

Fibula metastasis as the presenting feature of vaginal cancer

W.A. Tjalma¹, J. Somville²

¹Department of Gynecology and Gynecologic Oncology,

²Department of Orthopedic Surgery, Universitair Ziekenhuis Antwerpen (Belgium)

Summary

Background: Metastatic bone involvement in vaginal carcinoma has not been reported in the literature. **Case:** A 74-year-old woman was referred for a painful fibula to the orthopedic surgeon. A work-up revealed an isolated metastatic bone lesion in the right fibula of a primary squamous carcinoma of the vagina. Rather surprisingly this lesion had been missed during all previously regular clinical gynecological examinations. Palliative therapy including bone resection and radiotherapy of the metastatic lesion were given. **Conclusion:** This case highlights: (1) the unique presentation of a vaginal cancer by pain in the lower leg secondary to a metastasis in the fibula; (2) that a speculum examination can mask a mid-vaginal lesion; (3) the importance of aggressive treatment of a solitary bone metastasis in order to provide effective palliation.

Key words: Vaginal; Bone; Metastasis, Squamous, Cancer.

Introduction

Identifiable bone metastases are rare events in gynecological cancer. However the true incidence is unknown. Apparently low rates may be due to the fact that skeletal metastases generate symptoms mimicking benign conditions. As investigations become more accurate and tumor specific it is possible that these figures are going to rise. Currently the incidence of bone metastases in squamous cell carcinomas of the cervix is 15-29% [1]. Metastases of endometrial and ovarian cancer to the bone have a clinical incidence of respectively 5-6% and 2-4% [2, 3]. Vulvar bone metastases vary between 0.8% to 3.4% [4]. An English literature search with the terms: vaginal cancer, metastases and bone failed to identify any article on bone metastases in vaginal cancer.

Primary vaginal malignancies account only for 1-2% of all gynecological cancers [5, 6]. The majority of vaginal cancer patients present with vaginal discharge (62%) [5]. Less frequent symptoms are positive cytology (16%), tumor mass (13%), pain (4%), dysuria (2%) or incidental symptoms (3%) [5]. Bone metastasis has not been reported as an initial symptom. Seven out of ten patients are diagnosed in early stages (Stage I and II, respectively 49% and 22%); while 29% will be diagnosed in advanced stages (Stage III and IV, respectively 11% and 18%) [5]. These figures suggest that vaginal cancers may be missed at clinical examination. Other factors that may contribute to the relatively late presentation include patient reticence in reporting symptoms and failure to examine the patient vaginally. It is also possible that a standard speculum examination for a cervical smear may hide a vaginal cancer. If during removal of the speculum, visual inspection of the vagina is not performed a lesion lying in the anterior or posterior wall of the vagina may be overlooked.

Vaginal cancers have a tendency to spread into the surrounding tissues by direct infiltration and disseminate widely throughout the vaginal via the 'sub-mucosal' lymphatic plexus rather than by hematogenous pathways. Preoperative examinations routinely do not include a bone scan. FIGO staging is based on clinical examination and not on surgicopathologic findings.

This report describes a case of a bone metastasis in a patient with vaginal carcinoma presenting with pain in the right fibula due to a pathologic fracture.

Case

A 74-year-old woman with a painful swelling in the lower one-third of the right leg of a few weeks duration presented to her primary care physician. Initially this was treated with a non steroidal anti-inflammatory medication. This management gave no improvement. A conventional X-ray was done revealing a bone fracture of the right fibula. Consequently she was referred to an orthopedic surgeon. Past medical history included an infected wound on the right foot four years earlier. One month prior to the bone swelling she had reported blood stained vaginal discharge. The patient was referred to a gynecologist. Clinical examination was recorded to be within normal limits and a cervical smear was reported as negative. Clinical examination by the orthopedic surgeon showed an expanded right lower leg which was very painful on touch. A bone scan revealed an increased uptake in the lower right leg. Additional imaging with magnetic resonance imaging (MRI) scan showed bone metastasis with central necrosis in the distal right fibula. A computerized tomography (CT) guided biopsy was performed and pathological examinations revealed an invasive squamous carcinoma. The gynecological examination was repeated suggesting a vaginal lesion. However, due to the narrow introitus no proper speculum could be placed and thus only a pediatric speculum and no adequate internal examination could be performed. CT revealed a vaginal mass, without any signs of intra-abdominal or retroperitoneal disease. No other metastases were identified. Surgical resection of the bone metastases was planned. A gynecological examination under anesthetic

Revised manuscript accepted for publication June 8, 2010

revealed a circular mid vaginal tumor over a length of 5 cm. After installing a normal size speculum, necrotic tissue could be visualized in the middle of the vagina. The macroscopic appearance of the cervix and the upper vagina were normal. On rectovaginal examination both parametria were involved by spread of the cancer, the left parametrium completely and the right parametrium midway to the pelvic side wall. A biopsy of the cancer was taken and microscopic examination showed a moderate to poorly differentiated squamous cell carcinoma of the vagina.

The distal part of the right fibula except for the last 2 cm was resected and an allograft was installed. Macroscopically the lesion was 6.7 cm in diameter and microscopically represented metastasis of a poorly differentiated squamous carcinoma, compatible with the vaginal tumor. The cancer was staged as a vaginal cancer FIGO Stage IV. An uneventful recovery was made. Further management consisted of radiotherapy to the right lower leg. Systemic treatments were discussed including biphosphates, after consulting the patient no further therapy was given. During a period of two months the patient had a minimal of pain and according to herself a reasonable quality of life. Thereafter she presented with a shortness of breath and a chest X-ray revealed multiple small lesions suggestive of metastases. These lesions were not present at the initial chest X-ray. Supporting palliative therapy was given. The patient slowly deteriorated over a period of two months. She succumbed six months after the initial diagnosis.

Discussion

Osseous metastases as a presenting symptom in gynecological tumors is extremely rare. In Table 1 the percentage of bone metastases in gynecological tumors are shown. If bone metastases do occur then the vertebrae are the most common site and the pelvic bones, femur, ribs, sternum, mandibula and skull are the less frequent sites. Combined autopsy and radiological series showed that the incidence of bony lesions in the bones of the forearm, hands, legs and feet vary between 1-4%, and none of them was a single lesion [2, 7]. The most common primary tumor site for metastatic bone lesions in the leg and foot are the colon, rectum, lung and kidney [8].

The present case is exceptional and peculiar in various ways. First of all this is the first report of bone metastasis in vaginal cancer. Secondly it was a single bony lesion and thirdly it was in a fibula.

There are two possible factors that could explain why bone metastases are a rare event in gynecological cancers. First of all gynecological tumors in general tend to spread locally and through the lymphatic system rather than by the hematogenous route. Only the latter route can cause spread to the limbs [9]. An explanation for bone metastasis in the lower legs could be the retrograde venous flow of tumor emboli [9], which is similar to skin metastasis development [10]. The second important fact that could contribute to the low incidence is the fact that skeletal metastases can be asymptomatic and only detected during autopsy or imaging [2].

Every new symptom in a cancer patient should be approached with care [11]. Bone pain in a cancer patient is a metastatic lesion until proven otherwise. Further examinations including plain X-ray or whole body bone

Table 1. — *The percentage of bone metastases in gynecological tumors.*

Vulva cancer: 0.8-3.4%
Vagina: the present report is the first case
Cervical cancer: 0.8-23%
Uterine cancer: 5-6%
Ovarian - and tubal cancer: 1-4%

scan should be done immediately in order to deny or confirm a lesion. CT and/or MRI are only to be used once the diagnosis is established in order to describe the extent of tumor involvement in soft tissue and bone marrow. It is tempting to suggest that skeletal pain is due to more general conditions like inflammation, trauma or arthritis. It is therefore important, as stated previously, that technical examination are performed in the follow-up of gynecological cancer patients based on symptoms and not on routine examinations [12].

The fact that vaginal and vulval cancers still have a delay in diagnosis of several months to years is intriguing. These cancers generally have clear symptoms and can be seen by the naked eye. Clinical gynecological examination should include a direct visualization of the cervix together with the entire vagina and an internal examination.

In general, distant metastases have to be regarded as an ominous sign [10]. The average duration of survival for patients with bone metastases is ten months or less [2, 3]. Decisions regarding therapeutic or palliative management can only be made if the complete extent of the disease is known. Bone metastases are often just a tip of the iceberg and in case of widespread disease palliative therapy with symptom management is the rule. In the literature there are only a handful of reports of single bone metastasis in patients with gynecological malignancies [13, 14], some having long-term survival [15, 16]. However this is probably an overestimation in that many clinicians will only report on a success story of long-term survival and leave the short-term survival unknown. Nevertheless, aggressive treatment in a patient with a good clinical condition and a single bone metastasis should be considered.

Palliative treatment with radiation alone or in combination with orthopedic surgery is very effective in controlling symptoms. Furthermore biphosphonates should be considered to prevent or reduce skeletal complications [16, 17]. In animal models of bone metastases early biphosphonate administration followed by radiation led to improved remineralization and restabilization of osteolytic lesions [18]. The role of systemic treatment for symptomatic bone metastases is not well described.

The presence of bone metastases in vaginal cancer has not been reported previously. Based on the relatively rareness of vaginal cancer and the fact that this is the first report of bone metastasis in vaginal cancer patient, one can not recommend the use of a bone scan in the preoperative setting nor in follow-up. It is important to consider

osseous metastases as a possible diagnosis in a patient with skeletal pain not responding to conservative measures in general and in cancer patients in particular.

References

- [1] Fischer F., Kuhl M., Feek U., Rominger M., Schipper M.L., Hadji P. *et al.*: "Bone metastases in vulvar cancer: a rare metastatic pattern". *Int. J. Gynecol. Cancer*, 2005, 15, 1173.
- [2] Abdul-Karim F.W., Kida M., Wentz W.B., Carter J.R., Sorensen K., Macfee M. *et al.*: "Bone metastasis from gynecologic carcinomas: a clinico-pathologic study". *Gynecol. Oncol.*, 1990, 39, 108.
- [3] Chang K.H., Lee J.P., Ryu H.S.: "Rare case of stage IA epithelial ovarian cancer with bone as the first site of recurrent metastasis". *Int. J. Gynecol. Cancer*, 2006, 16, 322.
- [4] Ferrandina G., Testa A.C., Zannoni G.F., Poerio A., Scambia G.: "Skull metastasis in primary vulvar adenocarcinoma of the Bartholin's gland: a case report". *Gynecol. Oncol.*, 2005, 98, 322.
- [5] Tjalma W.A., Monaghan J.M., de Barros Lopes A., Naik R., Nordin A.J., Weyler J.J.: "The role of surgery in invasive squamous carcinoma of the vagina". *Gynecol. Oncol.*, 2001, 81, 360.
- [6] Tjalma W.A., Monaghan J.M., de Barros Lopes A., Naik R., Nordin A.: "Primary vaginal melanoma and long-term survivors". *Eur. J. Gynaecol. Oncol.*, 2001, 22, 20.
- [7] Ali Z.A., Wimhurst J.A., Ali A.A., Tempest M.E., Edwards D.J.: "Endometrial cancer metastasis presenting as a grossly swollen toe". *Int. J. Gynecol. Cancer*, 2003, 13, 909.
- [8] Brufman G., Krasnokuki D., Biran S.: "Metastatic bone involvement in gynecological malignancies". *Radiol. Clin.*, 1978, 47, 456.
- [9] Libson E., Bloom R.A., Husband J.E., Stoker D.J.: "Metastatic tumours of bones of the hand and foot. A comparative review and report of 43 additional cases". *Skeletal Radiol.*, 1987, 16, 387.
- [10] Tjalma W.A., Watty K.: "Skin metastases from vulvar cancer: a fatal event". *Gynecol. Oncol.*, 2003, 89, 185.
- [11] Tjalma W.A., van Dam P.A., Makar A.P., Cruickshank D.J.: "The clinical value and the cost-effectiveness of follow-up in endometrial cancer patients". *Int. J. Gynecol. Cancer*, 2004, 14, 931.
- [12] Tjalma W.A., van Dam P.A., Makar A.P., Cruickshank D.J.: "Routine follow-up in cancer patients appears to be a precious ritual". *Int. J. Gynecol. Cancer*, 2005, 15, 933.
- [13] Dosoretz D.E., Orr J.W. Jr, Salenius S.A., Orr P.F.: "Mandibular metastasis in a patient with endometrial cancer". *Gynecol. Oncol.*, 1999, 72, 243.
- [14] Manolitsas T.P., Fowler J.M., Gahbauer R.A., Gupta N.: "Pain in the foot: calcaneal metastasis as the presenting feature of endometrial cancer". *Obstet. Gynecol.*, 2002, 100, 1067.
- [15] Cooper J.K., Wong F.L., Swenerton K.D.: "Endometrial adenocarcinoma presenting as an isolated calcaneal metastasis. A rare entity with good prognosis". *Cancer*, 1994, 73, 2779.
- [16] Tjalma W.A., Buytaert P.M., Berneman Z.N.: "Reduction of visible bone metastases by clodronate therapy in breast cancer". *Eur. J. Gynaecol. Oncol.*, 2001, 22, 215.
- [17] Osanai T., Tsuchiya T., Ogino T., Nakahara K.: "Long-term prevention of skeletal complications by pamidronate in a patient with bone metastasis from endometrial carcinoma: a case report". *Gynecol. Oncol.*, 2006, 100, 195.
- [18] Krempien R., Huber P.E., Harms W., Treiber M., Wannenmacher M., Krempien B.: "Combination of early bisphosphonate administration and irradiation leads to improved remineralization and restabilization of osteolytic bone metastases in an animal tumor model". *Cancer*, 2003, 98, 1318.

Address reprint requests to:
 W.A. TJALMA, M.D., Ph.D.
 Department of Gynecology
 and Gynecologic Oncology,
 University Hospital Antwerpen,
 Edegem (Belgium)
 e-mail: wiebren.tjalma@uza.be