Muscle metastasis of low-grade endometrial carcinoma seven years after diagnosis: A case report

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Summary

Background: Early-stage low-grade endometrial carcinoma has an excellent prognosis. In few cases local relapse and/or distant metastases can occur. We report the muscle as an unusual site of metastasis. *Case:* A 69-year-old woman underwent surgery for FIGO Stage IA, grade 1 endometrioid adenocarcinoma of the endometrium. After four years she had local relapse without response to chemoradiation, requiring pelvic exanteration. Three years later she was diagnosed with a deltoid muscle metastasis confirmed histologically and bone metastases. After failing hormone therapy, chemotherapy was administered. She died eight months after diagnosis of the bone and muscle metastases. *Conclusion:* Low-risk endometrial carcinoma can behave like a high-risk group. Furthermore, this report describes, to our knowledge, the first case of endometrial carcinoma muscle metastasis.

Key words: Endometrial cancer; Early stage; Muscle metastasis; Bone metastases.

Introduction

Endometrial carcinoma is the most common gynaecological cancer. The majority of cases are diagnosed at an early stage, FIGO Stage I, with a 5-year overall survival of 80%-90% [1]. Pelvic recurrence, although relatively uncommon, is usually associated with distant metastases involving the liver and lung. Bone metastases are infrequent but there are a few cases reported in the literature [2].

We report an unusual evolution of Stage IAGI endometrial cancer. The main unexpected feature was the diagnosis of deltoid muscle metastasis. As far as we know, no previous case of muscle metastasis of endometrial cancer has been reported.

Case Report

A 69-year-old woman underwent surgery for endometrial carcinoma with total abdominal hysterectomy and bilateral salpingo-oophorectomy. The final diagnosis was FIGO Stage IA, grade 1 endometrioid adenocarcinoma.

Four years after surgery, the patient presented with vaginal bleeding. A computed tomography (CT) scan showed a large mass infiltrating the floor of the vagina and sigma. Following diagnosis of pelvic recurrence, she was moved to another institution where she received treatment with concurrent chemoradiotherapy. External pelvic radiation was delivered to the pelvis with a total dose of 45 Gy in 25 fractions. Two courses of chemotherapy based on cisplatin (75 mg/m^2) plus paclitaxel (135 mg/m^2) were administered on the first and last day of radiation therapy. A CT scan performed after treatment showed a minor response, so total pelvic exenteration was performed. The vagina, the sigma, the bladder and the surrounding soft tissues were infiltrated by moderate, grade 2, endometrial adenocarcinoma.

Three years later, the patient came to our office complaining of swelling of her left upper arm. On physical examination, there was a fixed mass measuring 4 x 4 cm in diameter. Magnetic resonance imaging (MRI) showed a large 4 cm mass in the deltoid muscle (Figure 1). A bone scan revealed multiple metastases in the spine and a body CT scan was unremarkable. A muscle biopsy was performed. The pathology showed adenocarcinoma that resembled endometrioid adenocarcinoma positive for estrogen and progesterone receptors (ER/PR), CK7 positive and CK20 negative (Figure 2). Since the tumour had positive hormonal receptors, we decided to start treatment with progestins. After three months of hormonal therapy, we documented disease progression with spine pain getting worse and new bone lesions in her bone scan. A course of palliative radiation was given to the painful bone metastatic sites. Hormonal therapy was stopped and the patient was put on chemotherapy with paclitaxel plus carboplatin. After two courses of treatment, the patient was hospitalized due to dyspnea. A large pleural effusion and liver metastases were documented. Unfortunately, the patient died two months later.

Discussion

The large majority of Stage I endometrial cancer cases without poor prognostic factors have a 5-year overall survival ≥ 90% [1]. However, approximately 11% of endometrial cancer patients develop a recurrence [3]. The distribution of recurrent disease is varied, with some studies demonstrating local recurrence in 50% of patients and others reporting that the majority of recurrences are distant or multifocal [4, 5]. A small number of women will develop an isolated central pelvic recurrence. The role of surgery in this group of women is undefined. Nevertheless, in those women who have previously received radiation therapy or who have failed to respond to radiation, pelvic exenteration may represent the only potentially curative option with overall 5-year survival rates of approximately 20%-40% [6, 7].

Although haematogenous metastases are infrequent in endometrial cancer, the incidence may be higher in patients with pelvic failure. In these cases, metastases to the lung and liver may be observed. Bone metastases are

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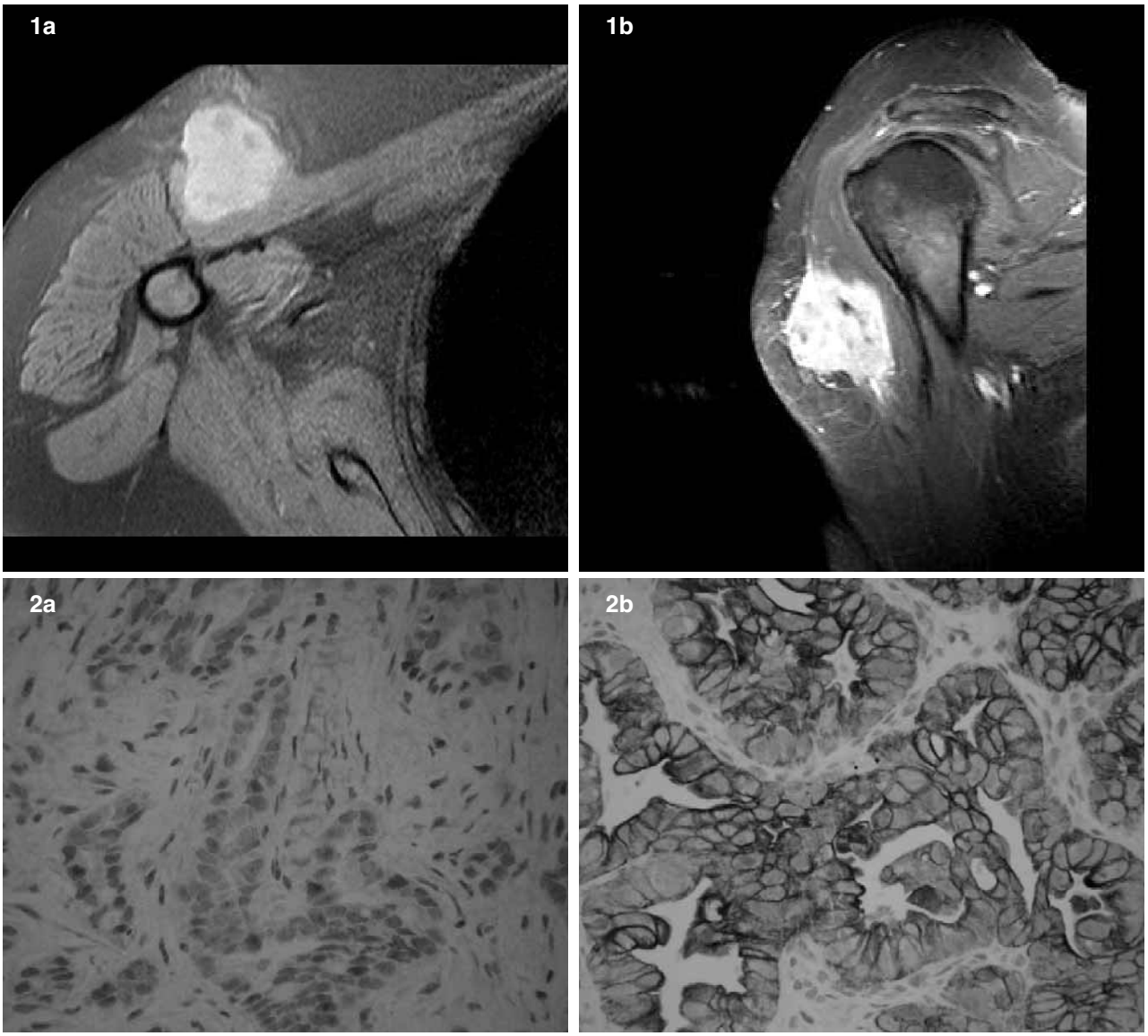

Figure 1. — MRI of the deltoid muscle mass: saggital section (1a) and cross section (1b).
Figure 2. — Immunohistochemistry of the deltoid muscle biopsy confirming an adenocarcinoma of gynaecologic origin: CK20 negative (2a) and CK7 positive (2b).

relatively uncommon with a reported incidence from 2% to 6% [2].

Our case is interesting for different reasons. Firstly, spine metastases were diagnosed three years after the pelvic exenteration and seven years after initial diagnosis. The average length reported in the literature is three years from initial diagnoses. Secondly, an unexpected lesion, deltoid muscle metastasis, was discovered at the same time.

Endometrial cancer usually disseminates by direct invasion or via the lymphatic route. Dissemination to the vertebrae occurs via Batson's plexus and the vertebral venous plexus. In our case, taking into account the simultaneous metastases to multiples sites in the spine and in the deltoid muscle must be the result of bloodstream dissemination [8].

Once endometrial cancer has recurred, the treatment options are quite limited, either hormonal therapy or chemotherapy. The majority of studies of hormonotherapy employing oral progestins, including medroxyprogesterone acetate (MPA) and megestrol acetate, have shown response rates of 11%-56%. Although the majority of responses are relatively short, some patients remain free from disease progression for more than 12 months. The relative lack of side-effects of progestins compared to chemotherapy initially led to their widespread use in unselected patient populations. In recent years, their use has often been confined to the better differentiated cases, which usually correspond with those demonstrating positive hormone receptors [9].

In our case, the metastatic disease was confined to bone

and muscle, but the tumour was moderately differentiated and ER/PR positive so we started MPA. Unfortunately, it did not work and we had to switch to carboplatin (area under of the curve of 6) and paclitaxel (175 mg/m^2) (CP). Results of second-line chemotherapy are generally poor, and only taxanes have response rates greater than 20% in this setting. The most active regimen tested in randomised trials to date is the triplet of cisplatin (50 mg/m^2), doxorubicin (45 mg/m^2), and paclitaxel (160 mg/m^2; TAP). This regimen produces a high percentage of grade 3-4 haematology toxicity and requires granulocyte growth factor support [10]. CP is widely used because of its relative ease of administration and the results from phase II studies [11]. The TAP regimen is being compared with CP in a large Gynecologic Oncology Group trial (GOG #209) which includes women with Stage III or IV disease or recurrent endometrial carcinoma.

This case illustrates that Stage IA well differentiated endometrial cancer can relapse as high grade tumours even in unusual sites. The prognosis of metastatic endometrial cancer remains poor with our current therapy. The emerging results with drugs targeting the PI3K-PTEN-AKT pathway are promising [12, 13].

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