**SINGLE BONE METASTASIS OF A SQUAMOUS CELL CARCINOMA OF THE CERVIX: IN THE CLAVICLE**

Abstract:

Cervical cancer occurs around the age of 40-45, and can be localized or metastatic.

Metastatic sites vary: lymph nodes, lungs and other sites. Bone metastases are uncommon, and require histological study to confirm their secondary nature, especially in the case of unusual localizations. Case report: we report the case of a young patient followed since 2022 for a moderately differentiated, infiltrating and keratinizing squamous cell carcinoma of the uterine cervix, classified IIb, treated with concomitant radio-chemotherapy. In early 2024, a surveillance thoraco-abdomino-pelvic CT scan showed a mixed lesion of the sternal end of the left clavicle. A PET-FDG scan showed an intense, heterogeneous, hypermetabolic condensing lesion. A biopsy confirmed the diagnosis: bone localization of a moderately differentiated squamous cell carcinoma. The patient was treated with chemotherapy, followed by surgery and local radiotherapy. Conclusion: a clavicular metastasis of a cervical cancer represents a rare entity, especially in the presence of a single secondary lesion, with no other metastases elsewhere.

KEY WORDS: clavicle, bone metastasis, single lesion, cervical cancer.

INTRODUCTION:

Globally, cervical cancer is the second most common cancer in terms of both incidence and mortality in women of reproductive age [1].

It is a squamous cell carcinoma in 80% of cases, adenocarcinoma in 15%, adeno-squamous carcinoma in less than 5%, and rarely an undifferentiated carcinoma [2].

Its incidence is declining in developed countries thanks to screening, but remains a cause for concern in developing countries and constitutes a genuine public health problem [3].

The most common metastatic site for cervical cancer is the lung [4].

Other sites include the bladder, the sigmoid, the brain and the bone [5].

Bone metastases are less frequent than lung lesions, and usually occur in the axial skeleton, mainly the spine, ribs and pelvis [6].

In this article, we describe the occurrence of a clavicular metastasis in a 36-year-old female patient previously treated for a squamous cell carcinoma of cervical cancer.

CLINICAL OBSERVATION:

This is a 36-year-old patient with no particular history, followed up in 2022 for a moderately differentiated, infiltrating and keratinizing squamous cell carcinoma of the uterine cervix, classified IIb, treated with concomitant radio-chemotherapy (06 weeks of radiotherapy with weekly cisplatin at a dose of 70 mg). **Then regular follow-up every 3 months, including a clinical examination, a biological assessment, and a PET-FDG that comes back normal at each check-up.**

A surveillance cervico-thoraco-abdomino-pelvic CT scan performed in early 2024 showed a mixed lesion of the sternal end of the left clavicle, with no other distant lesions.

Cervicothoracic MRI confirmed the existence of a swelling in the medial end of the left clavicle, without being able to rule out an inflammatory or infectious origin.

The MDP-Tc99m bone scan showed intense hyperfixation at the sternal end of the clavicle, which was suspicious.

We completed the scan with PET-FDG: an intense, heterogeneous, hypermetabolic, condensing lesion of the medial end of the left clavicle, SUVmax = 7.9, suspicious (Fig. 1, Fig.2).

 

**Figure 1:** PET-CT axial section showing an intense, heterogeneous hypermetabolic lesion of the left clavicle.

**Figure 2:** PET-CT axial section (MIP image).

In February 2024, a clavicular biopsy was performed, confirming a bone localization of a poorly to moderately differentiated squamous cell carcinoma already known.

**According to the recommendations of scientific societies (notably the European Society for Medical Oncology, the National Comprehensive Cancer Network, and others), in the case of metastatic squamous cell carcinoma of the cervix: cisplatin-based doublets with topotecan or paclitaxel have demonstrated their superiority over cisplatin monotherapy in terms of response rates and progression-free survival.
The combination of paclitaxel and carboplatin could be considered as an alternative for patients who are not candidates for cisplatin.
Although a Japanese randomized clinical trial comparing the two treatment regimens showed similar efficacy, the combination with cisplatin proved superior to carboplatin in patients who had never received cisplatin before [19].**

**Our patient has already been treated with cisplatin at the locally advanced stage of the cancer.**

**Based on this data, and after conducting a medical staff meeting, the decision made was to administer 03 to 06 cycles of chemotherapy with paclitaxel + carboplatin, then surgery +/- local radiotherapy.**

After 03 cycles of chemotherapy, the mass was still stable, with no progression or regression, so chemotherapy was continued until 06 cycles.

The patient underwent surgery in July 2024: resection of the tumor and invaded structures, notably bone (sternal manubrium, sternoclavicular joint, 2/3 of the clavicle and the anterior part of the 1st rib) and a part of the pectoralis major muscle, followed by placement of a muscle flap (pectoralis minor).

**On the anatomic-pathological data: the surgical specimen measured 10.8\*5\*3.4 cm, including a clavicle measuring 4.8\*1.4\*0.8 cm and a sternal fragment measuring 5.3\*4.6\*0.7 cm.
On sectioning, presence of a neoplasm with a major axis of 4.7 cm.
Histologically, the various samples taken showed bone tissue infiltrated by a poorly differentiated carcinomatous tumor process. The tumor cells were evidently atypical.
Presence of mitotic figures, without vascular emboli
All resection margins were clear.
An immunohistochemical study conducted showed: staining of tumor cells by anti-AE1/AE3 and CK5/6.**

**After recovery, we ordered a FDG-PET scan, which showed a moderate hypermetabolism in the left supraclavicular region, with a postoperative (inflammatory) appearance (Fig. 3, Fig. 4).**

 

**Figure 3:** PET-CT frontal section showing a moderate and diffuse hypermetabolism in the left supraclavicular region, with a postoperative (inflammatory) appearance.

**Figure 4:** PET-CT (MIP image).

**The patient was then referred for radiotherapy, and a continuous monitoring (with no sign of recurrence so far).**

DISCUSSION:

The frequency of bone metastases in cervical cancer does not exceed 7%, and so they are less frequent than pulmonary secondary lesions, which are the primary metastatic site in this disease [7], [8].

**The pathophysiological mechanism of tumor cell dissemination to the bone is represented as follows: tumor cells first interact with the stroma in the primary cancer, then migrate and enter the systemic circulation.
At this level, malignant cells interact with certain cell types (erythrocytes, T lymphocytes, neutrophils, and platelets), then migrate to the bone marrow, pass inside it, and communicate with its cells to survive and activate osteoclasts, forming a metastatic bone focus [9].**

The most common mechanism of bone involvement due to carcinoma of the uterine cervix was extension of the neoplasm from para-aortic nodes, with involvement of adjacent vertebral bodies [10].

In cervical cancer, metastatic spread to the bone is rarer than to the lung, since the latter has the densest capillary bed in the body, and is made up of a network of delicate membranes that easily trap tumor cells [11].

Bone metastases from cervical carcinoma usually occur in the axial skeleton, mainly the thoracic spine, lumbar spine, sarcum, pelvis and ribs. However, extra-skeletal metastases may occur, such us in the tibia or in the humerus [12], [13].

A retrospective cohort analysis of women with cervical cancer metastatic to bone, diagnosed between 2014 and 2015 was undertaken; in this study, the prevalence of bone lesions in the pelvis and lumbar spine was the highest (35%), given the anatomical location, followed by the thoracic spine (28%), sarcum (20%), ribs (16%), and other less frequent (skull, cervical spine, femur...) [14].

Clavicular localizations are rarer than other sites, and a case of clavicular metastasis was described in the same study, using FDG-PET in an asymptomatic patient [14].

In metastatic cervical cancer with multiple metastases, the therapeutic decision is obvious: chemotherapy, bevacizumab and immunotherapy depending on PDL-1 expression by the tumor, the patient's performance status and comorbidities [15], [16].

For patients unsuitable for systemic treatment, management is limited to supportive care [17].

However, in the case of oligo-metastatic disease, or in the case of a single metastasis as in our patient's case, treatment cannot be palliative, or aimed at improving progression-free survival, but must rather be curative [18].

- When local treatment is possible: we have to propose surgical resection with or without external radiotherapy (sometimes high dose external radiation), while discussing chemotherapy [18],[19], [20].

- When local treatment is impossible: therapeutic approaches are similar to those for poly-metastatic disease (chemotherapy, targeted therapy, immunotherapy) [21],[22].

In our patient's case, the disease was certainly oligo-metastatic and qualified for local therapy, but the rarity of this case put us outside the standard, and a medical staff was necessary before deciding on chemotherapy followed by surgery and radiotherapy.

CONCLUSION:

Bone metastases from cervical cancer are often associated with other secondary lymph node, liver and lung localizations, testifying to their late onset during the course of this disease; and thus their presence would be correlated with a poor prognosis.

The particularity of our patient's case was the occurrence of a single bone metastasis, and the exceptional location: the clavicle.

**I declare that NO generative AI technology such as large language models (ChatGPT, COPILOT, etc.) and text-to-image generators was used during the writing or revision of this manuscript.**

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