



Ca Cervix with Bilateral Ovarian Metastasis: An Interesting Case Report with Review of Literature

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Abstract: Early stage invasive squamous cell carcinoma of the cervix rarely presents with bilateral ovarian metastasis. Usually, ovarian metastasis is associated with bulky, advanced cervical squamous cell carcinomas with extensive involvement of the uterus. We are here reporting case of a 45 year old woman with clinical stage Ib2 of cervical carcinoma who presented with abnormal vaginal discharge with blood stained. A CECT of whole abdomen with Pelvis revealed bulky cervix measuring 3.5 x 3cm with ill defined heterogeneity, likely suspicious of malignancy. Patient underwent Radical hysterectomy with bilateral salpingo-oophorectomy with lymph node dissection. Microscopic findings, revealed cervical grade II non keratinizing squamous cell carcinoma with involvement of myometrium and left fallopian tube. Bilateral ovaries were positive for tumor metastases. This case brings attention to the non-conventional metastatic route of invasive cervical carcinoma

Keywords: Carcinoma cervix, Bilateral Salpingo-oophorectomy, Ovarian metastasis, Squamous cell carcinoma

1. INTRODUCTION

Globally the estimated age-standardised incidence of cervical cancer was 13.1 per 100,000 women and with varied rates ranging from 2 to 75 per 100,000 women in different countries [1]. In India overall cervical cancer incidence is 8.4% [2]. For patients with early stage cervical cancer Ib₁, Ib₂ and IIa₁, Radical hysterectomy with pelvic lymphadenectomy with Bilateral Salpingo ophorectomy is a reasonable therapeutic option [3]. For locally advanced stage Concurrent-Chemoradiation is the primary Radical treatment modality [4]. Ovarian Metastases from squamous cell carcinoma (SCC) of the cervix are rare and reported in less than 1% of early stage cervical SCC [5]. Studies reported that greater than 1.3% of cell carcinomas of cervix present with ovarian metastases [5–7]. Ovarian function preservation is critical for quality of life, especially for young patients (<45 years old). Preservation can be performed directly in situ or by ovarian transposition during surgery. Here, we are presenting a very unusual rare case of Ca Cervix with Bilateral Ovarian metastasis along with literature review.

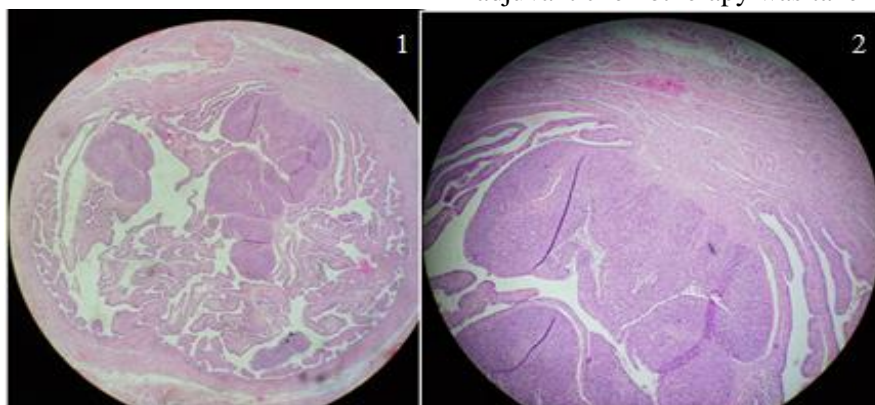
2. CASE PRESENTATION

A 45 year old P5L5 with biopsy proven cervical cancer presented to the Gynae - oncology outpatient department with chief complaints of per vaginal whitish discharge occasionally blood stained for 4 months. No history of weight changes or constipation. There was no history of associated pain, fever or any significant past or medical history. General physical and breast examination was unremarkable. On local clinical examination, As ulceroproliferative growth of less than 3.5 cm was found at cervix and cervix was deviated to right. Bilateral parametrium and fornices were free. No clinically palpable pelvic nodes. Ultrasonography of pelvis revealed a bulky uterus (8.8 x 5.3 cm) with adenomyosis along with thickened endometrium (ET-13mm) with mild endometrial collection. A CECT of whole abdomen with Pelvis was also done. It revealed bulky cervix measuring 3.3 x 3cm with ill defined heterogeneity and mild hydrometra, likely suspicious of malignancy. The fat planes with and bladder was maintained. Provisional clinico-radiologically diagnosis at this stage was

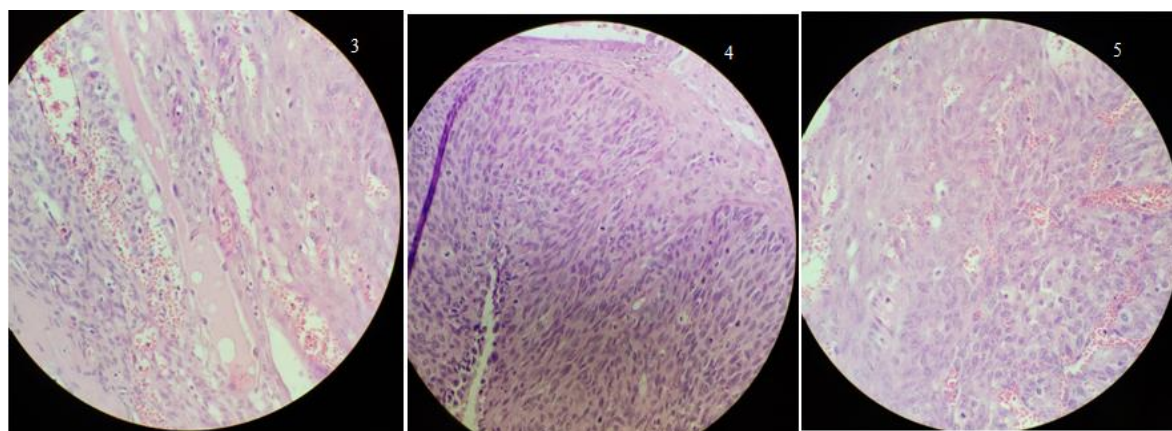
cervical malignancy without evidence of parametrial invasion (FIGO 2018 Stage Ib2). Complete hemogram and routine blood biochemistry parameters of the patient were within normal limits. Chest radiograph of the patient was normal. Patient underwent Radical hysterectomy with Bilateral Salpingo-oophorectomy with lymph node dissection.

Pathologic findings (Fig 1-5) revealed uterus and cervix measured 8 x 6cm. On cut section, Grey white area seen in cervix measuring 3x2x2cm. Microscopic findings revealed

cervical grade II non keratinizing squamous cell carcinoma. Tumor involved more than 50% of the cervical stroma. Endometrium was non secretory and free of tumor cells. Myometrium was involved by tumor. Bilateral parametrium were free of tumor metastases. Bilateral ovaries and left fallopian tube were positive for tumor metastases. Right fallopian tube was free of tumor. All lymph nodes were negative for tumor metastases. The case was presented in multi-disciplinary tumour board, and a decision for concurrent chemo radiation followed by adjuvant chemotherapy was taken.



1 Section from scanner view of FT along with metastatic squamous cell, 2 Section from FT 10x view Shows Island of malignant squamous cell deposit adherent to FT epithelium



3- Section from ovary at 10x shows sheet of squamous cells having hyperchromatic nuclei infiltrating stroma of ovary. 4- H and E stain section at 40x views shows malignant squamous cells infiltrating ovary with adjacent vascular proliferation. 5- H and E stain from ovary at 40x shows ovarian stromal cells and blood vessel with adjacent malignant squamous cells. Demarcation between both types of cell population are clearly visible in the above micro pictograph.

3. DISCUSSION

Around 40% of cervical cancers seen in women of childbearing age (8). Preserving functional ovaries is an important issue. Ovarian Metastasis is very rare in carcinoma cervix and its incidence is more in advanced stage .Incidence of ovarian metastases is 0.5% in SCC and 1.7% in adenocarcinoma, so ovarian

preservation at the time of surgery may pose a small risk of microscopic disease [9].

The standard surgical treatment for early stage cervical cancer is Radical hysterectomy and pelvic lymphadenectomy. The decision to do oophorectomy or not is usually based on the pathological type of the tumor and the patient's age. Menopausal symptoms, Risk for

cardiovascular diseases and poor long-term quality of life can be avoided with ovarian preservation [10]. Few studies have shown that preserving the ovaries can improve the quality of life after surgery [11].

Ovarian metastases rate of squamous variant of cervical cancer is lower than 2% and for adenocarcinoma is relatively high; ranged from 6.3% to 12.9% [6, 7, and 12]. Ovarian

metastases are associated with poor prognosis. Therefore, diagnosis of high-risk patients with ovarian metastases (OM) is very important. Due to lack of randomized trials, there is still no consensus on the selection criteria for ovarian preservation [13-14]. **Table 1** lists the studies evaluating incidence and the risk factors for OM.

S. No	Authors	No.	Stage	Ovarian Metastases No. (%)	Squamou cell Ca No. (%)	Adeno Ca No. (%)	Risk Factors
1	Le zhou et al 2018	3292	I-II	115 (3.49%)	56/2794 (2%)	59/498 (11.8%)	LVI, lymph node metastases, Histologic subtype, Corpus Invasion
2	Lu H et al 2016	101	I-II	5 (4.95%)	na	5/101 (4.95%)	Pathological grade, LVSI, lymph node metastasis, Tumor size, depth of stromal invasion, junction of cervix and uterine corpus
3	Hu T et al 2013	1889	IB-IIB	22 (1.2%)	12 (0.7%)	5 (2.7%)	lymph node metastasis, Corpus Invasion, Paramet. Invasion, Histology and NACT
4	Kasamatsu T et al 2009	578	<IIB	12 (2.06%)	6/455 (1.3%)	6/123 (5%)	lymph node metastasis, Stage IIB Adenocarcinoma
5	Kim MJ et al 2008	625	<IIB	14 (2.2%)	2/473 (0.4%)	8/151 (5.2%)	Histologic type and Uterine corpus Involvement
6	Landoni et al 2007	1695	IA ₂ -IIA	16 (0.9%)	7/1284 (0.5%)	9/380 (2.4%)	Pathologic type, pelvic lymph node metastases Age>45, adenoca., Higher stage
7	Shimada et al 2006	3471	IB-IIB	52 (1.5%)	29/2925(0.8%)	29/546 (5.3%)	Adenocarcinoma
8	Yamamoto et al 2001	631	IB-IIB	14 (2.2%)	2/485 (0.4%)	12/146 (8.2%)	Histologic type and Blood vessel invasion
9	Nakanishi et al 2001	1304	IA-IIB	29 (2.2%)	14/1064 (1.3%)	15/240 (6.3%)	Uterine inv, pelvic lnode mets, parametrial invasion, stage
10	Wu H S et al 1997	1507	IB-IIB	10/1413 (0.7%)	6 (0.42%)	4 (0.2%)	Lymph node mets and Uterine Involvement
11	Suttons et al 1992	990	IB	6 (0.6%)	4/750 (0.5%)	2/121 (1.7%)	Extracervical lesion
12	Toki et al 1991	597	IB-IIIB	3 (0.5%)	1/524 (0.19%)	2/36 (5.5%)	deep myometrial invasion, corpus invasion, and lymphatic permeation

Shimada et al reported 0.79% of incidence of Ovarian Metastasis from squamous cell carcinoma of cervix [5].

In a large retrospective study of 3292 patients by Zhou et al, they reported 3.49% incidence of ovarian metastases (S.C.C vs AdenoCa- 2% vs 11.8%). Histologic type, lymph node metastases, LVSI, and corpus invasion were associated with ovarian metastases independently [15].

Lu H et al reported 4.95% incidence of ovarian metastases in 101 cervical adenocarcinoma patients. Identified risk factors were pathological grade, LVSI, lymph node

metastases, tumor size, depth of stromal invasion, involvement of junction of cervix and body of uterus. [16]

In a series of 1889 patients by Hu T et al, 1.2% (S.C.C vs AdenoCa- 0.7% vs 2.7%) of patients had ovarian metastases. Associated risk factors were lymph node metastases, corpus uteri invasion, parametrial invasion, histology and NACT. [17]

Kasamatsu et al analysed 578 patients and reported 2.06% of ovarian metastases. 1.3% seen in squamous cell carcinoma patients and 5% in adenocarcinoma patients. [18]

Kim M J et al in 625 patients reported 2.2% had ovarian metastases. The Ovarian metastases rate was 0.4% for squamous cell carcinoma and 5.8% for adenocarcinoma. They concluded that histologic type and uterine corpus involvement were important risk factor for ovarian metastases. [19]

Landoni et al studied 1695 patients with early stage carcinoma cervix and reported 0.9% incidence of ovarian metastases. Metastases rate for squamous cell carcinoma was 0.5% and 2.4% for adenocarcinoma. Pathologic type, pelvic lymph node metastases, age >45yrs, adenocarcinoma and higher stage were the most important risk factors. [13]

Yamamoto et al published data of 631 patients and they reported 2.2% incidence of ovarian metastases in their study population. Adenocarcinoma was associated with high incidence of ovarian metastases as compared to squamous cell carcinoma i.e 8.2% vs 0.4%. Important risk factors identified were histologic type and blood vessel invasion. [6]

Another study by Nakanishi et al in 1304 patients with early stage cervical cancer had shown 2.2% incidence of ovarian metastases. 1.3 % for squamous cell carcinoma and 6.3% for adenocarcinoma. They concluded uterine metastases, pelvic lymph node metastases, parametrial invasion and stage were important risk factors associated with ovarian metastases. [17]

Similarly Toki et al showed that deep myometrial invasion, lymph node metastasis and uterine corpus invasion are risk factors associated with ovarian metastasis. [22]

Previous studies have analysed the risk factors for ovarian metastasis (OM) (6) and the identified risk factors are pathological grade, LVSI, lymph node metastases, tumor size, depth of stromal invasion, involvement of body of uterus. Out of these Histologic type and corpus invasion were the most important risk factors.

Due to a lack of large, randomized, controlled studies, there is no consensus on adjuvant treatment in ovarian metastasis from cervical cancer. Based on literature review, the treatment approaches includes adjuvant chemotherapy alone, radiation therapy individually or in combination with chemotherapy.

Most of the ovarian metastases reported are microscopic, unilateral, confined to ovarian

parenchyma and detected postoperatively [2, 20, 23, and 25]. Routes of spread in metastasis to ovaries in cervical cancer have been controversial. Wu et al. Postulated that lymphatic spread and transtubar implantation might be possible pathways of metastases from cervix to the ovaries [21]. However, Tabata et al. suggested that haematogenous spread of cervical carcinoma to ovaries might be a pathway [24].

Our patient had an extremely rare presentation, with exoophytic cervical carcinoma of squamous cell type with normal endometrium, invading myometrium and fallopian tube with bilateral parenchymal involvement of the ovaries. In our case Hematogenous route with transtubar implantation might have been a plausible route of spread.

4. CONCLUSION

Patients with ovarian metastasis has very dismal outcome, showing that ovarian metastasis is an important prognostic marker in patients with cervical cancer. If the above mentioned patient did not undergo salpingo-oophorectomy, the micrometastasis to ovary would have remained occult. In our case, endometrial involvement is a risk factor for ovarian metastasis. The unusual spread to bilateral ovaries in this case suggests to revisit the pathogenesis of squamous cell carcinoma of cervix.

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