Case Report

Synchronous HPV-associated cancer of the cervix and anal canal in a non-HIV infected patient treated simultaneously

Bhavana Rai, Promod Singh, Firuza Darius Patel, Suresh Sharma, Nalini Gupta[1], Mini P Singh[2]

Departments of Radiotherapy and Regional Cancer Centre, [1]Cytology and Gynaecology Pathology, [2]Virology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

ABSTRACT

Synchronous malignancies are uncommon. The oncogenic viruses like Human Papilloma Virus (HPV) 16 and 18 have been implicated in the development of cancers of the cervix and anal canal and an increased risk occurs in Human Immunodeficiency Virus-infected (HIV) individuals. Though cervical screening for HPV infection is recommended in female patients with anal cancers, synchronous presentation of cancer cervix and anal canal is rare. We present a case of a 72-year-old lady with synchronous cancer cervix and anal canal with HPV 16 positivity by polymerase chain reaction (PCR) treated with external radiotherapy, followed by brachytherapy to both the sites.

Key words: Anal canal, cancer, cervix, HPV, synchronous

INTRODUCTION

A strong causal relationship between infection with Human Papilloma Virus (HPV) and cancers exist. About 90% of cervical cancers and 70% of cancers of the anal canal are associated with HPV 16, 18 infections. Though cancer of the cervix is one of the commonest malignancies in women, cancer of the anal canal is relatively uncommon.[1] An increased risk of cervical cancers and anal cancers are seen in HIV-infected patients and development of multiple malignancies is not uncommon.[2] However, synchronous malignancy of the anal canal and cancer cervix is extremely rare and to the best of our knowledge has not been reported so far. We, hereby, present the first case of synchronous cancer cervix and anal canal positive for HPV 16 in a non-HIV infected patient treated simultaneously.

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CASE REPORT

A 72-year-old, HIV-negative female patient was presented with complaints of intermittent bleeding per vaginum and rectum along with itching in the anal region for one year. The patient was a post menopausal lady with hypertension and had six living children. There was no history of multiple sexual partners or of anal intercourse. Her vaginal examination revealed a 3 × 3 cm ulcero proliferative growth at the cervix with involvement of the right lateral vaginal wall in the upper third. Bilateral parametria appeared indurated in medial third. On rectal examination, there was a ulcero proliferative growth felt at the anal verge extending upto 4 cm along the lateral wall of the anal canal. Both these biopsy samples were processed for the detection of HPV 16 by polymerase chain reaction (PCR) and were found to be positive using type specific primers [Figures 1 and 2]. Computer-aided Tomograohy (CT) scan of the abdomen and pelvis done was suggestive of a growth in the cervix. A soft tissue thickening was seen in the anal canal along the right lateral wall extending upto 3.5 cm from the anal verge. There was no associated pelvic lymphadenopathy. The CT of the chest was normal. The cancer of the cervix was staged as FIGO stage II B and the cancer on the anal canal was staged as Stage II (T2N0M0).

Address for correspondence: Dr. Bhavana Rai, Department of Radiotherapy and Regional Cancer Centre, Post Graduate Institute of Medical Education and Research, Chandigarh - 160 012, India. E-mail: bhavrai@yahoo.com

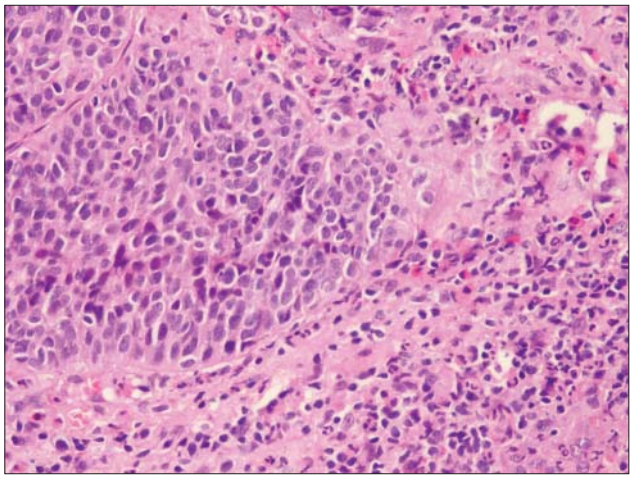

Figure 1: Micro-photographs showing sheets and nests of tumor cells separated by fibrous septae. The tumor cells show squamoid differentiation (H and E, ×40)

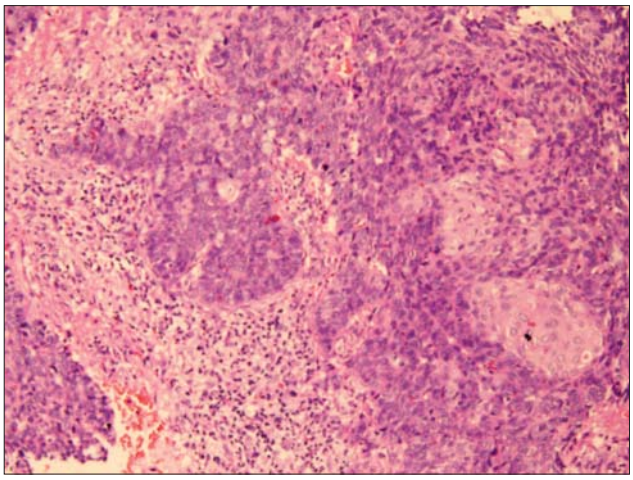

Figure 2: Micro-photographs showing sheets, cords and nests of tumor cells separated by fibrous septae. The tumor cells show squamoid differentiation (H and E, ×40)

The patient was planned for external radiotherapy with 15 MV photons with parallel opposed anterior posterior fields. The upper border of the field was kept at L4-L5 junction and the lower border was 2 cm below the anal verge. Total dose planned was 46 Gy in 23 fractions delivered over four and a half weeks. Keeping in mind the age of the patient and the large treatment field, she was not given concurrent chemotherapy. A treatment gap of one week was given in view of grade 3 reactions in the perineum. The patient was assessed for brachytherapy towards the end of external radiation and was found suitable for brachytherapy to both the sites. Prior to the brachytherapy procedure, an examination under anaesthesia was performed which revealed minimal residual disease around the external os involving both the lips of cervix. Bilateral parametria were smooth. On rectal examination, there was 1.5 cm induration along the right lateral wall of anal canal starting from the anal verge. An intracavitary application was done with a high dose rate (HDR) micro selectron applicator for the cervical cancer. This was followed by a simultaneous interstitial implant in the anal canal. Total five interstial needles were implanted from 6-8'ocloock position in the anal canal. A CT-based treatment planning was done using the Oncentra software. A dose of 9 Gy HDR was planned per fraction and two fractions were planned one week apart for the intracavitary brachytherapy. For the anal implant a dose of 3 Gy (HDR) per fraction in six fractions were planned over three days. Two fractions were delivered per day with a minimum interval of six hours. The intracavitary brachytherapy dose was delivered on the day of the procedure. The treatment for the interstitial implant for the anal canal began from the next day. The second fraction of the intracavitary brachytherapy implant was done after one week of the first intracavitary brachytherapy implant. The patient showed a good response. At one-year follow up, the patient continues to be disease-free without any treatment related complications.

DISCUSSION

Multiple primary malignant tumors in a single patient are relatively rare with reported incidence ranging from 0.73-11.7%.[3] They may be synchronous or metachronous depending on the interval between their diagnosis. They are classified into four types: Multicentric, if two distinct carcinoma arise in the same organ or tissue; systemic, if they arise on anatomically or functionally allied organs of the same system (e.g., colon and rectum); in paired organs, as in the breasts; and random, if they occur as a co-incidental association in unrelated sites.[4] In our patient, both the tumors occurred at random sites. Cancers of cervix and anal canal have been associated with HIV infection. Though the association between cancer and Human Immunodeficiency Virus (HIV) is not completely understood, but the link likely depends on the weakened immune system. Many patients affected with HIV are also infected with other oncogenic viruses like the Human Papilloma Virus (HPV) and Epstein Barr Virus (EBV), which have been implicated in the development of these cancers.[2] HPV infections are one of the most common sexually transmitted infections. Of the few subtypes categorized as high-risk oncogenic HPV, HPV 16 and 18 are the most common subtypes implicated in the development of cancer.[5] Our patient was a HIV-negative and was not immunocompromised. However, HPV 16 was demonstrated by PCR in both the tissue specimens and this could have played an important role in the pathogenesis of both the cancers. Studies have shown that patients with high initial HPV viral load can be favorably treated with radiotherapy alone and may have a better clinical outcome as compared to HPV-negative patients.[6] Our patient also, who was treated with radiotherapy alone, saw a good response with complete clinical regression of both the

cancers and she continues to be disease-free at last follow up for one year.

In conclusion, synchronous cancer of the cervix and anal canal is extremely rare. The prevalence of HPV is currently on high and its prevention and detection constitutes a major medical challenge. The HPV vaccine may help in reducing the incidence of disease in the near future and contribute significantly in reducing cancer related mortality.

REFERENCES

1. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer 2010;127,2893-917.
2. Engels EA, Biggar RJ, Hall HI, Cross H, Crutchfield A, Finch JL, *et al*. Cancer risk in people infected with human immunodeficiency virus in the United States. Int J Cancer 2008;123:187-94.
3. Demandante CG, Troyer DA, Miles TP. Multiple primary malignant neoplasms: Case report and a comprehensive review of the literature. Am J Clin Oncol 2003;26:79-83.
4. Moertel CG. Multiple primary malignant neoplasms: Historical perspectives. Cancer 1977;40:1786-92.
5. Schiffman M, Castle PE, Jeronimo J, Rodriguez AC, Wacholder S. Human papillomavirus and cervical cancer. Lancet 2007;370:890-907.
6. Datta NR, Kumar P, Singh S, Gupta D, Srivastava A, Dhole TN, *et al*. Does pretreatment human papillomavirus (HPV) titers predict radiation response and survival outcomes in cancer cervix?: A pilot study. Gynecol Oncol 2006;103:100-5.

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