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# **RESEARCH ARTICLE**

# DEVELOPMENT OF GALLBLADDER CARCINOMA IN A CERVICAL CANCER SURVIVAL – A CASE REPORT

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#### **ABSTRACT**

Cervical cancer survivors have a higher propensity for the development of second cancer when compared to general population especially HPV, Smoking and radiation related cancer. In our report, unusual carcinoma like gallbladder cancer developed after 7 years in a non-smoker cervical cancer survivor treated with radical cholecystectomy and adjuvant chemotherapy. Till last reporting, she is doing well and leading a normal life with an ECOG 0.

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# INTRODUCTION

Cervical cancer is the fourth most common cancer in women worldwide. In India, cervical cancer is the second most common cancer in women accounting for 22.9% of all cancer cases in women and 12.1% of all cancer cases in both men and women. Cervical cancer is the 2<sup>nd</sup> largest cause of cancer mortality in India accounting for nearly 9.9% of all cancer related deaths in the country (Globocon 2012). Curative therapy for cervical cancer results in large numbers of long term survivors who develop second cancers very late in life. Radiation is an important cause of this increase and there is no evidence that risk returns to normal level (Kleinerman et al., 1995). Here, we present a case of carcinoma cervix post hysterectomy and post CT+RT in 2010 was on follow up, subsequently developed right hypochondrial pain in 2017 for which investigations were done and diagnosed as gallbladder cancer. Radical cholecystectomy was done, and adjuvant chemotherapy given. At present she is leading a normal life and her ECOG is 0.

**Case History:** 56-year-old female from district Begusarai presented to Mahavir Cancer Sansthan, Patna (India) on 20<sup>th</sup> May 2010 with a diagnosed case of cancer cervix.

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She had undergone TAH+BSO outside on 09th May 2010. Histopathology report showed squamous cell carcinoma. Grade IV. Pelvic lymphadenectomy was not done. External Beam Radiotherapy planned by Co-60. 50Gy/25#/2Gy per fraction was given between 28-05-2010 to 01-07-2010 with concurrent cisplatin 40mg/m<sup>2</sup> weekly 4 times. 2# CVSA (6 Gy per fraction) were given on 15-07-2010 and 22-07-2010. She tolerated whole treatment uneventfully, and she was kept on standard follow-up in Aug-Sep 2010. She was on regular follow up and was doing well. In Aug 2017, she developed right hypochondrial pain. The pain was progressive in nature. USG whole abdomen was done on 11-08-2017 at Mahavir Cancer Sansthan, which shows 24.5 x 30.3 mm size heterogeneous mass is seen in gallbladder. Subsequently, CT scan whole abdomen was done on 12-08-2017 which shows 30 x 28mm size heterogeneously enhancing mass is noted in fundus of the gallbladder. The lesion is infiltrating the hepatic surface. CA 19.9 > 1200.00 U/ml. Radical Cholecystectomy with resection of liver segment IVB, V, VI (anatomical resection) with hepatoduodenal lymph node dissection on 01-9-2017. Histopathology report showed Adenocarcinoma grade II, tumor infiltrates up to liver parenchyma. Serosa is involved by the tumor. Liver resection margin is free of tumor. 1/8 hepatoduodenal lymph node positive. 3/3 interaortocaval lymph node is negative. She was taken on adjuvant chemotherapy (Gemcitabine 1 gm/m<sup>2</sup> D1 and D8 + Cisplatin 75 mg/m<sup>2</sup> D1) on 18-09-2017. Last date of chemotherapy (C6D8) was 29-01-2018.





Fig. 1. CT scan abdomen showing GB Mass (Before radical cholecystectomy)

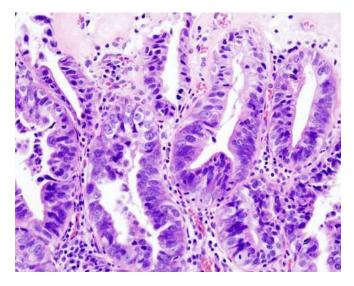


Fig.2. Adenocarcinoma grade II in GB specimen

She tolerated the whole chemotherapy very well and uneventfully. After completion of 6 # chemotherapy, CT scan whole abdomen was done, which shows normal report. She is now on follow up and doing well with ECOG 0.





Fig. 3. Post cholecystectomy and post adjuvant chemotherapy CT scan

# **DISCUSSION**

Cancer survivors often live with long-term consequences of the disease and its treatment, besides being at a higher risk of developing new primary cancers. This risk has been quantified to be 14% higher in cancer survivors in the U.S. when compared to the general population; for cervical cancer survivors this was 32% (Curtis, 2016). A report from Australia found a 24% increased risk after 23 years of followup, which was most pronounced in smoking-related cancers (Karahalios et al., 2009). To explore the long-term cancer risks of cervical cancer survivors, researchers evaluated information from cancer registries in Denmark, Finland, Norway, Sweden and the United States. The researchers conclude that risks of radiation-related, HPV-related, and smoking-related cancers are significantly increased among cervical cancer survivors (Chaturvedi et al., 2007). In Population-based study from the Taiwan, Netherlands and Korean Central Cancer Registry, the incidence of a second primary cancer increased after the diagnosis and treatment of cervical cancer, with an SIR of 1.36%, 1.8% and 1.08%

respectively (Chao-YuChen, 2012; Melina Arnold et al., 2014; Myong Cheol Lim, 2016). There was a greater risk for cancers of the esophagus, stomach, small intestine, rectum, lung, bone, non-melanoma skin, uterine corpus, vagina/vulva, bladder, kidney, and leukemia mainly due to HPV, smoking and treatment related. Korean central cancer registry and Taiwan Cancer registry which shows SIR of 0.96 and 1.00 respectively for developing biliary tract cancer in survivor of carcinoma cervix (Chao-Yu Chen et al., 2012; Myong Cheol Lim et al., 2016). In our report the patient was on regular follow-up for 7 years, then he developed gallbladder cancer. Since the patient is non-smoker, gallbladder was out of radiation field and also there is no any direct relation of HPV in gallbladder cancer, so, there must be some another cause for the development of carcinoma gallbladder. Northeastern states of India have different ethnicity and lifestyles, food-habits, tobacco consumption from rest of the country. So, gallbladder cancer has serious impact in North-eastern states (Amit Das, 2016). Unisa S et al. in a study concluded that a higher risk of GBD was observed in older, multiparous women and men with diabetes, intake of chickpeas, unsafe water and villages with heavy metal water pollution (Unisa, 2011). Higher Incidence of gallbladder cancer in eastern Uttar Pradesh and western Bihar regions of India suggests that environmental factors might be playing an important role in its causation. Both these regions lie downstream of the river Ganges which is the main source of water for all uses such as drinking water and for irrigation. The river Ganges receives an extremely high load of pollutants in the form of untreated domestic sewage, industrial and agricultural effluents containing aromatic hydrocarbons, nitrosamines and chemicals such as nitrates and nitrites which are by-products from domestic sewage. Pesticides which are frequently used in agricultural industry can also play a role in Ca GB. Typhoid infection is prevalent in this region which may also be associated with the gallbladder carcinogenesis. Lifestyle and smoking have also been correlated with the Ca GB. Adulteration in our cooking oil (mustard) by sanguinarine and diethylnitrosamine has also been found to be linked with Ca GB. It is possible that carcinoma of the gallbladder is the disease of multifactorial etiology (Ruhi Dixit, 2014).

### Conclusion

The incidence of a second primary cancer significantly increased after the diagnosis and treatment of cervical cancer especially HPV, smoking and treatment related cancers. But unusual cancer like gallbladder carcinoma can also develop. So, cancer surveillance should continue among cervical cancer survivors and early investigation for new symptom can diagnose a second cancer in very early stage and treatment started promptly.

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