response evaluation. Few recent studies have evaluated the role of FDG-PET/CT in response to tyrosine kinase inhibitors in metastatic RCC.[19]

Many surgeons consider KTs as a definite marker of incurable metastatic disease and are dissuaded by attempting a surgical treatment. This is because of the belief that KT is a marker of peritoneal dissemination and unresectable disease at surgical laparotomy. In the current clinical practice, surgery is preferred in young patients with limited disease. In majority of the cases, palliative surgery is considered for symptomatic relief. However, it is still uncertain whether surgery of ovarian deposits and/or primary tumor could improve the overall survival. Intraperitoneal chemotherapy has been preferred in multiple intra-abdominal deposits. The prognosis for patients with this type of metastatic tumor is poor, as most die within the 1st year of evolution. There are rare cases in which patients survive for several years.[8]

Conclusion

KTs have been a tough nut to crack. It is difficult to distinguish the KTs from the primary ovarian neoplasm; however, application of the clinical-radiological knowledge, serum markers, and ancillary diagnostic clues help in evaluating the cause of the KTs. PET/CT has been in the market since few decades, but its potential diagnostic use in this clinical entity is yet to be explored. FDG-PET/CT may be extremely helpful these cases by not only diagnosing KT, but also revealing other intra- and extra-abdominal metastatic sites, helping in therapeutic decision, therapeutic response evaluation, and overall prognostication.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

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