Case study

Skin as a site of recurrence in carcinoma ovary- an unusual presentation.

Abstract: Cutaneous metastases from various malignancies have been reported in literature but skin as a site of recurrence in cancer ovary has been seldom reported. We hereby report one such case of a 47 year old, follow up case of ovarian cancer, which progressed after two lines of chemotherapy and presented with abdominal skin nodule as site of metastatic recurrence, nearly 32 months after diagnosis of ovarian cancer

Key-words: *cutaneous metastases, refractory ovarian cancer, recurrence*.

Introduction: Cutaneous metastasis is a late presentation in ovarian carcinoma which is rarely encountered. Heavy disease burden like bulky abdominal nodes or peritoneal carcinomatosis are known risk factors for this entity. The prognosis of such cases is uniformly poor and the gap between diagnosis of ovarian cancer and documentation of skin metastases is supposedly the most important prognostic factor for survival. The optimum line of management is not yet decided. We report here a similar case in a 47 year old female who developed skin recurrence nearly 32 months after diagnosis of ovarian cancer. Documentation of these rare cases is crucial to building an optimum line of management hopefully be in future.

Case report: A 47 year old female patient presented to our clinic in May, 2013 with complaints of pain abdomen and abdominal distension for last 3 months. On examination, the abdomen was tense, distended and per rectal examination revealed nodularity in Pouch of Douglas (PoD).Contrast enhanced CT (CECT) scan of abdomen done outside showed well-defined solid cystic lesion in left adnexa measuring 4.3x 4x5.7cm and multiple enhancing peritoneal deposits, largest 2.2x1cm .There was no pelvic or retroperitoneal lymphadenopathy; visceral organs were unaffected. Ascitic fluid tapping was done and cytology was suggestive of metastatic adenocarcinoma. Serum CA 125 was hugely elevated - 2051U/ml. The patient was evaluated by gynaecology oncology team and was referred for neo-adjuvant chemotherapy (NACT). Patient was started on three weekly NACT with

paclitaxel (175 mg/m2) and carboplatin (AUC 6) initially for 3 cycles and later on reassessment 3 more cycles was given. Post NACT, she underwent Total Abdominal Hysterectomy with Bilateral salpingo-oophorectomy and Infra-colic omentectomy in October, 2013. Post-operative histopathology revealed poorly differentiated serous carcinoma of left ovary. She received 2 more cycles with same chemotherapy regimen, last cycle in Dec, 2013. There was no evidence of residual disease in CECT abdomen done 6 weeks after chemotherapy and serum CA-125 level was 8 U/ml. Patient was loco-regionally disease free with CA-125 levels below 15U/ml till Sept, 2014 when pelvic examination revealed nodularity in the PoD. Serum CA-125 was raised to 555.9U/ml. Fine needle aspiration cytology (FNAC) from PoD mass came as metastatic high grade serous adenocarcinoma. CECT abdomen showed multiple peritoneal deposits in sub diaphragmatic and perihepatic regions. Second line chemotherapy regimen with liposomal doxorubicin (50 mg/m2) and carboplatin (AUC 6) q 4weekly was prescribed for 6 cycles, last cycle being completed in April, 2015. Local examination and CECT abdomen showed complete response & CA-125 was 30.46 IU/ml. Patient was once again kept on periodic follow up. In Jan 2016 a solitary firm nodule of 3x3 cm was detected on left lower flank which was non-tender and fixed to skin (Fig-1). Careful enquiry and review of operative records showed that the nodule didn't develop on the site of drain positioned during surgery nor was it close to incision sites.

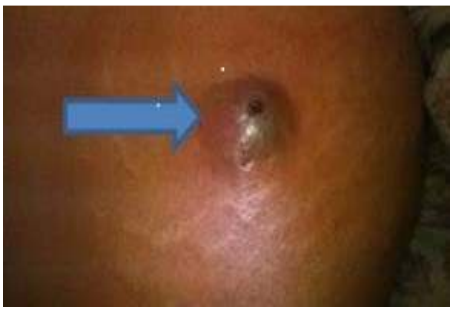

Fig1-Cutaneous nodule (Marked by arrow)

FNAC from the skin nodule came as adenocarcinoma metastatic (Fig -2A &2B).

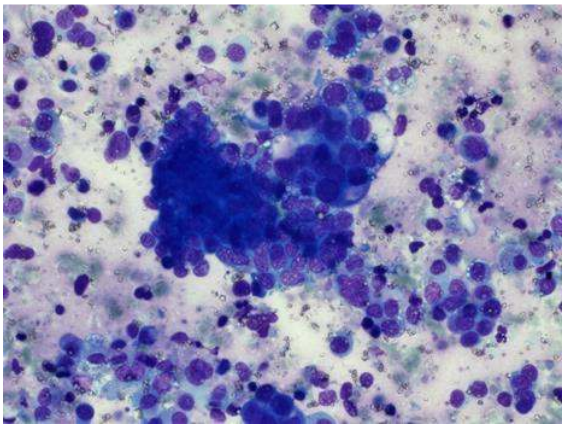

Fig. 2a-Micro-photograph showing loosely cohesive clusters as well as dispersed population of tumor cells having vacuolated cytoplasm (MGG x40X).

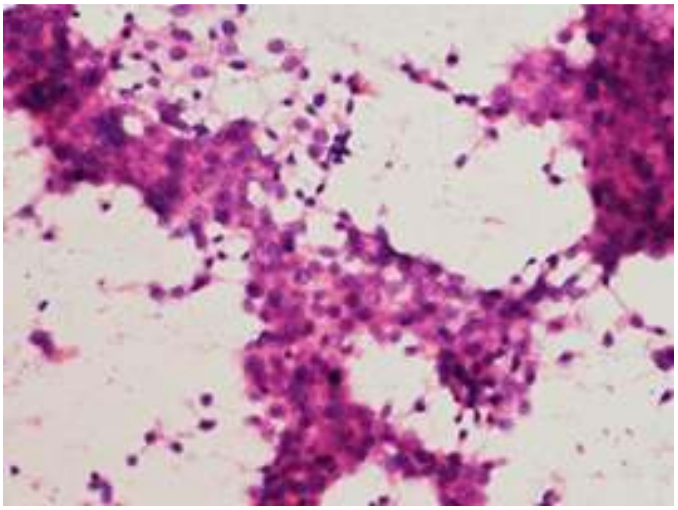

Fig.2b-Micro-photograph showing clusters of tumor cells showing moderate nuclear pleomorphism, coarse chromatin and prominent nucleoli (H&E x40X).

CECT abdomen in the same month showed a heterogeneously enhancing mass in PoD-7x7x4.1 cm (Fig-3).

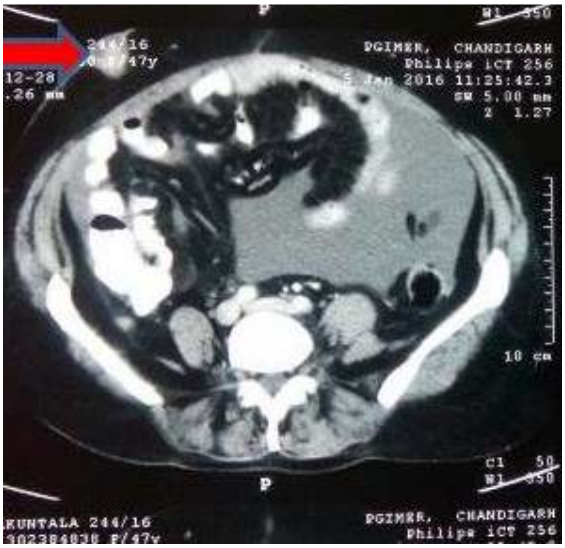

Fig 3-CECT showing cutaneous metastasis (red arrow).

Soft tissue deposits were seen in perihepatic and left sub phrenic region with gross ascites- all suggestive of peritoneal carcinomatosis. Patient was started on third line salvage chemotherapy with Gemcitabine (1gm/m2) and oxaliplatin (100 mg/m2) q 3 weekly. Post therapy patient has been kept on palliative and best supportive care with poor prognosis of the disease explained to her and her care-givers as not much significant clinical response could be achieved after completion of salvage therapy.

Discussion-

Cutaneous metastasis is a rare sequel of ovarian cancer with an incidence being reported in 2-3% of cases [1] .Cormio et al has described nine such cases in a retrospective review of 220 cases in a span of 10 years [2] .Other case series reports the incidence to be even less than 1%

[3, 4, 5].Most of these recurrences reportedly occurred in the scar sites or sites of drainage [4,5].The average time of appearance of skin metastases after the diagnosis of ovarian cancer has been reported to be 23.4 +/- 12 months (range 4 to 37) [2] .They may be single or multiple with a diameter between 0.5-3cm^2 .In our case, the lesion was solitary with a maximum diameter of 3cm. Dauplat et al has reported malignant ascites, peritoneal carcinomatosis, large metastatic disease within the abdomen, and retroperitoneal lymph node involvement at the time of the initial surgery to be significant risk factors for distant metastases[1] .Presence of malignant ascites and peritoneal deposits

were the risk factors in our case .In our case also, the cutaneous metastases appeared as late as nearly 32 months after diagnosis.However, the nodule didn't develop in scar/drainage sites.

Management of cutaneous metastases is mostly palliative and not well standardised. Systemic therapies include chemotherapy with pegylated liposomal doxorubicin or etoposide or hormonal agents like letrozole and tamoxifen[6, 7]. Local therapies like electrocoagulation, phototherapy, electro chemotherapy and topical Imiquimod have had various responses rates. In our case we tried with Gemcitabine-Oxaliplatin combination chemotherapy with minimal clinical response achieved on completion.

The prognosis is unanimously poor in all case series. The median survival after diagnosis of skin metastases was only 4 months in the series reported by Cormio et al [2] .The time interval till documentation of skin metastases is reportedly the single most important prognostic factor for survival [2].

This report emphasises on the fact that an oncologist must be aware of this entity during follow-up of ovarian cancers. Since standard line of management is not yet decided, documentation of this rare entity is much needed so as to investigate further therapeutic modalities that may benefit the patient in future.

Conclusion-

Skin is a potential site of recurrence in carcinoma ovary hence a thorough examination should be done in patients of carcinoma ovary on follow up.

Consent Disclaimer:

As per international standard or university standard written patient consent has been collected and preserved by the authors.

References:

1. Dauplat J, Hacker NF, Nieberg RK, Berek JS, Rose TP, Sagae S. Distant metastases in epithelial ovarian carcinoma. Cancer.1987; 60: 1561 – 1566.

2. Cormio G, Capotorto M, Vagno GD, Cazzola A, Carriero C, Selvaggi L. Skin metastases in ovarian carcinoma: A report of nine cases and review of literature. GynecolOncol. 2003;90:682–5.

3. Eckman I, Brodkin RH, Rickert RR. Cutaneous metastases from carcinoma of ovary.Cutis. 1994;54:348–50. [PubMed]

4. Robinson W.R., Beyer J., Griffin S., Kanjanavaikoon P. Extraperitoneal metastases from recurrent ovarian cancer. Int. J. Gynecol. Cancer. 2012;22(1):43–46. [PubMed]

5. Cheng B., Lu W., Xiaoyun W., YaXia C., Xie X. Extra-abdominal metastases from epithelial ovarian carcinoma: an analysis of 20 cases. Int. J. Gynecol. Cancer. 2009;19(4):611–614.

6. Rose P.G., Bleseing J.A., Mayer A.R. HomesleyHD. Prolonged oral etoposide as second line therapy for platinum resistant and platinum-sensitive ovarain carcinoma: a gynecologic oncology group study. J. Clin. Oncol. 1998;16:405–410.

7. Ramirez P.T., Schmeler K.M., Milam M.R. Efficacy of Letrozole in treatment of recurrent platinum- and taxane-resistant high grade cancer of the ovary or peritoneum. Gynecol. Oncol. 2008;110:56–59.