

Breast cancer metastases to uterine leiomyomas – a clinical and patomorphological analysis of two cases

Paweł Blecharz¹, Joanna Szpor², Kazimierz Karolewski¹, Janusz Ryś²

The phenomenon of one tumor metastasising to another one is extremely rare. Breast cancer metastases to the female genital system are relatively common, but the diagnosis of metastases to uterine leiomyomas remains a casuistry. The histological type of these metastases is usually hormono-dependent, lobular breast carcinoma. This clinical finding is generally accidentally made during histopathological examination.

Przerzuty raka piersi do mięśniaków macicy – analiza kliniczna i patomorfologiczna dwóch przypadków

Zjawisko przerzutowania jednego nowotworu do drugiego jest bardzo rzadko stwierdzanym przypadkiem. Przerzuty raka sutka do kobiecych narządów płciowych są stosunkowo częste, jednak umiejscowienie przerzutu w mięśniaku macicy pozostaje dotychczas wyłącznie kazuistyką. Najczęściej stwierdzanym typem histologicznym tego rodzaju przerzutów jest hormonozależny, zrazikowy rak gruczołu piersiowego. Obecność komórek raka, typowych dla gruczołu piersiowego, w tkance mięśniaka macicy stwierdzana jest z reguły przypadkowo, podczas badania histopatologicznego materiału operacyjnego.

Key words: breast cancer, uterine leiomyoma, metastasis

Słowa kluczowe: rak piersi, mięśniaki macicy, przerzut

The phenomenon of one neoplasm metastasising to another is an extreme clinical rarity. Although breast cancer metastases to the female genital organs are common, yet their localization within uterine leiomyomas is purely casuistic. In case of this entity the most common histopathological type is the hormono-dependant lobular type of breast cancer. The presence of breast cancer cells within the myoma is usually a chance finding made during routine histopathological examination of the surgical specimen.

Introduction

Breast cancer is the most common malignancy in women, and remains the second most common cause of cancer death of female patients. Poland is a country in which breast cancer incidence is estimated to be moderate – there are approx. 11000 new cases and 5000 deaths noted *per annum* [1].

Breast cancer metastasises mainly to the lungs, the bones, the liver, the skin and the brain. Ductal carcinoma accounts for some 70-75% of invasive cancer of the breast, while lobular carcinoma for about 5-20% of cases.

Studies have shown that lobular carcinoma is more apt to metastasise to the genital organs, especially if it is found to have hormone receptors [2]. Most metastases of extragenital tumours (incl. breast cancer) to the female genital organs locate within the ovaries and the vagina, being rare within the uterus. The most common primary site of these metastases is the gastrointestinal tract [3].

Metastases located in the uterus usually infiltrate its entire wall. Opinions vary as to whether the more common site of these metastases is the endometrium [4] or the myometrium [5]. Sole endometrial infiltration, with free myometrium, is rare [4]. The most common clinical symptom is metrorrhagia. Diagnosis bases upon endometrial biopsy or excochleation of the uterine cavity. If infiltration is limited to the uterus one may assume that the tumour metastasised along the blood vessels. If the initial metastatic site was within the ovaries uterine involvement occurred probably due to local reversed dissemination via the lymphatic drainage [2].

It is difficult to state whether the uterine tumour is primary or metastatic, especially if the patient had been treated with tamoxifen [6]. Although most malignancies are aggressive, yet their dissemination into another neoplasm is a very rare clinical oddity. Literature reports concerning the presence of breast cancer metastases within uterine myomas are very rare. The aim of this

Department of Gynecologic Oncology
Maria Skłodowska-Curie Memorial Cancer Center
and Institute of Oncology, Kraków Branch, Poland

paper is to present two cases of such metastases, both derived from the material of the Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology in Cracow.

Material

Case 1

A 46-year old woman was found to have, both on examination and in mammography scans, isolated tumours of approx. 1 cm in diameter in both breasts. The tumors were suspected to be malignant. The patient underwent radical mastectomy *modo* Patey (left breast) and synchronous lumpectomy of the tumour of the right breast. On histopathological examination of the left breast specimen a tumour of 1 cm in size was found on the verge of the two upper quadrants. It was pronounced to be infiltrating lobular carcinoma with an additional "*in situ*" component. The cancer cells contained a mucous substance stained by Mayer's mucicarmine dye (Figure 1 – insert). Immunohistochemical examination has shown the cells to possess estrogen and progesterone receptors with concomitant negative reaction to E-cadherin (Table I). Apart from this tumour microscopic foci of cancer were also found within the two external quadrants of the left breast and in the vicinity of the nipple. 9 out of the 13 examined lymphnodes were found to be metastatic, with extracapsular extension.

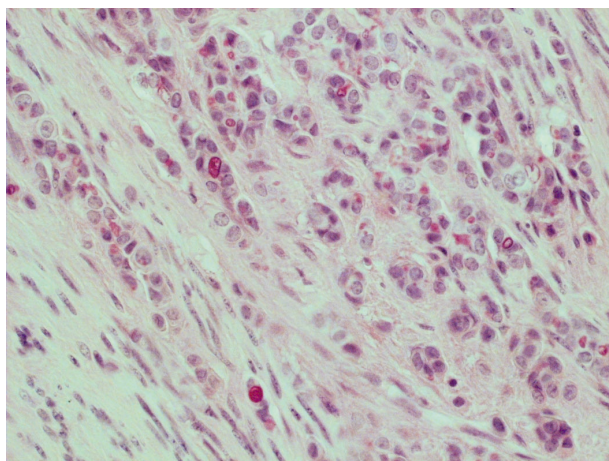


Figure 1 – insert

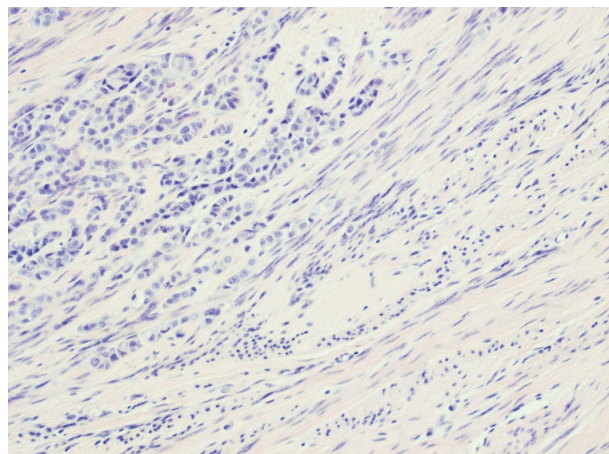


Figure 1. Focus of lobular carcinoma within a leiomyoma of the uterine corpus. HE stained. Inset – staining for mucus with Mayer's mucicarmine

Table I. Results of immunohistochemical analyses of assorted markers and of staining for mucus

Examined tumour (Specimen No.)	Mucicarmine	CK 7	CK 19	ER	PgR	E-cadherin
Patient 1						
Tumour of left breast (256905)	+	+	+	+	+	-
Tumour of right breast (256906)	+	+	+	+	+	-
Carcinoma within leiomyoma (269772)	-	+	+	+	+	-
Patient 2						
Specimen from tumour of right breast (236442)	+	+	+	+	+	+
Carcinoma within leiomyoma (272503)	+	+	+	+	-	+
Carcinoma of uterine cervix (272505)	-	+	+	-	-	+

Abbreviations: CK 7 – cytokeratine 7, CK 19 – cytokeratine 19, ER – estrogen receptor, PgR – progesterone receptor, (+) – positive reaction, (-) – negative reaction

The material obtained from the right breast was found to contain intralobular carcinoma, therefore mastectomy *modo* Patey was also performed on the right breast. Next, the patient was administered 6 courses of chemotherapy according to the ADR + CTX + 5FU regime.

On gynecological examination the uterus was found to be significantly enlarged. Ultrasonography of the genital organs revealed an irregular mass projecting over the right adnexa, which corresponded to myomatous masses. Hysterectomy and adnexectomy was performed at the Clinic of Gynaecological Oncology of the Maria Skłodowska-Curie Memorial Cancer Centre and Institute of Oncology in Cracow. Within the uterus there were numerous tumours histologically pronounced as leiomyomas, however in one of them we discerned a focus of lobular carcinoma (Figure 1). On examination its cells were estrogen receptor positive (Figure 2) and progesterone receptor and cadherin E negative (Table I).

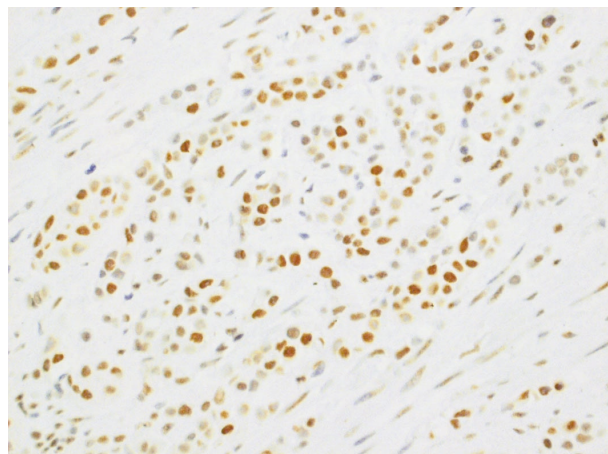


Figure 2. Lobular cancer tissue within a leiomyoma of the uterine corpus. Positive immunohistochemical reaction for the presence of estrogen receptors

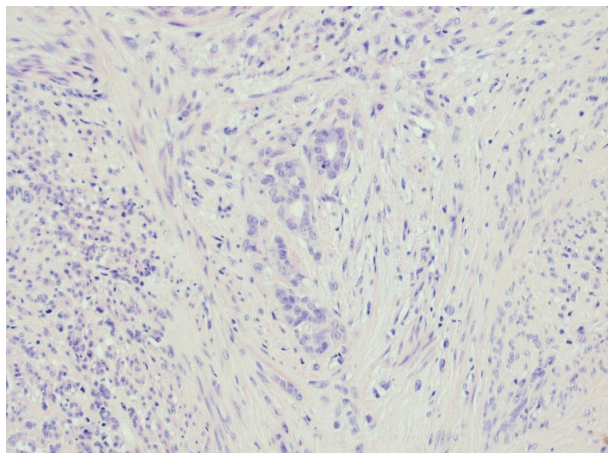


Figure 3. Focus of ductal carcinoma within a leiomyoma of the uterine corpus. HE stained

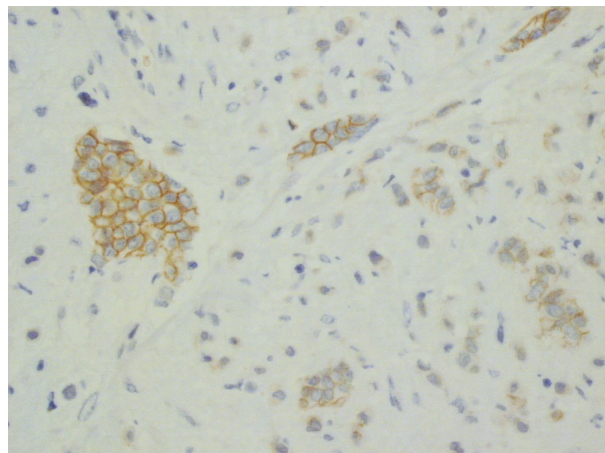


Figure 4. Foci of ductal carcinoma within a leiomyoma of the uterine corpus. Positive immunohistochemical reaction for the presence of E-cadherin

Tamoxifen therapy was initiated and the patient remained under careful follow-up of the Outpatient Clinic both the Clinic of Gynaecological Oncology and the Clinic of Chemotherapy. 16 months after gynaecological surgery the patient was found to have bone metastases (incl. the vertebrae). She was administered aromatase inhibitors and biphosphonians and underwent palliative radiotherapy of the thoracic and lumbal vertebrae. At present, 43 months after the initial diagnosis, the patient is alive, with symptoms of an active malignant process.

Case 2

A 61-year old woman reported with an ulcerated tumour of the right breast and palpable axillary nodes. On histopathological examination we found foci of infiltrating ductal carcinoma. The cancer cells were characterized by a positive reaction identifying intracytoplasmatic mucus (mucicarmine dye); estrogen and progesterone receptor positive and cadherin E positive (Table I)

Due to the initial diagnosis (cancer the right breast with lung metastases) the patient was referred for chemotherapy, of which received 7 courses according to the NAV+CTX+5FU regime. She was additionally treated with tamoxifene. We achieved complete local regression and complete regression of the metastases. The patient was followed-up at the Outpatient Clinic of the Clinic of Chemotherapy. For 37 months she showed no symptoms of cancer. Due to irregular metrorrhagia she underwent abdominal ultrasonography, which revealed an enlarged, probably myomatous, uterus. After the completion of chemotherapy the patient underwent excochleation of the uterine cavity, which revealed the presence of poorly-differentiated carcinoma planoepitheliale. Hysterectomy and adnexectomy was performed. Macroscopically, within the body of the uterus, there were numerous myoma-like tumours, while in the vicinity of the external orifice of the uterus there was a brittle papillary tumour. Microscopically one of the myomas was found to contain a focus of highly differentiated ductal carcinoma (Figure 3). Its cells were estrogen receptor and E-cadherin positive (Figure 4, Table I). Histologically the cervical malignancy was found to be *carcinoma transitionale*. Its cells were both mucus negative and hormone receptor negative, which enabled us to differentiate it from the breast cancer metastasis to the uterine myoma.

Due to the diagnosis of dissemination we initiated treatment with aromatase inhibitors. The patient remains under close scrutiny of the Outpatient Clinics of the Clinic of Gynaecological Oncology and of the Clinic of Chemotherapy with no signs of progression.

Discussion and conclusions

Autopsies have shown that breast cancer metastases to the female genital organs are most common in the ovaries (42%), and definitely more rare within the uterus (8%) [7]. Weingold and Boltuch [8], having analysed 150 patients with extragenital malignancies metastasising to the pelvis, have found that only in 6 cases the metastases were found in the leiomyomas. In 2 of these cases the primary site was breast cancer. Literature data shows that uterine metastases from breast cancer are most common in case of hormono-dependent lobular carcinoma [5, 9-11]. Both our patients also had estrogen and progesterone receptor positive breast tumours (Table I). As for the metastases – in the 1st case (bilateral breast cancer) the metastatic cells showed the same hormonal expression, while in the 2nd case the metastatic cells had a different phenotype (ER+PR-). Metastases of breast cancer to uterine leiomyomas are most common in the case hormono-dependant tumours, probably because the development of both these malignancies arises from an excessive level of estrogens inadequately balanced by progesterone.

According to literature reports uterine metastases of breast cancer appear mainly as lobular carcinoma. Lobular carcinoma is approximately three times less common than ductal carcinoma. Therefore, one may presume that its metastases to the uterine corpus or to uterine leiomyomas are caused by a specific mechanism or brought on by cancer cell characteristics. When analyzing literature reports on breast cancers metastasising to the uterus one finds that the diagnosis of the histological type of breast cancer had been made without any additional laboratory investigations – such as immuohistochemical reactions determining the presence of E-cadherin (positive membrane reaction in ductal carcinomas and negative in lobular carcinomas – see Table I). This last test is particularly valuable for the differentiation of lobular and poorly-differentiated ductal carcinoma with a minimal tendency towards tubule

development. In view of this one may assume that in the cases described in literature lobular carcinoma was in fact less common.

In view of the relatively high frequency of myomal metastases of breast cancer [7] one cannot fail to wonder why such cases are not reported more often. It is likely that the post-surgical or autopsy specimens of patients with breast cancer and uterine myomas are not analysed carefully. Therefore, from the histopathologists' point of view, it would be advisory to perform more detailed histological examinations of leiomyoma specimens obtained from breast cancer patients. The examination should include numerous cross-sections of each specimen so as not to miss small foci of cells typical for breast cancer [12-14].

Pawel Blecharz MD

Department of Gynecologic Oncology
 Maria Skłodowska-Curie Memorial Cancer Center
 and Institute of Oncology, Kraków Branch
 ul. Garncarska 11, 31-115 Kraków, Polska
 e-mail: pawel.blecharz@interia.pl

References

1. Krzakowski M. et al. Onkologia kliniczna. In: *Rak piersi*. Pieńkowski T. (ed.). 1st edition. Warszawa: Borgis Wydawnictwo Medyczne; 2001, 87-8.
2. Dessole S, Cherchi PL, Ruiu GA et al. Uterine metastases from breast cancer in a patient under tamoxifen therapy. Case report. *Eur J Oncol* 1999; 5-6: 416-7.
3. Mazur MT, Hsueh S, Gersell DJ. Metastases to the female genital tract: analysis of 325 cases. *Cancer* 1984; 53: 1978-84.
4. Taxi JB, Trujillo YP. Breast cancer metastatic to the uterus. Clinical manifestations of a rare event. *Arch Pathol Lab Med* 1994; 118: 819-21.
5. Le Bouedec G, de Latour M, Kauffmann P et al. Uterine metastases originating from breast cancer. Apropos of 12 cases. *Arch Anat Cytol Pathol* 1993; 41: 140-4.
6. Martinez-Montero I, Dominguez-Cunchillos F, Maruzabal JC et al. Uterine metastases from breast cancer. *Acta Obstet Gynecol Scand* 1999; 78: 165-7.
7. Abrams HL, Spiro R, Goldstein N. Metastases in carcinoma: Analysis of 1000 autopsied cases. *Cancer* 1950; 3: 74-85.
8. Weingold AB, Boltuch SM. Extragenital metastases to the uterus. *Am J Obstet Gynecol* 1961; 82: 1267-72.
9. Kemp B, Schroder W, Hermann A et al. Uterine metastasis of invasive lobular breast carcinoma. Case report and review of the literature with reference to differential diagnostic problems and clinical consequences. *Zentralbl Gynakol* 1997; 119: 500-2.
10. Mohseni H, Truong P, Hadjseyd M et al. Uterine and ovarian metastases 28 years after the discovery of breast cancer. *Presse Med* 2003 Jan 18; 32: 67-9.
11. Le Bouedec G, Kauffmann P, De Latour M et al. Uterine metastasis of breast cancer. Report of 8 cases. *J Gynecol Obstet Biol Reprod (Paris)* 1991; 20: 349-54.
12. Beattie GJ, Duncan AJ, Paterson AJ et al. Case Report. Breast Carcinoma Metastatic to Uterine Leiomyoma. *Gynecologic Oncology* 1993; 51: 255-7.
13. Liebmann RD, Jones KD, Hamid R et al. Fortuitous diagnosis in a uterine leiomyoma of metastatic carcinoma of the breast. *Histopathology* 1998; 32: 577-8.
14. Banooni F, Labes J, Goodman PA. Uterine leiomyoma containing metastatic breast carcinoma. *Am J Obstet Gynecol* 1971; October 1: 427-30.

Paper received: 14 May 2003

Accepted: 12 February 2004