#### **ORIGINAL ARTICLE**

# "Ovarian Metastases from Colorectal Cancer: Our Experience"

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Abstract Ovarian metastases from colorectal cancer are uncommon and can present synchronously and metachronoulsy. Role of prophylactic oophorectomy for colorectal cancer is controversial and there is no definitive evidence to support it. A retrospective analysis of all the patients with colorectal cancer who had attended a single unit at our center have been analysed. Clinical presentation, Pathological features and image findings were analyzed. We had 7 patients with ovarian metastases who had presented synchronously or metachronously at our institute. Five patients presented synchronously at the time of primary surgery and 2 patients had presented metachronously after the treatment of primary. Three patients had malignancy in ascending colon and 2 had in sigmoid colon, one in rectosigmoid junction and one case in rectum. The mean overall survival rate was 12.4 months (range 6–20 months). All the patients received adjuvant chemotherapy. Ovarian metastases is rare in colorectal and occurs in younger patients.

**Keywords** Ovarian metastases in colorectal cancer · Colorectal cancer · Computer tomography findings of ovarian metastases

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# Introduction

The incidence of ovarian metastases in patients with colorectal cancer is uncommon and varies from 0 to 30 % depending on whether it is an autopsy or clinical series [1–4]. They can present synchronously or metachronously. The incidence of metachronous metastases is less than 5 % and usually occurs within 2 years of diagnosing the primary [5, 6].

The diagnosis of synchronous metastases may be challenging in few patients who are asymptomatic for lower gastrointestinal malignancies. The prognosis of synchronous and metachronous metastases may vary. Prophylactic oophorectomy was first described by Schenk and Sitzenfrey in 1907, but there is no definitive evidence on the role of routine oophorectomy at the time of surgery for primary [7].

Here we would like to describe clinicopathological features, radiological findings, management and prognosis of patients of colorectal cancer with ovarian metastases.

## **Materials and Methods**

A retrospective analysis of operative and medical records of patients who were operated for colorectal cancer from 1st January 2009 to 31st December 2011 in a single unit in a tertiary care center. The presenting symptoms, clinical findings, ultrasound reports, computed tomography scan findings, treatment given and follow up were noted and analysed.

## **Results**

Of the 150 women with colorectal cancer treated at our institute in a single unit, 7 patients had ovarian metastases. The mean age of the patients was 42 years (range 24–65 years). Five patients had synchronous metastases



Table 1 CT findings of ovarian metastases

Patient	Site of primary	Side and size of ovary	Solid vs cystic	Calcification	Septa	Enhancement
1.	Sigmoid	Left	Cystic	×	×	Wall enhancement
2.	Rectosigmoid (Fig. 1)	Bilateral	Solid and cystic	+	×	Minimal enhancement
3.	Sigmoid	Bilateral	Solid and cystic	×	×	Minimal enhancement
4.	Rectum	Bilateral	Solid	+	×	Minimal enhancement
5.	Ascending colon	Right	Solid cystic	×	×	Minimal enhancement
6.	Ascending colon (FAP <sup>a</sup> ) (Fig. 2)	Bilateral	Cystic	×	+	Wall enhancement
7.	Ascending colon	Bilateral	Solid cystic	×	×	Minimal enhancement

<sup>&</sup>lt;sup>a</sup> FAP Familial adenomatous polyposis

and 2 had metachronous metastases (Table 1). The site of primary malignancy was caecum and ascending colon in three patients, sigmoid colon in two, rectosigmoid junction in one and in one it was from rectum. Four patients had mucin secreting adenocarcinoma. Three patients had adenocarcinoma grade 3, three had grade 2 and one patient grade 1. Of the 4 patients with mucinous adenocarcinoma of colon metastasing to ovary, two had calcific specks within ovarian metastases (Fig. 1). One patient was a case of Familial Adenomatous polyposis with bilateral ovarian metastases and underwent total abdominal proctocolectomy with hysterectomy and bilateral salpingoophorectomy (Fig. 2).

CEA was elevated in all patients with a mean of 37.17 (Range 5.5–108.4). CA 125 was less than 35 IU in 6 patients and in only in one patient it was 40.6. Two patients had associated peritoneal deposits along with ovarian deposits and one presented with local recurrence. Three patients underwent immunohistochemistry for diagnosis.

All patients received adjuvant chemotherapy, 6 cycles of FOLFOX regimen. Two patients were lost to follow up and 5 are in follow up. The mean overall survival rate was 12.4 months (Range 6–20 months) (Table 2).

Fig. 1 a Computer tomography of pelvis of a patient showing rectosigmoid anastamotic recurrence 2 years after initial surgery with ovarian metastases and calcific specks in the ovarian mass. b A Contrast enhanced Computer tomography (CECT) scan showing enhancement of the ovarian metastases after contrast





#### Discussion

The risk of ovarian metastases in colorectal cancer varies from 1.2 to 10 % for synchronous and 1.3–2.4 % for metachronous metastases [3, 4, 8, 9]. Various routes of spread to ovaries described are hematogenous, lymphatic, direct or transcoelomically. As it affects younger age group, who has high chance of having raw surface due to menstruation, transcoelomic spread of cancer cells and deposition of cancer cells on ovarian surface is one hypothesis. Most of them have bilateral ovarian involvement (43-70 %) and 15-20 % has associated liver metastases [10, 11]. As most of the ovarian metastases occur bilaterally have an intact capsule and affect younger age group, hematogenous spread was thought. The risk is higher in younger individuals because the vascularity of ovaries is higher in this group. Arteriographic studies have shown free vascular communication between both the ovaries through fundic branches and hence they need to be carefully examined at the time of surgery for colorectal cancers [12].

Because of the risk of ovarian metastases, few authors have advocated routine prophylactic oophorectomy in colorectal cancer patients. Ovaries act like sanctuary sites and do not respond well to chemotherapy hence, surgery is considered as the main mode of treatment. There is only one trial comparing



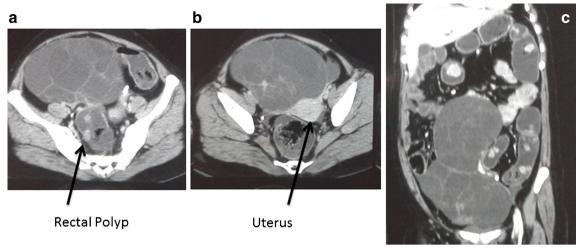


Fig. 2 A CECT scan of a patient showing septated ovarian metastases with enhancement of septal walls after contrast  $\{2(\mathbf{a}), 2(\mathbf{b})\}$  and Multiple polyps (arrow head) seen involving whole of the colon and rectum  $\{2(\mathbf{c})\}$ 

role of prophylactic oophorectomy in which 155 patients were randomized to two arms. In patients who underwent prophylactic oophorectomy, survival benefit was there for initial 2 or 3 years, but Kaplan–Meier survival analysis indicated that this was not statistically significant and the benefit did not persist for 5 years. The 5 year disease free survival improved from 65 to 80 % in patients who underwent prophylactic oophorectomy, but it was not statistically significant [5].

The tumor markers, CEA (carcinoembryonogenic antigen) and CA 125 are used commonly in colorectal cancer and ovarian lesions. CA 125 is usually elevated in epithelial cancers of ovary. It can also be raised in endometrium, fallopian tube, breast, pancreatic cancers and metastatic ovarian lesions [13]. In our series only one patient had raised levels. CA 125

has been found to be useful as a prognostic factor in krukenberg tumors in which levels of > 75 IU/ml are associated with lower 5 year survival rate [14, 15].

A recent analysis, evaluated imaging findings in detection of metastatic lesions in comparison with primary ovarian malignancies. They had evaluated mass character, surface of the ovarian mass, peritoneal seedling, ascites, enhancement of cystic wall and solid component within the lesion. They concluded that smooth margin of mass and more cystic nature favors colonic metastases than a primary ovarian neoplasm. Presence of calcification indicates metastatic mucinous carcinoma [16]. We had two cases of metastatic mucinous carcinomas to ovaries in our study and both had calcification (Fig. 1). Imaging in our study showed solid metastases in

Table 2 Clinicopathologic findings and prognoses of the patients with metastatic ovarian cancers

S.No.	Age	Primary site	TNMGrade	Metastases at onset	Other sites of spread	CEA	CA125	Mucin producing tumor	Prognosis
1	65	Sigmoid colon	T3N1cG1	Synchronous	×	108.4	7.1	+	18 months on follow up
2	47	RectoSigmoid colon	T4aN2aG2	Metachronous (2 years later)	Anastomotic recurrence, peritoneal deposits	45.53	6.38	+	7 months on follow up
3	50	Ascending colon	T3N1bG3	Synchronous	×	5.5	40.6	_	20 months lost to follow up
4	24	Ascending colon	T3N2aG2	Synchronous	×	11.62	28.8	+	16 months on follow up
5	35	Ascending colon with multiple polyps	T3N1aG2	Synchronous	×	24.2	19.2	_	6 months on follow-up
6	35	Sigmoid colon	T3N2aG2	Metachronous (8 months later)	Peritoneal deposits	45.2	5.8	_	8 months lost to follow up
7	38	Rectum	T3N1bG3	Synchronous	×	20.16	6.47	+	12 months follow up



one patient, solid cystic in four and cystic metastases in 2 patients.

Five-ten % of ovarian masses are metastatic and are frequently mistaken for primary [17, 18]. To differentiate primary ovarian neoplasms from metastatic lesions, histopathological features play an important role. Young and Scully proposed a classification based on histological aspects of metastatic ovarian cancers. They proposed that metastatic ovarian cancers show prominent garland and cribriform structures with intraluminal dirty necrosis, cytological atypia and high mitotic index [19]. In doubtful cases, immunohistochemistry may help in diagnosis. Lack of CA125 expression, expression of CK 20, vimentin and absent staining for CK 7 is present in most of the metastatic colonic neoplasms. In our study three patients, underwent immunohistochemistry for diagnosis of metastases using CK 7 and CK 20.

Whether oophorectomy improves overall survival and disease free survival is another question to be answered? Whether there is difference in survival in patients with synchronous and metachronous ovarian metastases? In a study done by Ramesh et al. of 180 patients with colorectal cancer, patients with metachronous metastases had better survival than synchronous metastases (20 months vs 10 months) [20]. In other study by Garrett et al., a retrospective analysis of ovarian metastases in 110 patients among 3776 female colorectal cancer patients at M. D. Anderson center, showed better survival in patients with metachronous metastases (mean survival of 50 months) compared to patients with synchronous metastases (mean survival of 39.4 months). The same study showed significant survival benefit in patients who underwent palliative oophorectomy for metachronous or synchronous disease compared to patients who did not undergo oophorectomy. But overall 5 year survival rate is very low in patients with ovarian metastases [21].

Most often in patients with ovarian metastases survival depends on disease elsewhere like peritoneal disease or distant metastases (apart from liver). Patients with disease elsewhere do not perform well compared to those with isolated ovarian metastases.

#### Conclusion

Ovarian metastases from colorectal cancer are rare and usually occur in younger patients. Patients who develop synchronous or metachronous metastases may need to be treated with palliative oophorectomy.

#### Conflicts of Interest Nil



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