ORIGINAL ARTICLE

Coexisting genital malignancies with tuberculosis: A case series with review of literature

Avantika Gupta, Sangeeta Gupta, Usha Manaktala, Nita Khurana

Department of Obstetrics and Gynaecology, Maulana Azad Medical College, New Delhi, India

ABSTRACT

Objective: To study a case series of genital malignancies coexisting with genital tuberculosis.
Materials and Methods: A series of three cases with known genital malignancies were found to have coexisting genital tuberculosis on subsequent workup.
Results: First case was a 45 years old lady who underwent staging laparotomy for ovarian cancer. On histopathology examination, there was coexisting tuberculosis with papillary serous carcinoma. Second case was 53 years old postmenopausal lady who underwent extrafascial hysterectomy along with pelvic lymph node dissection. Histopathology showed tubercular changes along with endometrial malignancy. Third patient was a 50 years old postmenopausal lady with stage IIA carcinoma of cervix. She underwent radical hysterectomy and histopathology revealed tubercular changes in pelvic lymph nodes. All patients were given antitubercular therapy for 9 months in postoperative period along with adjuvant therapy.
Conclusion: Although diagnosed as an incidental finding in the case series, genital tuberculosis may present in patients with malignancies as a result of immunosupression.

Key Words: Carcinoma cervix, endometrial carcinoma, tuberculosis

INTRODUCTION

The precise incidence of genital tuberculosis cannot be determined with certainty as some cases are asymptomatic and uncovered accidentally during investigation. In India, the incidence of genital tuberculosis is about 18%.[1] Peritoneal tuberculosis has common symptoms with advanced ovarian carcinoma including pelvic pain, mass, ascites, and elevated CA-125 levels. We present here three different cases of coexisting genital carcinoma along with tuberculosis diagnosed on histopathology. Tuberculosis complicating malignant disease may occur in regions with a high prevalence of disease; with a resurgence of tuberculosis worldwide, this association may not be uncommon. The diagnosis and treatment of tuberculosis in a patient with cancer assume importance as a high morbidity has been seen in patients with coexistent disease. Whether tuberculosis, a chronic inflammatory condition, facilitates carcinogenesis is yet to be determined.

Address for Correspondence: Dr. Avantika Gupta, House No. 93-94, Pocket 2, Sector 22, Rohini, New Delhi - 110 085, India.
E-mail: dravantikagupta@gmail.com

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CASE REPORTS

Case 1

We present a case of a 45-year-old para 4 female who reported to the gynecological outpatient department with a complaint of lump abdomen since 1 year, which

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was gradually increasing in size and had reached up to umbilicus. There was associated dull aching pelvic pain and amenorrhea for last 7 months. On examination, she had a body mass index (BMI) of 22.5 with minimal pallor and no lymphadenopathy. On bimanual examination, a firm mass of size approximately 15 cm × 12 cm × 12 cm felt arising from left adnexa. Her hemoglobin was 9.7 gm%, total leukocyte count of 11,900/mm^3, and erythrocyte sedimentation rate (ESR) of 30 mm in 1st h. CA-125 level was raised to 1000 units/mL. Liver function test and blood sugars were normal. Chest X-ray showed normal findings. Her HIV serology was negative. Uterus and the right ovary were normal, and there was no associated ascites. Magnetic resonance imaging (MRI) pelvis was done which also showed a smoothly marginated complex multiseptated predominantly cystic lesion with solid component within the dependent portion, arising from the left ovary and was 10.6 cm × 14.3 cm × 16.8 cm in size. There was no ascites. Her risk of malignancy index 2 score was calculated to 4000.

A provisional diagnosis of ovarian malignancy was made and a staging laparotomy followed by total abdominal hysterectomy and optimum debulking surgery was performed in this patient. Intraoperatively, there was a large right-sided ovarian sized 15 cm × 15 cm × 12 cm occupying almost whole of the pelvis. The capsule was intact with large feeding vessels over surface. Large gut was densely adherent to the mass, which had to be separated. Uterine surface and left-sided fallopian tube showed deposits. Right fallopian tube and ovary looked normal. Cut section of the tumor showed multiple septa with irregular surface inside. Thick cheesy material was expressed from the tumor and a solid area of size 6 cm × 3 cm × 3 cm was present inside the tumor. Histopathology report showed moderately differentiated papillary serous cystadenocarcinoma involving left ovary spreading to the ipsilateral fallopian tube. The tumor involved the capsule which showed focal dense chronic inflammation comprising caseating epithelioid granulomas indicative of tuberculosis [Figure 1]. Right ovary was unremarkable. Right fallopian tube showed multiple epithelioid granulomas, few with caseation suggestive of tuberculosis [Figure 2]. Ziehl–Neelsen stain for acid-fast bacilli was negative. Parametrium and uterus were free of tumor and tubercular changes. Omentum was free of tumor but showed caseating granulomas.

Finally, Stage IIA ovarian carcinoma was made. Postoperatively, skin reaction to injection of purified protein derivative was of 20 mm. The WHO Category 1 antitubercular therapy was started on postoperative day 10 and one cycle of chemotherapy comprising carboplatin and paclitaxel was given. CA-125 levels after 1st cycle of chemotherapy decreased to 400 U/mL. She has taken antitubercular treatment for 6 months and received 6 cycles of chemotherapy after surgery and is doing fine.

Case 2

A 53-year-old female postmenopausal since 5–6 years presented with three episodes of postmenopausal bleeding over the last 6 months. She had a significant weight loss over the last 1 year. On examination, she had a BMI of 21.0 with mild pallor and no lymphadenopathy. An endometrial biopsy was performed which showed endometrial mucinous adenocarcinoma. Her hemoglobin was 9.0 gm%, total leukocyte count of 12,000/mm^3, and an ESR of 35 mm in 1st h. Her liver function test, kidney function test, and blood sugars were within normal limits. Chest X-ray showed normal findings. She was seronegative for HIV. Transvaginal ultrasound showed an enlarged uterus of size 10 cm × 5 cm × 4 cm with disrupted endomyometrial junction. MRI also confirmed the findings suggestive of endometrial carcinoma. She underwent staging laparotomy followed by extrafascial hysterectomy along with pelvic lymphadenectomy. Cut section of the uterus showed growth inside the endometrial cavity invading the myometrium.

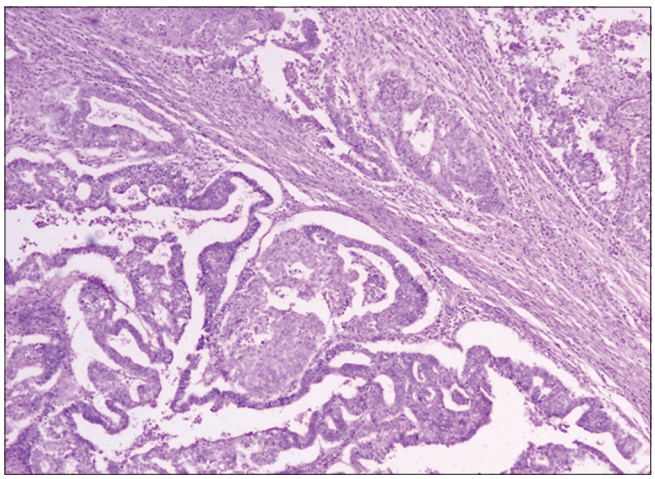

Figure 1: Ovarian tissue showing moderately differentiated papillary serous adenocarcinoma along with features of tuberculosis

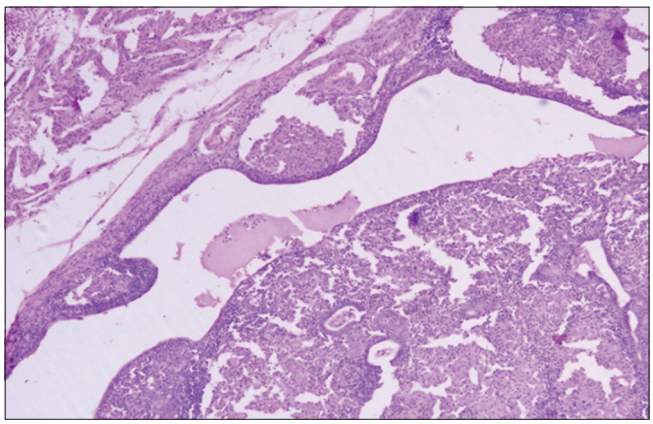

Figure 2: Tubal mucosa showing infiltration of carcinoma along with tubercular changes

Final histopathology showed Grade III mucinous adenocarcinoma involving up to half of the myometrium. However, the adnexa, parametrium, and ovaries were free of invasion. Six out of 13 lymph nodes dissected showed caseation along with epithelioid granulomas without any evidence of malignancy. Ziehl–Neelsen stain for acid-fast bacilli was, however, negative. A final diagnosis of Stage IB Grade III endometrial mucinous adenocarcinoma with coexisting tuberculosis was made. The WHO Category I antitubercular therapy was started on postoperative day 10, and she received adjuvant radiotherapy. She took antitubercular therapy for 6 months along with adjuvant treatment for carcinoma and is doing well on follow-up.

Case 3

A 50-year-old postmenopausal female presented with a complaint of postmenopausal bleeding since 3 months. She had minimal pallor and no lymphadenopathy. On per speculum examination, growth was seen on the anterior lip of cervix of size 2 cm × 2 cm. All the fornices, bilateral parametria, and rectal mucosa were free of tumor growth. Punch biopsy from the cervical growth revealed well-differentiated squamous cell carcinoma. A final diagnosis of Stage IB carcinoma cervix was made. Her hemoglobin was 10.2 gm% and a thin-layer chromatography of 7800/mm^3. Her chest X-ray was unremarkable, and her liver function test, kidney function test, and blood sugar were within normal range. Her HIV test was negative. She underwent modified radical hysterectomy for carcinoma cervix. Intraoperatively, tumor was found limited to only cervix. Vaginal cuff, bilateral parametria, and adnexa were free of tumor. Histopathology of the lymph nodes showed tubercular changes without any malignant involvement. Ziehl–Neelsen stain for acid-fast bacilli was, however, negative. She took antitubercular therapy under the WHO Category I for 6 months and is doing well on follow-up.

DISCUSSION

Pelvic tuberculosis infection is usually caused by reactivation of organisms from systemic distribution of *Mycobacterium tuberculosis* during primary infection. The most common organ involved in genital tuberculosis is fallopian tube (95%–100%) followed by endometrium (50%–60%), ovary (20%–30%), cervix (5%–15%), and vulva and vagina (1%).[2] The symptoms of chronic pelvic pain, abdominal mass, and weight loss along with the formation of adnexal mass with or without ascites can be present in both pelvic tuberculosis and ovarian carcinoma. Thus, it can be difficult to distinguish both the conditions. Various authors have reported pelvic tuberculosis mimicking an advanced ovarian carcinoma;[3-11] however, none reported coexistence of ovarian carcinoma with tuberculosis.

First case presented with a complex adnexal mass and elevated CA-125 levels which led us to the diagnosis of ovarian cancer preoperatively. The diagnosis of coexisting underlying pelvic tuberculosis was made on histopathological evaluation. The presence of epithelioid granulomas along with caseation confirmed the presence of tuberculosis.

Whether tuberculosis, a chronic inflammatory condition, facilitates carcinogenesis is yet to be determined. The coexistence of tuberculosis and cancer cervix has been reported by very few authors. Yamabe *et al*. reported the coexistence of carcinoma cervix with tuberculosis diagnosed on histopathology in 1972.[12] Similarly, Hsu *et al*. reported two cases from China in 1985, where both the cases presented with postmenopausal bleeding.[13] Rajaram *et al*. reported a case of carcinoma cervix with coexisting endometrial tuberculosis in 2004.[14]

Even coexisting endometrioid adenocarcinoma and endometrial tuberculosis have been reported as an extremely rare condition. Due to rarity of the association, data regarding outcome of such patients, the influence of one condition over the other as well as survival are unavailable. In 1995, Castelo-Branco *et al*. reported a case of primary adenocarcinoma of the endometrium associated with genital tuberculosis.[15] Similar case was reported by Saygili *et al*. in 2002.[16]

It is controversial whether the coexistence of genital malignancy and tuberculosis is an incidental finding or whether cancerous cachexia offers a good nutritional basis for dormant tuberculosis bacilli to survive or whether carcinoma was superimposed on chronic progressive tuberculosis. Usually, the patients are cachectic on presentation as both the malignancy and tuberculosis cause cachexia. Cancer cervix has been included in the list of acquired immune deficiency syndrome-defining illnesses in patients infected with HIV and tuberculosis too has resurged with the HIV pandemic. The immune suppression caused by HIV infection is a risk factor for the development of cancer cervix as well as tuberculosis, thus cancer cervix occurring along with tuberculosis may increase in the HIV era. However, all the above three patients were HIV negative. Data regarding outcome of such patients, the influence of one condition over the other as well as survival are unavailable due to the rarity of the association. Thus, a regular follow-up of such patients is necessary.

Although we could not show an acid-fast microorganism by Ziehl–Neelsen stain from the specimens obtained at laparotomy in any of the cases, histological findings confirmed tuberculosis along with carcinoma. Since genital

tuberculosis is a paucibacillary form of the disease, smears and cultures are usually negative. Microscopic examination of acid-fast bacilli requires at least 10,000 organisms/mL in the sample.[17] Although polymerase chain reaction DNA is a rapid and sensitive molecular method DNA for diagnosing *M. tuberculosis* in extrapulmonary samples, it was not done as it is not routinely performed at our institution.

CONCLUSION

Further research is needed to determine if tubercular infection being a chronic inflammatory condition facilitates carcinogenesis. Since coexisting tuberculosis with carcinoma is a histopathological diagnosis, it is important to keep its diagnosis in mind while reporting genital cancer.

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Conflicts of interest
There are no conflicts of interest.

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