



Original Article

Skin metastases in genital malignancy

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Abstract

Objectives: To study the incidence, clinicopathological characteristics, and prognosis of skin metastases in patients suffering from genital malignancy. **Methods:** A retrospective review of 1012 patients with different types of genital malignancies was undertaken in our tertiary center. Relevant clinicopathological information, treatment of primary site and documentation of skin metastases were noted. Survival time was calculated from the time of diagnosis of skin metastasis. **Results:** Out of the 1012 patients only nine patients (four suffered from carcinoma cervix and five from ovarian carcinoma) had skin metastases. The average time of appearance of skin metastasis after diagnosis of primary malignancy was 18.9 months. Six patients died of the disease. Two patients are still alive. One patient did not follow up. Median survival time after diagnosis of skin metastasis in eight cases was 4.5 months. **Conclusions:** Skin involvement occurs rarely in genital malignancy. Prognosis after skin metastasis is poor.

Key words: skin metastases, genital malignancy.

Introduction

Cervical carcinoma is the most common cause of death from gynecological malignancy in developing countries, whereas ovarian carcinoma is the leading cause of death from genital malignancy in the developed countries. The most common route of dissemination in ovarian cancer is intraperitoneal. Lymphatic spread is also common. Haematogenous spread usually occurs late in the course of the disease. Carcinoma of the cervix

spreads predominantly by either direct invasion or lymphatic permeation. Endometrial carcinoma spreads by invading the myometrium. The more deeply it invades, the greater is the likelihood of lymphatic invasion or less commonly vascular involvement. In vulvar cancer the tumor spreads slowly infiltrating local tissue before metastasizing to the groin nodes.

Metastasis to skin occurs rarely in gynecological cancers especially in cervical carcinoma¹. The aim of the present study was to find out the incidence, clinicopathological characteristics and prognosis of skin metastases in genital malignancy.

Methods

A retrospective study was conducted on 1012 patients suffering from different types of genital malignancies

Paper received on 19/04/2008 ; accepted on 19/02/2009

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Figure 1. Showing multiple nodular skin metastases in umbilicus and suprapubic region



Figure 2. Showing single nodular skin metastasis in infra umbilical region



Figure 3. Showing single nodular skin metastasis in laparotomy scar



Figure 4. Showing multiple blister like skin metastasis in laparotomy scar



Figure 5. Showing mould therapy

from January 1998 to December 2007. (This includes patients attending for primary malignancy and patients receiving treatment for primary site outside and subsequently referred to our hospital). Pertinent clinical information, pathological data, treatment for primary disease, appearance of cutaneous metastases and their management were reviewed in each patient.

FIGO staging at the time of primary diagnosis (those attending our hospital for primary malignancy) was done, which was not possible in most of the referred cases as staging was not mentioned in the discharge certificate. All the patients had undergone surgical procedures for their primary disease but only few patients received subsequent adjuvant radiotherapy or chemotherapy.

Cutaneous metastases after histological confirmation were recorded. Survival time was calculated from the diagnosis of skin metastases.

Results:

Among the 1012 patients with different types of genital malignancies, nine were found to have skin metastases. Four patients had carcinoma cervix and five suffered from ovarian cancer. Clinicopathological characteristics of these patients are summarized in Table 1.

The mean age of the patients at the time of diagnosis of genital malignancy was 40.2 years (range 24-60 years). FIGO staging at the time of diagnosis was not known in four cases. The remaining five patients had stage Ib and IIa cervical cancer, stage IVa, stage IIIc, and stage Ia ovarian cancer respectively. Three patients received treatment for primary disease (case no. 1, 5 and 9) in our hospital and six cases were referred from outside (after having surgery for primary malignancy). Adequate surgery was not done in two referred cases (case no. 2 and 7). One patient received postoperative adjuvant chemotherapy and radiotherapy (case 8). Case no. 9 did not receive any further treatment as she had history of primary infertility and stage Ia granulosa cell tumor, which is very slow growing.

No skin metastasis was found in endometrial, vulvar or vaginal cancer patients. Table 2 shows clinicopathological characteristics of skin metastases. One patient had skin metastasis at the time of diagnosis of ovarian cancer (case no. 5). In rest of the cases the average time of appearance of skin metastasis after the diagnosis of genital malignancy was 18.9 months (range 0-8 years). Skin lesions vary from 1.5-5cm in diameter. Six patients had single deposit whereas three patients had multiple deposits. Skin metastases were found in surgical scar (laparotomy scar), umbilicus, and lower abdomen.

The treatment of skin metastases consisted of surgery, chemotherapy and radiotherapy, either alone or in combination. Prior to chemotherapy or radiotherapy, surgery (excision of the lesion) was done in case no. 1 and 9. Case no. 8 refused surgery. Details of the chemotherapeutic agents are mentioned in table 2. External radiotherapy was administered by parallel opposed AP & PA fields in three cases (case no. 1, 7, 9).

Table 1. Clinicopathological characteristics of genital malignancy patients having skin metastases.

Case	Age-years	Ref case / Firstvisit at NRS	Primary site	Primary treatment	FIGO staging	Histology
1	24	NRS	Cervix	RadHys (rt tube and ov preserved)	Ib	Sq cell carcinoma
2	60	Ref	Ovary	Rt SO	Not known	Androblastoma
3	25	Ref	Ovary	Rt SO	Not known	Poor diff. malig. germ cell tum
4	37	Ref	Cervix	RadHys-Inc-RT	Not Known	Mod. diff. sq. cell carcinoma
5	48	NRS	Ovary	Debulking operation	IVa	Ser. pap. cyst. adeno carcinoma
6	35	Ref	Cervix	RadHys-RT	IIa	Mod. diff. sq. cell carcinoma
7	43	Ref	Cervix	Sub total Hys	Not known	Poor. diff. sq. cell carcinoma
8	47	Ref	Ovary	TAH BSO & ICO-Ad chemo (PAC & CDDP) Ad EBRT	IIIc	Mod. diff. adeno carcinoma
9	43	NRS	Ovary	Rt SO (pr inf) after 5 yrs TAH & Lt SO (DUB)	Ia	Rt ova-gr cell tumor endom & Lt ova-NAD

RadHys – Radical hysterectomy. SO-Salpingo-oophorectomy. Inc-Incomplete. RT-Radiotherapy. gr-ganulosa. Endom-Endometrium. Ad-Adjuvant. Ser pap-serous papillary. ICO-Infra colic omentectomy. PAC-Paclitaxel. CDDP- Cisplatin – Sq – Squamous

Table 2. Characteristics of skin metastases.

Case Number	Shape & site	Maximum diameter (cm)	Interval time	Concomitant disease between diagnosis of prim malig & skin meta	Treatment	Status & survival	
1	Single	Nodular, just above lap scar	4	11m	Nil	Sur & EBRT	discharged, did not turn up.
2	Multiple	Nodular, lower abd (rt side)	2	3m	(Pelvis + liver)	CT (CDDP&CPM)	died during treatment 2m ASM
3	Multiple	Nodular, umbilicus & SPB region	3	20d	Liver	CT (BEP Rec)	died while planning, 45 days ASM
4	Single	Nodular, lap scar	1.5	5m	Pelvis	RT (M)	died 11m ASM
5	Single	Nodular, infra umbilical region	2	0	Pelvis + abdomen	CT (CDDP&CPM)	died during treatment, 3m ASM
6	Single lap scar	Nodular,	1.5	6m	Nil	RT (M)	discharged & died 24m ASM
7	Multiple	Blister like, lap scar	2.5	1m	Pelvis + abdomen	EBRT & ICRT	discharged and readmitted died 4mASM
8	Single	Nodular umbilical region	5	4y	Nil	Refused Sur, CT (Pacl & Carbo) & RT (M)	C.C.R. kept under F.U. for last 5 months
9	Single	Nodular lap scar	5	8y	Nil	Sur & EBRT	C.C.R kept under F.U. for last 10 months

Lap – Laparotomy, SPB – Suprapubic, Sur-surgery, CT-Chemotherapy, CDDP-Cisplatin, CPM – Cyclophosphamide, Pacl-Paclitaxel, Carbo-Carboplatin, BEP-Bleomycin, Etoposide Cisplatin, RT-Radio therapy, M-Mould therapy, ASM-After skin metastasis, C.CR-Complete clinical remission, F.U. – Follow up, Rec – Recommended, abd – Abdomen pri-Primary, malignancy, meta – metastases

For superficial skin lesions electron beam therapy is an ideal choice for radiation treatment. As linear accelerator machine is not available in our institution, radiation therapy was modified as follows. Thermoplastic mould of the body parts, where the nodules were present, was taken. Flexible interstitial plastic tubes were fixed over the mould at a gap of 1.2-1.5 cm. Dummy sources were placed within the tubes and orthogonal X-ray picture was taken with “C” arm. Computerized planning was performed and treated with Ir-192, remote controlled

HDR brachytherapy. Dose calculated at the depth of the nodule, was variable. Mould brachytherapy is a good alternative to electron beam therapy. Mould therapy was given to case no. 4, 6, and 8 who had previous radiotherapy.

Six patients died either during treatment for skin metastasis or during follow up. One patient (case no. 1) did not turn up. Two patients (case no. 8 & 9) are now in complete clinical remission and kept under follow

up. Median survival time from the diagnosis of skin metastasis in eight patients was 4.5 months (1.5 months – 2 years).

Discussion

Skin involvement from genital malignancy is uncommon. In our study cutaneous metastases were found in 0.88% (9 out of 1012) of the patients suffering from genital malignancy. It can be compared with the incidence of 1.3% which was reported by Imachi et al. in their study of 1190 patients with carcinoma cervix, where only 15 patients developed skin metastasis². Cormio et al in their retrospective study on 220 patients with ovarian carcinoma, found cutaneous metastasis in nine patients (4%)³.

In the present study skin metastases were found in surgical wound (laparotomy scar), umbilicus (umbilical metastasis from a malignant neoplasm is termed Sister Mary Joseph's Nodule)⁴ and lower abdomen. Cormio et al found cutaneous metastasis in laparotomy scar, neck, chest, arm, groin and vulva in ovarian carcinoma³. Distant metastases such as in vulval region, scalp and gluteal region were also reported by other authors like Srivastava et al⁵, Park⁶ and Krasagakis et al⁷ in cervical cancer. Skin metastases originating from endometrial and vulvar cancer were reported by Faught⁸ and Tobias et al⁹ respectively. In our study we did not get any skin metastasis originating from endometrial, vulvar or vaginal cancer.

In our study the time interval between the diagnosis of genital malignancy and detection of skin metastases is 18.9 months (0-8 years). Similar time intervals of 16.9 months and 24 months were also recorded by Imachi et al² and Cormio et al³ respectively. Different case reports were published regarding the nature, site and appearance of skin metastases in genital malignancy. Pertzborn found metastasis on the hand at points of recent skin puncture at the time of diagnosis of a case of cervical cancer¹⁰. Behtash et al reported a case of skin metastasis four years after the completion of treatment of cervical cancer¹.

Several theories have been postulated to explain the pathogenesis of skin metastasis in genital malignancy. In ovarian malignancy the cutaneous metastasis may be due to direct invasion from underlying growth, continuous extension of the tumor cell through lymphatic and accidental implantation of the tumor cells during surgical procedures. Haematogenous, lymphatic

and venous spread; all represent valid mechanisms of tumor spread from gynecological cancer. Hockel proposed that most scar recurrences are regarded as the result of interaction of minimal residual microscopically occult cancer with the surgical wound environment (wound volume, and extent of ischemia within a wound) inside a developmentally defined tissue or organ compartment¹¹.

In the present study skin metastases are mainly nodular in nature. Only one patient presented with a blister like skin lesion. Cormio et al also found nodular lesions in most of the cases². Cutaneous metastasis resembling herpes zoster lesion was reported by Schonmann et al¹². Traiman reported a huge (20 cm x 20 cm) cauliflower type of skin metastasis, six years after the diagnosis of a case of ovarian carcinoma¹³.

Till now no definite guideline is available to decide a therapy for skin metastasis. The intent of treatment remains palliation by radiation, chemotherapy and surgery either alone or in combination. In our study two patients received only chemotherapy and three patients received radiotherapy only, and one patient succumbed while planning for chemotherapy. Remaining three patients received combination therapy. Chemotherapy alone or in combination with surgery was also the modes of treatment in the study of Cormio et al³. Imachi et al² preferred surgical extirpation followed by radiotherapy. In the present series median survival time from diagnosis of skin metastases was 4.5 months (45 days - 2 years). Similar median survival of four months (2 months - 65 months) from diagnosis of the skin metastases was also reported by Cormio et al³.

Conclusion

Skin metastasis is a rare presentation in genital malignancy, both at the time of diagnosis and during the course of the disease process. Prognosis after skin metastasis is poor and the most important prognostic factor is the interval time between the diagnosis of genital malignancy and the appearance of skin metastasis whether metastasis is isolated or part of systemic recurrence. Earlier the metastasis, worse is the prognosis. The intent of treatment remains palliation either by radiation, chemotherapy or surgery alone or in combination. Careful handling of tissue during operation, extension of radiotherapy fields to include the wound and obviously proper primary treatment (which was lacking in our study in some of the referred cases) might prevent the development of skin

metastases. Research oriented on the mechanism of local cancer spread and the interaction of cancer cells with the surgical wound environment may improve the knowledge of skin metastases and clinical prognosis.

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