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CASE REPORT

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Bone Involvement by Adenocarcinoma of the Uterine Cervix: A Rare Entity

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Summary

Background: Adenocarcinoma is the second most frequent cancer of the uterine cervix after squamous carcinoma, and the most frequent histotype is the mucinous one. Endo-cervical adenocarcinoma accounts for about 10–30% of all cervical cancers and clinically the lesion can be asymptomatic or, more frequently, presenting with anomalous bleeding and/or vaginal discharge.

Case Report: A 41-year-old woman with a diagnosis of adenocarcinoma of the uterine cervix was subjected to chemotherapy after radical surgery. During the follow-up, the patient underwent a Positron Emission Tomography integrated with Computed Tomography and pelvic Magnetic Resonance, which showed rapid and diffuse disease progression from the site of the lesion to the pelvic bones.

Conclusions: Bone involvement in patients with cervical cancer, being a rare event, is significant since it greatly reduces life expectancy. The majority of metastatic bone lesions in cervical cancer seem to be of osteolytic nature. In our patient, Positron Emission Tomography integrated with Computed Tomography and Magnetic Resonance were the imaging methods used during the follow-up and both techniques clearly showed diffuse and rapid tumour spread to the bones.

MeSH Keywords: Adenocarcinoma • Cervix Uteri • Magnetic Resonance Imaging • Pelvic Bones • Positron-Emission Tomography

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Background

Adenocarcinoma is the second most frequent cancer of the uterine cervix after squamous carcinoma. This tumour originates from the cells of the columnar epithelium of the cervical canal and generally presents an endophytic growth pattern [1]. Although there are several histological variants of cervical adenocarcinoma, the mucinous one is the most frequent histotype [2]. Clinically, the lesion can be asymptomatic or, more frequently, presenting with anomalous bleeding and/or vaginal discharge [3,4].

Case Report

A 41-year-old woman underwent in 2010 a radical excision of adenocarcinoma of the uterine cervix FIGO stage IIIB for involvement of the left parametrium, right ovary and regional lymph nodes. Next, she received chemotherapy with Carboplatin AUC 5 and Paclitaxel 175 mg/m^2 q3w for 6 cycles from August 2010 to January 2011, without evidence of residual disease.

After about two years (April 2013), during her follow-up, the patient had a PET-CT scan, which showed, at the site of previous surgery, an area of abnormal tracer uptake (SUV max 7). In addition, focal increased tracer uptake (SUV max

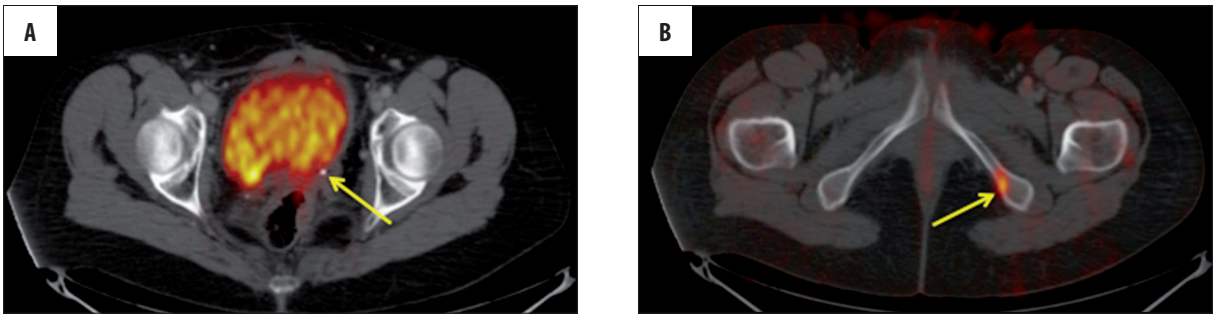

Figure 1. (**A**) Axial PET-CT image showing abnormal tissue in the posterior wall of the bladder with increased FDG uptake (SUV max 7), (**B**) Axial PET-CT image also demonstrated abnormal uptake (SUV max 5.2) in a millimetre osteolytic focus in the left ischio-pubic branch.

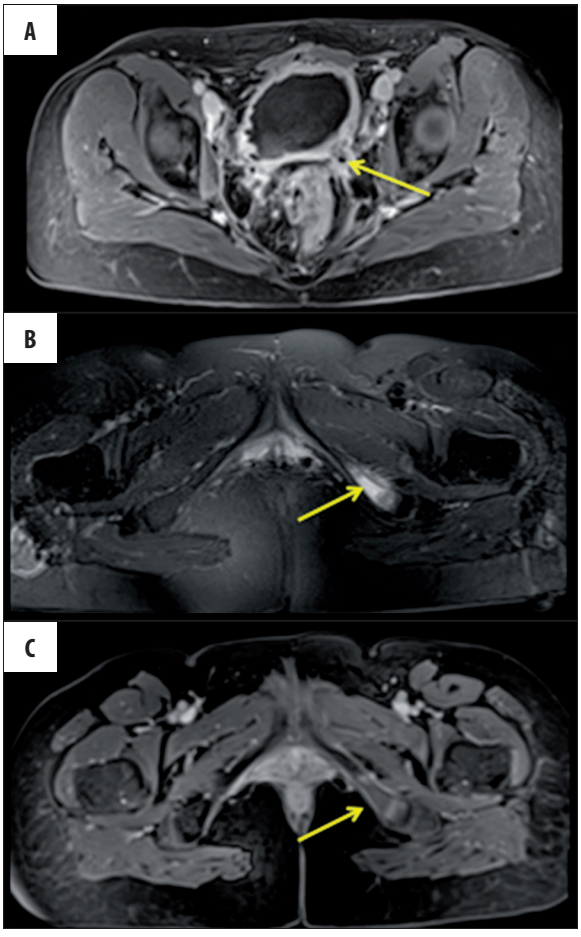

Figure 2. (**A**) VIBE T1 axial image confirms the presence of solid tissue in the posterior wall of the bladder showing contrast enhancement. (**B**) Axial TSE T2 image with fat suppression shows a hyperintense focus (16 mm) in the left ischio-pubic branch presenting contrast enhancement as shown on VIBE T1 axial image (**C**) obtained after administration of contrast medium (gadolinium)

5.2) was detected at the level of an osteolytic lesion located in the left ischio-pubic branch (Figure 1). After about one month, for further investigation of those findings, the patient underwent a pelvic MRI, which showed in the left posterior bladder the presence of irregular infiltrative tissue not dissociable from the ipsilateral ureteral meatus. Furthermore, a bone lesion of the left ischio-pubic branch was described, confirming the result of PET-CT (Figure 2).

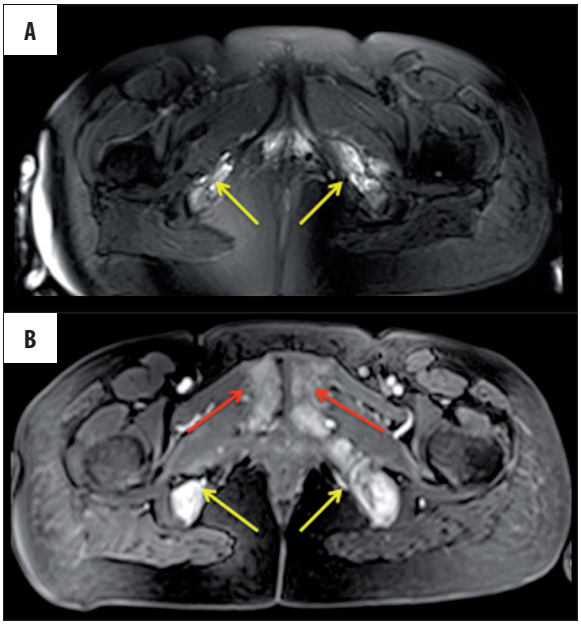

Figure 3. (**A**) Axial TSE T2 image with fat suppression showing dishomogeneous hyperintensity in the ischio-pubic branches presenting a swelling with cortical irregularity of the outline. In the axial VIBE T1 image (**B**), intense and diffuse enhancement in bone structures (yellow arrows) of the pelvis (red arrows) are present.

Based on the radiological signs of loco-regional disease recurrence, a cystoscopic evaluation was performed, confirming the disease recurrence. As a result, the patient resumed combination chemotherapy with Carboplatin and Paclitaxel for 6 cycles, from July 2013. The in-course evaluation included a pelvic MRI (October 2013) which showed a disease progression for the evidence of new bone lesions in the right ileo-pubic branch, with involvement of the pubic symphysis and both posterior acetabular pillars, particularly on the left, which was swollen and showed intense contrast enhancement (Figure 3). Additionally, two small sub-centimeter contrast-enhanced areoles were highlighted in the left acetabular roof and a focal abnormality in the medium-proximal third of the left femur. That focal structural bone alteration was subsequently confirmed by a second PET-CT study (Figure 4), performed in November 2013, after the fifth cycle of chemotherapy, that also showed a diffuse bone involvement. That clearly indicated diffuse bone abnormalities of the pelvis characterized by heterogeneity and structural deformity at the level of the ischial bones and the

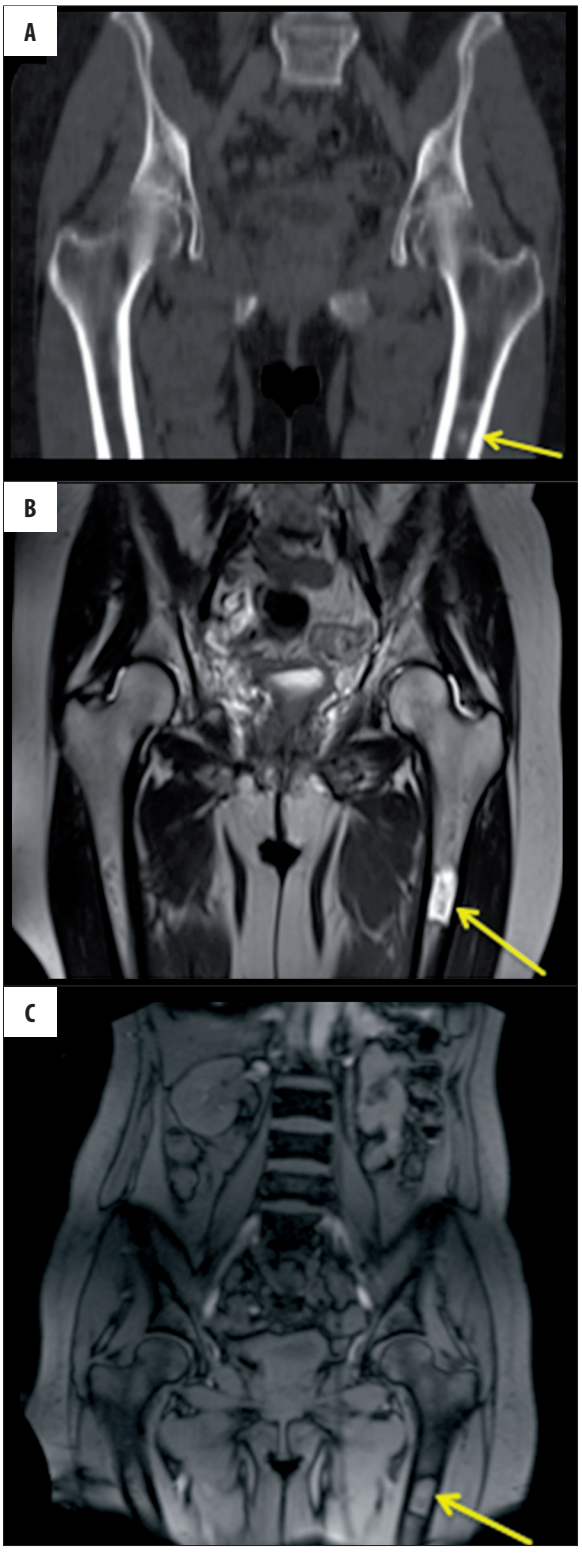

Figure 4. (**A**) Coronal CT image in which a focal structural alteration in the third proximal of the left femur is evident. (**B**) Coronal TSE T2 image in which an area of hyperintensity (3.2 cm) in the third proximal of the left femur is detected as in the coronal localizer (**C**).

ischio-pubic branches, especially on the left. Thickened bone marrow and cortical irregularity of the outlines were also

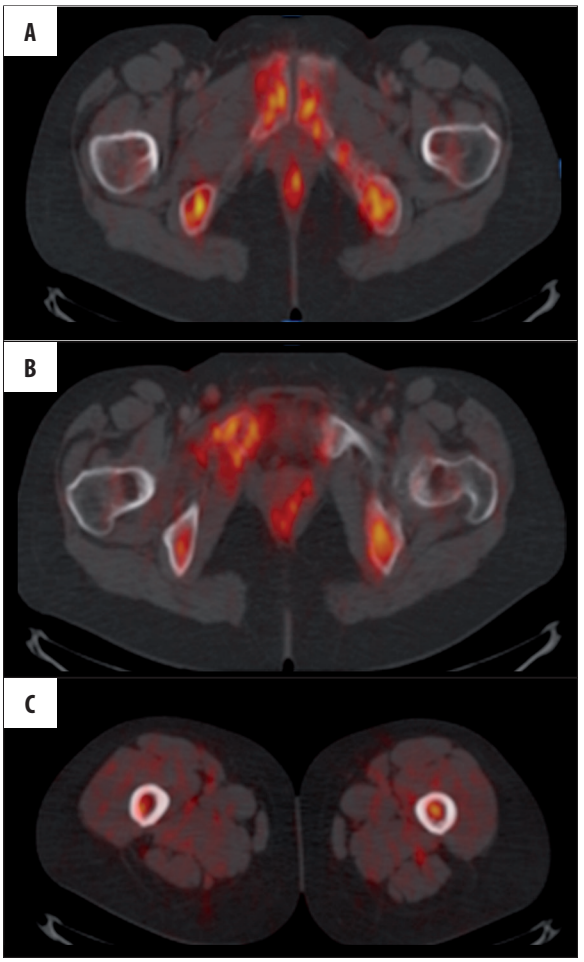

Figure 5. (**A, B**) Axial PET-CT images showing diffuse abnormal uptake in the bone structures of the pelvis (SUV max from 4 to 7) (**C**) Axial PET-CT image in which a focus of increased tracer uptake is also detected in the left proximal femur (SUV max 3).

noted. At that level, an abnormally increased tracer uptake with a SUV max from 4 to 7 was evident. Furthermore, in the proximal-middle third of the diaphysis of the left femur, in the context of the bone marrow, a shady pseudo-nodular area of hyper-density was shown. That was associated with cortical irregularity of the outline inside of the rear side and showed tracer uptake with a SUV max value of 2 (Figures 5).

The patient was successively monitored in the follow-up during the 6 cycles of chemotherapy.

Discussion

Adenocarcinoma is the second most frequent cancer of the uterine cervix after squamous carcinoma. This tumor originates from the cells of the columnar epithelium of the cervical canal and generally presents an endophytic growth pattern; although there are several histological variants of cervical adenocarcinoma, mucinous is the most frequent histotype. Clinically, the lesion can be asymptomatic or, more frequently, presenting with anomalous bleeding and/or vaginal discharge. Cervical carcinoma may also involve other pelvic structures, such as endometrium, vagina, bladder, ureters,

rectum, parametrium, ovaries and regional lymphnodes. Moreover, other atypical tumor sites could be involved, such as abdominal solid organs, lungs and bones [5]. Appropriate imaging techniques should be used for the assessment of loco-regional extension and systemic spread of the disease.

Endo-cervical adenocarcinoma accounts for about 10–30% of all cervical cancers. Barbu's analysis [6] showed that the clinical stage represents the most important prognostic factor in these forms of cancer of the uterine cervix. The typical evolution of carcinomas of the uterine cervix is the extension of the disease into pelvic organs. However extra-pelvic tumor spread in the abdomen, lungs and bones is rare but possible. According to Matsuyama et al. [7], the frequency of bone metastasis during the follow-up of cervical carcinoma increases with advancing stage of disease. The most frequent site of metastasis is the spine, particularly the lumbar spine (48%), followed by the pelvic bones. The majority of metastatic bone lesions in cervical cancer seem to be of osteolytic nature. Charles et al. [8] showed secondary bone involvement by adenocarcinoma of the uterine cervix in 15% of cases. According to Ratanatharathorn et al. [9], there are different models of tumour cell spread to the bone structures: a) direct extension into the bone from the parametrial extensions of the primary or recurrent pelvic tumour; b) direct extension into the bone from parenchymal metastasis to distant lymph nodes or lungs; c) regional hematogenous metastasis compatible with Batson's venous plexus distribution and systemic hematogenous metastasis to distant bones.

Bone involvement in patients with cervical cancer, being a rare event, is significant since it greatly reduces life expectancy. To our knowledge, there are a few described cases of bone metastases from carcinoma of the uterine cervix [10,11]. Our patient with an uncommon tumour of the uterine cervix (mucinous adenocarcinoma) presented in the follow-up a rapid and diffuse involvement of bone disease (pelvic bones and femoral diaphysis), which is a very rare event as demonstrated by CT images using a bone window. A limit to our report was the lack of histopathological confirmation of diffuse bone involvement by uterine carcinoma, but considering the imaging criteria, the concordance of the results of two advanced imaging techniques may be considered diagnostic for metastatic bone lesions. In line with the literature, bone metastases in our patient were osteolytic. MRI and PET-CT imaging may improve the detection of bone metastasis [12,13]. In particular, Liu et al. [14] reported the superiority of 18F-FDG-PET compared to CT and MRI, in the detection of bone metastases in patients with hematogenous advanced cervical cancer. In our case, both imaging methods were used during the follow-up and both techniques clearly showed diffuse and rapid tumor spread to the bones in the pelvis. Initially the patient was in clinical remission. However, later on the patient had loco-regional disease recurrence and focal bone involvement, and therefore she resumed chemotherapy for additional 6 cycles. In the course of the subsequent follow-up the patient showed a rapid and diffuse bone involvement, initially detected by MRI, and subsequently confirmed by PET-CT.

Conclusions

The patient is currently followed up but her clinical condition is significantly worse. In our patient the correlation of both morphological and functional imaging findings was strongly suggestive of diffuse bone involvement. Therefore, advanced tomographic imaging techniques are recommended in such patients, and particularly the "hybrid" modality is suggested. Bone metastatic lesions in the pelvis, observed in our patient, are a rare entity. In case of uterine cervix adenocarcinoma, these abnormalities need to be differentiated from other malignant bone lesions, and in particular: metastatic bone disease, plasma cell myeloma, Ewing's sarcoma and lymphoma are among tumours located primarily within hematopoietic marrows, as occurred in our patient [15]. Clinical history, anatomic location and imaging findings may be helpful in the differential diagnosis. Bone involvement by cervical adenocarcinoma may rarely occur; therefore, careful follow-up of such patients is required, and for this purpose, integrated diagnostic imaging such as PET-CT is recommended.

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