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The role of FDG PET/CT in the evaluation of treatment response in a case of calcified ovarian metastases

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ABSTRACT

Evaluation of calcified metastatic lesions by conventional imaging can be challenging. Ovarian cancer metastases can present with calcification which might increase in size and number following therapy. It is not entirely clear whether these calcifications are associated with tumor response or disease progression. Calcified lesions which do not change in size or configuration are particularly problematic when assessed by RECIST criteria. Positron emission tomography (PET)/computed tomography (CT) is of particular value as it demonstrates the metabolic activity of the calcified lesions, in addition, it might reveal metastases in unexpected sites. We report a case of serous papillary ovarian cancer with extensive abdomino-pelvic calcified metastases referred for evaluation of therapy response. Despite being reported as stable disease on CT evaluation, we observed increased metabolic activity in the calcified lesions both on CT-attenuation corrected and non-attenuation corrected images, which was indicative of inadequate response to therapy. PET/CT is an ideal modality in follow-up of patients with ovarian cancer presenting with calcified metastatic tumoral deposits.

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Introduction

Ovarian cancer is one of the most common cancers in women and a leading cause of cancer mortality (1). This malignancy has an indolent nature and is usually diagnosed at later stages (1). In ovarian cancers, calcifications might occur in tumoral deposits or metastatic lymph nodes which may change in size following therapy (2). There have been also reports of tumoral calcification following chemotherapy in other cancers (3, 4). In a report by Burkill et al. the change in calcification on serial CT scan was not associated with tumoral response (5). Thus, response evaluation criteria in solid tumors (RECIST) might not be the most suitable approach in evaluating calcified lesions. Herein we report a case of ovarian cancer with calcified metastases showing no morphologic changes on CT but increased metabolic activity by FDG PET/CT hence representing superiority of PET/CT over CT in the evaluation of therapy response.

Case Report

A 33-year-old woman with a history of ovarian cancer was referred to our center for the evaluation with FDG PET/CT. Her initial abdomino-pelvic sonography two years prior, revealed a large solid cystic mass in pelvis surrounding the uterus and rectum, extending to abdominal cavity. She had an elevated initial CA-125 level of 76.2 U/ml (normal ≤ 35). Consequently, she underwent total hysterectomy and bilateral

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salpingo-oophorectomy (June 2018). The pathology report confirmed involvement of both ovaries by low-grade serous papillary carcinoma accompanied by omental tumoral deposits (FIGO stage at least IIb). The patient underwent postoperative chemotherapy with doxorubicin and carboplatin. On serial CT scan examinations (from September 2018 to September 2019) number and size of the calcified tumoral deposits were increased (Figure 1).

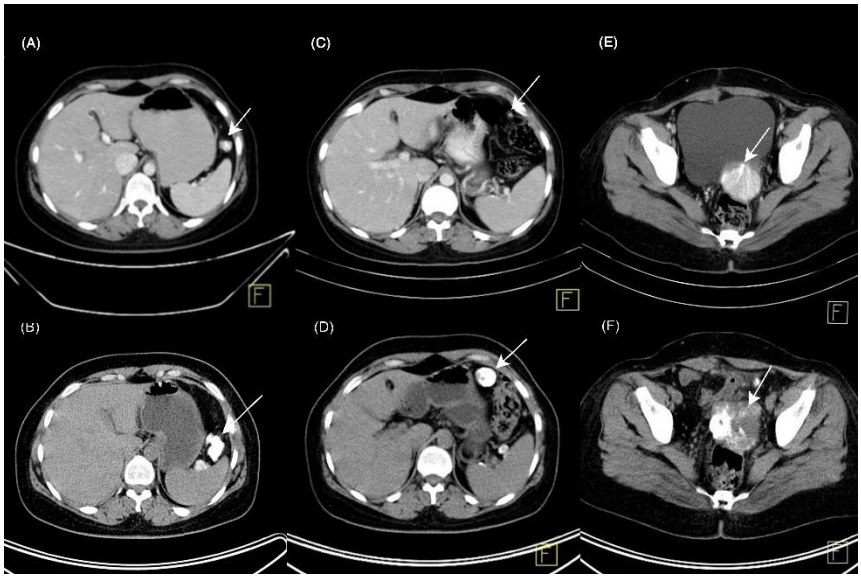

Figure 1. Comparison of CT images dated September 2018 (A, C, E) with the scan performed on September 2019 (B, D, F). Axial CT images reveal significant increase in size and heterogeneity of the tumoral deposits

At the current presentation, she was found to have mildly elevated CA125 level of 41.3 U/ml (normal ≤ 35), CEA level of 2.6 ng/ml (normal level <5.8) and CA19-9 level of 22 U/ml (normal up to 37). The recent CT-scan dated Jan 2020 demonstrated multiple calcified masses in pericapsular regions of the liver and spleen as well as in other parts of abdominopelvic peritoneal cavity (up to 82 mm) which showed no change in size or configuration of the lesions since the previous scan of September 2019. Her PET/CT scan performed 1.5 months after the last chemotherapy, on February 2020, also revealed several calcified masses with increased FDG uptake dispersed in the abdomino-pelvic cavity showing SUV_{max} up to 10.4 (Figure 2).

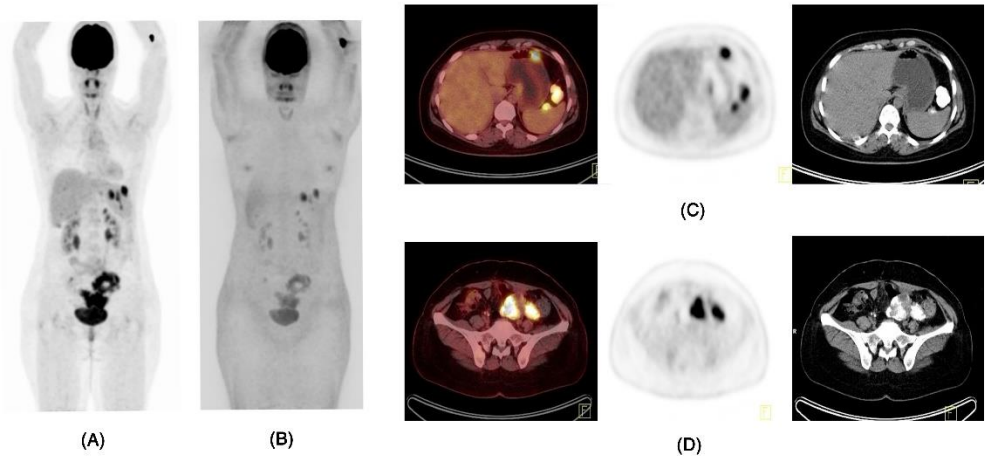

Figure 2. Maximum intensity projection (MIP), both CT attenuation corrected (A) and attenuation uncorrected images (B) demonstrate increased metabolic activity in calcified lesions in the abdominopelvic region. PET/CT fusion (right), PET (middle) and axial CT (left) images demonstrate calcified lesions with increased FDG uptake in the perisplenic and perigastric region (C) as well as in the left pelvic cavity (D)

There was also a lymph node with mild increased FDG uptake in the prevascular region of the mediastinum located posterior to the sternum (SUV_{max}= 2.3) (Figure 3). The patient was scheduled for further chemotherapy.

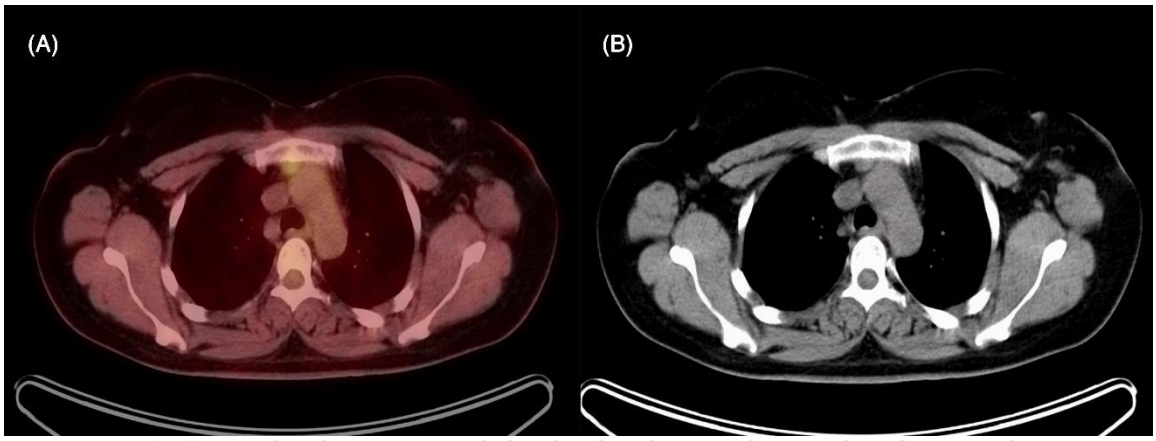

Figure 3. PET/CT fusion and axial CT images reveal a lymph node with increased FDG uptake in the prevascular space

Discussion

It has been reported that peritoneal calcification occurs in 8% to 16% of ovarian tumoral deposits. The calcification associated with serous papillary ovarian cancer appears to be related to psammoma bodies which is characterized as dystrophic calcification (2, 5). Other malignancies such as colon and gastric cancers have also been associated with peritoneal calcifications (6, 7). The pattern of peritoneal calcification on CT images was evaluated by Agarwal et al. (8) to distinguish between benign from malignant form. In their study, peritoneal calcifications associated with calcified lymph nodes were more likely characterized as malignant deposits. While the presence of sheetlike peritoneal calcification had significant association with benignity, these patterns however, could not completely rule out malignancy .

In a study by Ganeshan et al. (2) the change in calcification size or development of new calcifications following chemotherapy were evaluated and the results were correlated with CA-125 level. According to this study, in the case of incremental serum CA-125 the number and size of peritoneal deposits and calcifications were also increased. They concluded that increasing in calcification following chemotherapy should not be viewed as response to therapy. On the other hand, the evaluation of calcified lesions by conventional imaging following chemotherapy may be problematic as the lesions might not change in size and consequently the study may be falsely reported as stable disease. PET/CT is valuable in this setting as it demonstrates the tumoral viability and help to differentiate post-therapy changes from persistent/recurrent neoplastic tissue.

FDG PET/CT has potential role in evaluating ovarian cancer recurrences both in patients with normal and elevated CA-125 levels. Its accuracy is higher than CT for the detection of peritoneal metastases. The classic pattern of peritoneal spread is characterized as the involvement of the surface of liver and spleen, omentum, paracolic areas, pelvis and sigmoid mesocolon (9). The same pattern was noted in our patient demonstrating calcifications around the liver and spleen, sigmoid and pelvic regions .

The superiority of FDG PET/CT over conventional imaging is in evaluating disease activity. Hu et al. (10) reported two cases of calcified metastases from ovarian cancer depicted on PET/CT scan, in one case progressive disease was noted on serial examination, with the development of new lesions and increased metabolic activity of the previously calcified lesions. The second case demonstrated extensive calcified lesions with increased FDG uptake in the left hemi-pelvis, right subdiaphragmatic and supradiaphragmatic areas. Considering the rise of serum CA-125 level, the diagnosis of recurrent ovarian cancer was made and therapy was initiated. The authors indicated that PET/CT scan has invaluable potential in distinguishing benign from malignant calcifications. The PET/CT scan is advantageous in evaluating response to therapy in the presence of calcifications.

The potential additive value of PET/CT scan is also to determine the metastatic lesions in supradiaphragmatic lymph nodes as the lymphatic drainage of ovarian cancer commonly

occur through the cardiophrenic region followed by parasternal area (9). The presence of extrabdominal and inguinal lymph nodes upstages the disease from stage III to IVB. Considering our patient, a prevascular lymph node showing mild metabolic activity was observed in parasternal region, which is to be further evaluated to confirm metastatic involvement.

When increased SUV values are observed on attenuation corrected (AC) images due to deposits of high-density material such as calcium, there is always a potential for false positive interpretation of disease activity. In view of calcification in the metastatic lesions, both AC and non-AC images should be precisely reviewed to exclude the possibility of artifactual nature of activity. This fact was emphasized in a case report by Nikaki et al (11). In their study, a patient with a history of ovarian cancer and extensive calcified metastases in mediastinal, supraclavicular and retroperitoneal lymph nodes was examined for the evaluation of treatment response. The authors reviewed both AC and NAC images which demonstrated increased metabolic activity in both settings. We also thoroughly reviewed the non-AC and AC images of the lesions which confirmed considerable increased metabolic activity in abdominopelvic deposits, indicating inadequate response to therapy. It has been reported that when tumoral deposits demonstrate metabolic activity on FDG PET study, surgical resection might be a better therapeutic option, since these lesions might not be chemosensitive (9).

Conclusion

we presented a case of ovarian cancer with multiple calcified abdomino-pelvic metastatic deposits showing increased metabolic activity referred to us for evaluation of response to treatment, in the presence of a recent CT scan reported as indicative of stable disease. PET/CT scan was of particular value in this patient, demonstrating the increased FDG uptake which in the presence of elevated CA-125 levels was highly suggestive of inadequate response to treatment and she was rescheduled for further chemotherapy. In patients with extensive calcifications, the review of both non-AC and AC images are mandatory to differentiate true from false positive results and avoid misinterpretation due to attenuation correction artifact.

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