Observational Study

Medicine®

OPEN

Skin metastases in epithelial ovarian and fallopian tube carcinoma

Isao Otsuka, MD, PhD*, Takuto Matsuura, MD

Abstract

This study aimed to investigate the clinical features and outcomes of skin metastasis in ovarian and fallopian tube carcinomas.

We studied patients with epithelial ovarian or fallopian tube carcinoma who developed skin metastasis from 2001 through 2012, and were also treated with chemotherapy and/or surgery.

Skin metastases were classified as umbilical metastasis (Sister Joseph nodule [SJN]) and nonumbilical metastasis. Patients who developed skin metastases at paracentesis sites were excluded.

Of the 206 patients treated, 12 (5.8%) developed skin metastasis: 7 developed SJN, and 5 developed nonumbilical metastasis. Six patients had serous carcinoma, 3 had clear cell carcinoma, 2 had endometrioid carcinoma, and 1 had adenocarcinoma. Four patients out of the 7 who developed SJN had skin metastasis at initial diagnosis, and all 4 patients had SJN with concomitant peritoneal dissemination. Of the 4 patients, 3 received chemotherapy, and their survival ranged from 22 to 42 months. Of the 7 patients who developed SJN, 3 patients with stage IIIC disease developed an SJN at recurrence and were treated with surgery and/or chemotherapy. Their survival duration after recurrence ranged from 26 to 43+ months. Five patients developed nonumbilical metastases 3 to 53 months (median 34 months) after initial diagnosis: 3 cases occurred in incisional scars of primary surgery, and 2 in subcutaneous metastasis in the other sites. Survival after recurrence ranged from 56 to 140+ months in 3 patients with incisional scar recurrence, and it was 5 months in 2 other patients.

Sister Joseph nodule developed only in patients with peritoneal dissemination, and most patients with SJN survived for >24 months. Nonumbilical metastases occurring in incisional scars of primary surgery may carry a favorable prognosis.

Abbreviations: FDG = 18F-fluorodeoxyglucose, PET/CT = positron-emission tomography/computed tomography, SJN = Sister (Mary) Joseph nodule.

Keywords: ovarian carcinoma, fallopian tube carcinoma, skin metastasis, umbilical metastasis

1. Introduction

Ovarian carcinoma is a gynecologic malignancy with the highest mortality rate. It usually spreads directly to the peritoneal cavity, but may also metastasize through the lymphatic and hematogenous routes. Distant metastases may be noted at the time of ovarian cancer diagnosis or may occur during the course of the disease, and the most common sites are the pleura, liver, lungs, and lymph nodes.[1] Skin metastases are rare, occurring in 0.9% to 4% of patients.[1–3] Ovarian carcinomas were the primary tumors in 3.3% to 4% of women with skin metastasis.[4,5]

Skin metastases are classified as metastatic umbilical tumors, which are known as Sister (Mary) Joseph nodule (SJN), and nonumbilical metastasis. The prognosis of patients with skin metastasis has been shown to be poor: in previous studies, the median survival of patients with skin metastasis from ovarian cancer was 12 months.[1,6] However, in these studies, skin metastases at presentation and those developed after initial therapy were not analyzed separately. In addition, many patients did not appear to receive a current standard chemotherapeutic regimen, that is, platinum/taxane chemotherapy. Thus, survival data on patients with skin metastases who received platinum-based chemotherapy have not been sufficiently studied. In the present study, we retrospectively studied patients with epithelial ovarian or fallopian tube carcinoma to investigate the clinical features and outcomes of patients who developed skin metastases and were treated with platinum/taxane chemotherapy and/or surgery.

2. Patients and methods

A consecutive series of patients with epithelial ovarian or fallopian tube carcinoma treated at the Department of Gynecology, Kameda Medical Center, from January 2001 through December 2012, were identified from the tumor registry, and their medical records were reviewed to obtain clinical and pathological data. Of these patients, those who developed skin metastases at the time of diagnosis or during the course of the disease were included in this study. Patients with skin metastases found at autopsy, patients with borderline tumors, and patients who did not undergo treatment for cancer were excluded from this study. Patients who developed skin lesions at the site of

Editor: Laszlo Geza Boros.

The authors report no conflicts of interest.

Department of Gynecology, Kameda Medical Center, 929 Higashi-cho, Kamogawa, Chiba, Japan.

* Correspondence: Isao Otsuka, Kameda Medical Center, Kamogawa, Chiba, Japan (e-mail: otsuka.isao@kameda.jp).

Medicine (2017) 96:33(e7798)

Received: 9 May 2017 / Received in final form: 19 June 2017 / Accepted: 21 June 2017

http://dx.doi.org/10.1097/MD.0000000000007798

Table 1

Clinical features of skin metastases at initial diagnosis.

Case no.	Type of skin met	Age at diagnosis, y	Stage	Histotype	Symptoms related to skin met	Metastases concomitant to skin met	Treatment for skin met	Survival after skin met, mos	Status
1	SJN	72	IVB	Serous, G1	None	PeritD	Surgery, Chemo (TC)	27	DOD
2	SJN	70	IVB	Serous, G3	None	PeritD	Chemo (E, TC)	42	DOD
3	SJN	79	IVB	Endometrioid, G3	None	PeritD, LN (paraaortic)	Surgery*	7	DOD
4	SJN	61	IVB	Clear cell	None	PeritD	Surgery, Chemo (TC)	22	DOD

DOD = dead of disease, E = etoposide, LN = lymph nodes, PeritD = peritoneal dissemination, SJN = Sister Joseph nodule, skin met = skin metastasis, TC = paclitaxel/carboplatin.
* Case 3 did not receive chemotherapy because of medical comorbidities and older age.

paracentesis and colostomy were also excluded. This retrospective study was approved by the Institutional Review Board.

In this study, skin metastasis was diagnosed pathologically and radiologically. New skin lesions with an abnormal uptake of 18F-fluorodeoxyglucose (FDG) on integrated positron-emission tomography/computed tomography (PET/CT), and also skin lesions that increased in size during the clinical course, were diagnosed as skin metastases. Clinical and pathological factors examined included age, stage, histotype, the site of metastasis at initial diagnosis, initial treatment, time to skin recurrence, treatment for skin metastasis, and overall survival. We examined skin metastases separately by the site (SJN vs nonumbilical metastasis) and the time at which skin metastasis was noted (skin metastasis at presentation vs skin metastasis as a recurrent or a progressive disease). Differences in age were compared using Student *t* test.

3. Results

During the study period, 206 patients with epithelial ovarian or fallopian tube carcinoma were treated: 191 patients underwent surgery with or without chemotherapy and 15 patients received chemotherapy alone. These 15 patients had pelvic tumors with peritoneal dissemination on imaging studies and elevated serum CA-125 levels (range 127−3851 U/mL), and ovarian cancer was diagnosed with histologic examination of tissue biopsies or cytological examination of ascites fluid.

Of the 206 patients, 12 patients (5.8%) developed skin metastasis. All patients were initially treated at our institution. None of the patients received bevacizumab treatment, partly because bevacizumab use for ovarian cancer was approved in November 2013 in Japan. An SJN developed in 7 patients and nonumbilical metastasis developed in 5 patients. Skin metastasis developed at initial diagnosis in 4 patients (1.9%) and as a recurrent or progressive disease in 8 patients. Patients with skin metastasis at initial diagnosis were significantly older compared with those with skin metastasis as a recurrent or progressive disease (mean age at diagnosis of skin metastasis 71 years vs 57 years; $P = .015$). No significant difference in age was observed between the patients with SJN and those with nonumbilical metastasis (64 vs 58 years; $P = .28$). Six patients had serous carcinoma, 3 had clear cell carcinoma, 2 had endometrioid carcinoma, and 1 had adenocarcinoma.

3.1. SJN

Four patients developed an SJN at initial diagnosis (Table 1), occurring in 17% of the patients with stage IV disease (n = 23). These patients' symptoms were not associated with umbilical tumors. All 4 patients had peritoneal dissemination. Survival time of the 3 patients who received platinum/taxane chemotherapy ranged from 22 to 42 months.

Three patients developed an SJN as a recurrent disease (Fig. 1), and all the 3 patients had stage IIIC disease at initial diagnosis (Table 2). They developed an SJN after more than 2 years of being progression-free, and were treated with surgery and/or chemotherapy. Their survival after recurrence ranged from 26 to more than 43 months.

3.2. Nonumbilical metastasis

Five patients developed nonumbilical metastasis as a recurrent or a progressive disease (Table 2). The time from initial diagnosis to the development of skin metastasis ranged from 3 to 53 months. Nonumbilical metastases developed after abdominal peritoneal dissemination at presentation in 2 patients; however, metastases developed in 3 other patients who did not experience abdominal dissemination. Three patients developed nonumbilical metastases at abdominal incisional scars of primary surgery; these 3 patients survived more than 4 years after skin metastasis. Two other patients developed a subcutaneous nodule as a progressive disease during chemotherapy; both patients died of disease 5 months after the diagnosis of skin metastasis.

4. Discussion

This study indicates that survival of patients with skin metastases may not be as poor as previously reported.[1,6] Patients with SJN at presentation who received current standard chemotherapy survived more than 20 months. Even patients who developed skin metastases as recurrent disease survived more than 4 years when the recurrence developed at incisional scars of primary surgery.

Skin metastasis from epithelial ovarian carcinoma is rare. The incidence of skin metastasis in ovarian carcinoma patients ranged

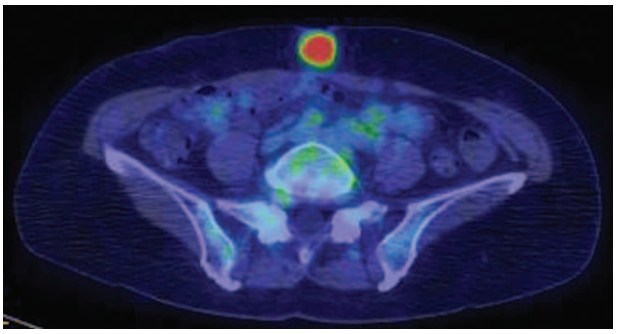

Figure 1. A case of umbilical metastasis (Sister Joseph nodule) (case 5). Axial PET/CT demonstrates abnormal FDG uptake by the umbilical tumor. FDG = 18F-fluorodeoxyglucose, PET/CT = positron-emission tomography/computed tomography.

Table 2

Clinical features of skin recurrences.

Case no.	Type of skin metastasis	Age at initial diagnosis, y	Stage	Histotype	Initial therapy	Time to skin rec, mos	Symptoms related to skin rec	Metastases before/ concomitant with skin rec	Treatment for skin rec	Survival after skin rec, mos	Status
5	SJN	49	IIIC	Endometrioid, G2	Chemo (TC), Surgery	115	Umbilical tumor	Pelvic tumor/none	Surgery	43+	AWD
6	SJN	58	IIIC	Serous, G1	Chemo (TC), Surgery	28	Umbilical tumor	Perit D, LN (inguinal)/PeritD	Chemo (DTX, LPD)	33	DOD
7	SJN	45	IIIC	Serous	Chemo (TC), Surgery	39	Umbilical tumor	PeritD/PeritD	Chemo (TC, CPT-11)	26	DOD
8	Nonumbilical (incision scar)	48	IC1	Clear cell	Surgery, Chemo (MMC+CPT-11)	8	None	None/none	Surgery, RT	140+	NED
9	Nonumbilical (incision scar)	53	IIIA1	Clear cell	Surgery, Chemo (TC)	16	None	LN (axillary, supraclavicular, paraaortic)/brain†	RT, immunotherapy	56+	NED
10	Nonumbilical (incision scar)	54	IIIC	Serous, G2	Surgery, Chemo (TC)	53	Skin tumor	Perit D/ Perit D, adrenal gland	RT, Chemo (DTX, LPD)	56	DOD
11	Nonumbilical (hip, breast)	49	IIC	Serous, G3	Surgery, Chemo (TC)	40	Subcutaneous tumor	Perit D, LN (paraaortic)/LN (mediastinal, paraaortic), muscle, breast	Chemo (TC, CPT-11, LPD)	5	DOD
12	Nonumbilical (anterior abdomen)	72	IVB	Adenoca, G3	Laparotomy, Chemo (TC, DTX)	3	None	LN (axillary, supraclavicular, inguinal, pelvic), PeritD	Chemo (primary therapy continued)	5	DOD

AWD = alive with disease, CPT-11 = irinotecan, DOD = dead of disease, DTX = docetaxel, LN = lymph nodes, LPD = liposomal doxorubicin, MMC = mitomycin-C, NED = no evidence of disease, PeritD = peritoneal dissemination, SJN = Sister Joseph nodule, skin rec = skin recurrence, TC = paclitaxel/carboplatin.

* In case 7, tumor could not be graded due to neoadjuvant chemotherapy.

† Case 9 underwent resection of brain tumor and γ-knife therapy before treatment of skin tumor. Immunotherapy was performed at an outside institution.

from 0.9% to 4% in previous studies in which skin metastases were confirmed by cytology or histology.[1–3] Its incidence was influenced by the chemotherapeutic regimens administered; autopsy data showed that the incidence of skin metastasis in patients who received the current standard chemotherapeutic regimens, such as platinum and taxane, was lower than that in patients who received older chemotherapeutic regimens that are not as effective as current standard regimens (4.3% vs 17.9%).[7] In our study, pathological examination and imaging studies revealed that 5.8% of patients with epithelial ovarian or fallopian tube carcinomas were diagnosed to have skin metastasis, although skin metastases at paracentesis sites were excluded. Skin metastasis at the stage IV disease site occurred in 17% of patients in our study, which was a higher percentage than that found in previous studies (0.91%–3.7%).[8,9] Reasons for this difference are unclear, but may include that Japanese populations are aging, as older women appear to be more likely to develop skin metastasis at presentation. The high rate in our study appears to reflect the high rate of older women living in our medical service area.

In women, ovarian carcinoma is the most common origin of SJN: 42% to 47.7% of women with SJNs had ovarian carcinoma.[10,11] The most significant risk factor of developing an SJN is peritoneal dissemination. In our 7 patients with SJNs, all patients had peritoneal dissemination before or concomitant with their SJN. A review of the literature showed that 21 of 22 (95%) patients with SJNs at presentation experienced peritoneal dissemination (Table 3).[10,12–25] Thus, the vast majority of SJNs appear to develop by direct invasion from the underlying intraperitoneal metastatic tumors. However, lymphatic or

Table 3

Ovarian or fallopian tube carcinoma patients with Sister Joseph nodule at presentation who received chemotherapy.

No.	Author	Age	Histotype	Symptoms related to skin metastasis	Metastases concomitant to skin met	Treatment	Survival, mos	Status
1	Brustman and Seltzer[10]	73	Papillary cystadenoca	Ulcerated, bleeding umbilical mass	PeritD	Surgery, Chemo (CAP-H)	2	DOD
2		59	N/A	N/A	PeritD	Surgery, Chemo (CAP-H)	20	DOD
3	Hashimoto et al[12]	47	Serous, G1	N/A	PeritD	Surgery, Chemo (TC, CTX)	11	NED
4		81	Serous, G2	N/A	PeritD	Surgery, Chemo (Carbo/CTX)	7	NED
5	Kato et al[13]	76	Serous papillary (FT)	Umbilical bleeding	PeritD	Surgery, Chemo (CAP)	5	Alive
6	Haneda et al[14]	74	Serous	Umbilical mass	PeritD, LN (retroperitoneal)	Surgery, Chemo (Carbo/CDDP)	14	DOD
7	Calista et al[15]	65	Adenoca, G3	Umbilical mass	PeritD, LN (retroperitoneal)	Surgery, Chemo (CAP)	6	DOD
8	Cormio et al[2]	67	Serous, G3	N/A	PeritD, Pleura	Surgery, Chemo (TC)	25	DOD
9	Matsubara et al[16]	59	Serous	Umbilical bleeding	PeritD, LN (pelvic)	Surgery, Chemo (CAP)	8	NED
10	Kirshtein et al[17]	54	Poorly diff (FT)	(umbilical hernia)	PeritD (implants)	Surgery, Chemo (Carbo)	13	NED
11	Mizuno et al[18]	70	Serous	Bleeding and itching umbilicus	PeritD, LN (retroperitoneal)	Surgery, Chemo (PTX)	6	NED
12	Kolwijck et al[19]	18	Serous	Abdominal pain, bleeding and itching umbilicus	PeritD, Pleura, LN (inguinal)	Surgery, Chemo (TC, CAP, TAM, LPD)	28	DOD
13	Haraguchi et al[20]	82	Adenoca, G2	Umbilical mass with discharge	None	Surgery, Chemo (TC)	31	AWD
14	Ohta et al[21]	51	Endometrioid, G3	Umbilical mass	PeritD, LN (inguinal)	Surgery, Chemo (TC)	10	NED
15	Yu et al[22]	82	Serous	Umbilical mass	PeritD	Surgery, Chemo (TC)	20	Alive
16	Kurt et al[23]	49	Mixed type (endometrioid G3 + serous)	Umbilical mass, abdominal pain	PeritD	Surgery, Chemo (TC)	15	DOD
17	Fukushima et al[24]	45	Serous, G3 (FT)	Umbilical mass	PeritD, LN (paraaortic)	Surgery, Chemo (CDDP, PTX)	33	DOD
18		65	Serous, G3	Umbilical mass	PeritD	Surgery, Chemo (TC)	25	AWD
19	Yokota et al[25]	70s	Endometrioid, G1	Umbilical bleeding	PeritD, LN (retroperitoneal)	Surgery, Chemo (TC)	17	NED
20	Present study	72	Serous, G1	None	PeritD	Surgery, Chemo (TC)	27	DOD
21		61	Clear cell	None	PeritD	Surgery, Chemo (TC)	22	DOD
22		70	serous, G3	None	PeritD	Chemo (Etop, TC)	42	DOD

AWD = alive with disease, CAP-H = cyclophosphamide (CTX)/adriamycin/cisplatinum (CDDP)/hexamethylmelamine, DOD = dead of disease, Etop = etoposide, FT = fallopian tube carcinoma, LN = lymph node, LPD = liposomal doxorubicin, N/A = not available, NED = no evidence of disease, PeritD = peritoneal dissemination, TAM = tamoxifen, TC = paclitaxel (PTX)/carboplatin (Carbo).

hematogenous spread is also involved in the development of SJNs, as SJNs can develop as a recurrent disease in patients without peritoneal dissemination.[26] Patients with an SJN at initial diagnosis often present with umbilical symptoms including an umbilical mass, umbilical bleeding, and pruritus.[10,13–16,18–25] Sometimes they have only umbilical symptoms without typical ovarian cancer symptoms. In a previous report, a patient with SJN who did not have abdominopelvic abnormalities on computed tomography (CT) scan at presentation developed an ovarian tumor 10 months later.[20]

Patients with SJN at presentation are expected to have similar survival as patients with other distant metastases (stage IV disease), if they receive platinum/taxane chemotherapy. In this study, 3 patients received paclitaxel/carboplatin chemotherapy and survived more than 22 months. Review of the studies in which treatment and survival data are provided shows that the median survival of patients with SJN at presentation, who received platinum and/or taxane chemotherapy, is 26 months,[2,10,12–25] which compares favorably with the 25-month survival of patients with stage IV disease who underwent primary debulking surgery.[27] Therefore, patients with SJN should be treated with the current standard treatment for an advanced ovarian carcinoma, that is, a combination of cytoreductive surgery including SJN resection and adjuvant platinum/taxane chemotherapy. On the contrary, patient survival with SJN developing as a recurrent disease may not be favorable; it is influenced by the time to recurrence and coexisting recurrent diseases.

Nonumbilical metastases in ovarian carcinoma are less likely to occur compared with SJN, and develop as a recurrent or progressive disease in almost all cases. In addition to hematogenous and lymphatic spread, nonumbilical metastases develop by contiguous spread and implantation. Skin metastasis after laparoscopy and paracentesis has been a well-known phenomenon in patients with advanced or recurrent ovarian cancer[1,2,28]; this type of metastasis is developed by implantation of cancer cells at the site of the procedures. Nonumbilical metastasis often develops in previous incisional scars.[29,30] Isolated incisional metastases occur by cancer cells contaminating surgical wounds.[29] Another explanation is "oncotaxis" in which otherwise dormant tumor cells may be distantly attracted to sites of tissue inflammation, such as surgical wounds, thus initiating local recurrence.[31] Scalp and limb metastases, both very rare, have been reported.[32,33]

Since almost all nonumbilical metastases occur as a recurrent disease, prognosis of patients with these metastases is poor. However, patients who develop skin metastases in previous incisional scars without coexisting metastatic diseases may have a long-term survival after developing this disease.[29,30] In our study, these 3 patients survived more than 4 years. Treatments for nonumbilical metastasis depend on the site of disease, presence or absence of coexisting diseases, and time to recurrence. Resection may be considered if the skin lesion is an incisional metastasis without coexisting diseases. Radiation therapy is effective in improving pruritus associated with skin lesions,[34,35] and may prolong survival in some patients.[36] Also, in endometrial carcinoma, patients with isolated incisional recurrence had better survival than patients with nonisolated incisional recurrence.[37] Prognosis of patients with a skin lesion outside previous surgical incision is poor, as this type of skin metastasis is a late manifestation associated with multiple metastases.[32,33,35,38]

The limitations of this study include the exclusion of patients with skin metastases developed at the site of paracentesis and colostomy, which resulted in the small number of the patients. These types of skin metastases were not necessarily evaluated fully, because they usually occurred in patients with refractory disease who required repeat paracentesis and whose survival time was inevitably short. Thus, survival time after diagnosis in patients with nonumbilical metastasis in the present study may be longer than that observed in previous studies. Another limitation is the diagnostic method for skin metastases. Skin metastases are traditionally diagnosed histologically or cytologically. However, in the present study, PET/CT was used to confirm the diagnosis of skin metastasis, because PET/CT has a higher diagnostic reliability compared with conventional imaging techniques, such as magnetic resonance imaging and CT.[39] Using PET/CT, skin ulceration sometimes occurring after biopsy of subcutaneous lesions can be avoided. Moreover, PET/CT can reveal unusual disease spread and be helpful for treatment planning.[39]

5. Conclusions

In conclusion, patients with SJN at presentation from epithelial ovarian or fallopian tube carcinoma may have a relatively long survival if they receive current standard chemotherapies. Therefore, these patients, including older women, may be referred to a cancer center and treated adequately. Recent studies have suggested that molecular targeted therapy using an antiangiogenetic agent (bevacizumab) may alter the patterns of recurrence and increase the incidence of brain and skin metastasis.[40,41] It is important for physicians to recognize symptoms or signs that would suggest skin metastasis.

References

[1] Dauplat J, Hacker NF, Nieverg RK, et al. Distant metastases in epithelial ovarian carcinoma. Cancer 1987;60:1561–6.
[2] Cormio G, Capotorto M, Di Vagno G, et al. Skin metastases in ovarian carcinoma: a report of nine cases and a review of the literature. Gynecol Oncol 2003;90:682–5.
[3] Cheng B, Lu W, Xiaonyun W, et al. Extra-abdominal metastases from epithelial ovarian carcinoma: an analysis of 20 cases. Int J Gynecol Cancer 2009;19:611–4.
[4] Brownstein MH, Helwig EB. Metastatic tumors of the skin. Cancer 1972;29:1298–307.
[5] Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. J Am Acad Dermatol 1993;29:228–36.
[6] Majmudar B, Wiskind AK, Croft BN, et al. The Sister (Mary) Joseph nodule: its significance in gynecology. Gynecol Oncol 1991;40:152–9.
[7] Güth U, Huang DJ, Bauer G, et al. Metastatic patterns at autopsy in patients with ovarian carcinoma. Cancer 2007;110:1272–80.
[8] Rafii A, Deval B, Geay JF, et al. Treatment of FIGO stage IV ovarian carcinoma: results of primary surgery or interval surgery after neopadjuvant chemotherapy: a retrospective study. Int J Gynecol Cancer 2007;17:777–83.
[9] Aletti GD, Podratz KC, Cliby WA, et al. Stage IV ovarian cancer: disease site-specific rationale for postoperative treatment. Gynecol Oncol 2009; 112:22–7.
[10] Brustman L, Seltzer V. Sister Joseph's nodule: seven cases of umbilical metastases from gynecologic malignancies. Gynecol Oncol 1984;19: 155–62.
[11] Papalas JA, Selim MA. Metastatic vs primary malignant neoplasms affecting the umbilicus: clinicopathologic features of 77 tumors. Ann Diagn Pathol 2011;15:237–42.
[12] Hashimoto T, Ezaki K, Yamada K, et al. Six cases of ovarian carcinoma with umbilical metastasis (in Japanese). Sanfujinka no Jissai 2000; 49:2063–7.
[13] Kato K, Koshiba H, Kikuchi N, et al. Sister Mary Joseph's nodule: report of a case of umbilical metastasis from the primary tubal cancer (in Japanese). Kyoto Second Red Cross Hospital Med J 2000;21:90–7.
[14] Haneda T, Kimura T, Sarukawa M, et al. Ovarian carcinoma with Sister Mary Joseph's nodule (in Japanese). Hifu-Rinsho 2001;42:342–3.

[15] Calista D, Florentini C, Landi G. Umbilical metastasis from ovarian carcinoma: Sister Mary Joseph's nodule. J Eur Acad Dermatol Venereol 2002;16:84–5.
[16] Matsubara M, Osada K, Ohara M, et al. A case of ovarian carcinoma presenting as an umbilical metastasis (in Japanese). Kanto J Obstet Gynecol 2004;41:377–82.
[17] Kirshtein B, Meirovitz M, Okon E, et al. Sister Mary Joseph's nodule as the first presenting sign of primary fallopian tube adenocarcinoma. J Minimal Inv Gynecol 2006;13:234–6.
[18] Mizuno M, Sumida K, Kuno T, et al. A case of ovarian carcinoma with Sister Mary Joseph's nodule. A case report (in Japanese). Inazawa Municipal Hospital J 2006;10:74–8.
[19] Kolwijck E, Boss EA, van Altena AM, et al. Stage IV epithelial ovarian carcinoma in 18 year old patient presenting with a Sister Mary Joseph's nodule and metastasis in both breasts: a case report and review of the literature. Gynecol Oncol 2007;107:583–5.
[20] Haraguchi K, Sekine M, Aoyama R, et al. Sister Mary Joseph's nodule presented 10 months before ovarian cancer detection (in Japanese). Hifubyo Rinsho 2007;29:837–40.
[21] Ohta S, Yamakawa Y, Hasegawa T, et al. Advanced ovarian cancer with Sister Mary Joseph's nodule: a case report (in Japanese). Gan to Kagaku Ryoho 2007;34:117–9.
[22] Yu S, Kurimasa E, Ohyagi C, et al. Five cases of Sister Mary Joseph's nodule treated at Sakai Municipal Hospital (in Japanese). Sakai Municipal Hospital J 2008;11:23–7.
[23] Kurt S, Camuzcuoglu H, Camuzcuoglu A, et al. Umbilical metastasis of serous component as a first sign of mixed type epithelial ovarian cancer. Eur J Gynaecol Oncol 2009;30:455–7.
[24] Fukushima J, Shinohara S, Tagaya H, et al. Two cases of advanced adnexal malignant tumor detected with Sister Mary Joseph's Nodule (in Japanese). Yamanashi Obstet Gynecol J 2014;4:53–9.
[25] Yokota Y, Suzuki K, Honda K, et al. Ovarian cancer with umbilical metastasis detected by scraping cytology (in Japanese). Niigata Obstet Gynecol J 2014;109:68–71.
[26] Gupta P, Kumari A, Kriplani A, et al. Sister Mary Joseph's nodule as the first and only sign of recurrence in a case of stage Ia carcinoma ovary. BMJ Case Rep 2014;2014:bcr2013201779.
[27] Trope CG, Elstrand MB, Sandstad B, et al. Neoadjuvant chemotherapy, interval debulking surgery or primary surgery in ovarian carcinoma FIGO stage IV? Eur J Cancer 2012;48:2146–54.
[28] van Dam PA, DeCloedt J, Tjalma WAA, et al. Trocar implantation metastasis after laparoscopy in patients with advanced ovarian cancer: can the risk be reduced? Am J Obstet Gynecol 1999;181:536–41.
[29] Kohler MF, Soper JT, Tucker JA Jr, et al. Isolated incisional metastases after intraperitoneal radioactive chromic phosphate therapy for ovarian carcinoma. Cancer 1991;68:1380–3.
[30] Traiman P, De Luca LA, Bacchi CE. An extremely large, cauliflower-type, cutaneous metastasis of ovarian cancer associated with good prognosis. Gynecol Oncol 1994;53:239–41.
[31] DerHagopian RP, Sugarbaker EV, Ketcham A. Inflammatory oncotaxis. JAMA 1978;240:374–5.
[32] Matsui H, Suzuka K, Yamazawa K, et al. Scalp metastasis of a serous ovarian cancer. Acta Obstet Gynecol Scand 2002;81:577–8.
[33] Kim YW, Srodon M, Bristow RT. Stage IV micropapillary serous ovarian carcinoma: a report of three cases. Int J Gynecol Pathol 2005;24:235–8.
[34] Merimsky O, Chaitchik S, Inbar M. Skin metastasis of ovarian cancer: report of three cases. Tumori 1991;77:268–70.
[35] Wiechert AC, Garrett LA, Lin G, et al. Management of a skin metastasis in a patient with advanced ovarian cancer. Gynecol Oncol Rep 2012;2:124–6.
[36] Demirci S, Yavas F, Ozsaran Z, et al. Palliative radiotherapy for the skin metastasis of ovarian cancer: a case report and review of the literature. Med Oncol 2010;27:628–31.
[37] Bogani G, Dowdy SC, Cliby WA, et al. Incisional recurrences after endometrial cancer surgery. Anticancer Res 2015;35:6097–104.
[38] Schonmann R, Altaras M, Biron T, et al. Inflammatory skin metastases from ovarian carcinoma: a case report and review of the literature. Gynecol Oncol 2003;90:670–2.
[39] Gadducci A, Cosio S. Surveillance of patients after initial treatment of ovarian cancer. Crit Rev Oncol Hematol 2009;71:43–52.
[40] Paez-Ribes M, Allen E, Hudock J, et al. Antiangiogenic therapy elicits malignant progression of tumors to increased local invasion and distant metastasis. Cancer Cell 2009;15:220–4.
[41] Robinson WR, Beyer J, Griffin S, et al. Extraperitoneal metastases from recurrent ovarian cancer. Int J Gynecol Cancer 2012;22:43–6.