Three in a row: A case series of cervical tuberculosis*

By Angelynn Santos Sianghio, MD and Elizabeth Espino-Strebel, MD, FPOGS, FSGOP

Department of Obstetrics and Gynecology, San Juan de Dios Educational Foundation, Inc. Hospital

ABSTRACT

Cases of cervical lesions have been rising steadily in the past decades. From inflammation to carcinogenesis, the cervix is never really spared of disease. In the presence of a cervical mass, malignancy is always a consideration. In this paper, we present three cases of cervical tuberculosis that were diagnosed in a tertiary private hospital in Pasay City. Women in their 3rd and 4th decade of life presenting with post coital spotting, copious vaginal discharge and amenorrhea were examined: The cervix was converted to a nodular friable mass, with extension to the fornices. On rectovaginal exam, both parametria were nodular but free from the pelvic sidewall. The primary consideration was a probable cervical carcinoma stage IIB. On tissue biopsy and further testing, cervical tuberculosis was confirmed. Quadruple anti-Koch's therapy was initiated, to which clearing of the cervix with decrease discharge was noted.

Keywords: Anti-Koch's therapy, Cervical tuberculosis, Epitheloid cells, Langhan's Giant cells, Tuberculosis (TB)

INTRODUCTION

Tuberculosis has long been plaguing men. It was once regarded as a fatal "wasting" disease until in 1952 when it was deemed curable with the discovery of anti-Koch's medications.

In the 17th century, genital tract tuberculosis comprised 7.7% of all cases of TB, which increased to 5-25% in the 20th century.[2]

According to the Global tuberculosis report of 2016, 6.1 million new TB cases were detected and reported worldwide; 18% of which came from the Philippines. Thirty-four percent of the 324,000 newly diagnosed cases of tuberculosis comprised of females, 87% percent belonging to the child-bearing age.[1]

TB mimics carcinoma, and is often times misdiagnosed as a malignancy. Meticulous history-taking and a high index of suspicion, coupled with laboratory examinations, aid in distinguishing between these two disease entities.

Among women, genital tuberculosis represents 5-10% of non-pulmonary cases. Cervical involvement appears in 5-15% of all cases of female genital tuberculosis, i.e. 0.1-0.65% of all tuberculosis cases.[3] Low detection rates and report rates for cervical tuberculosis may be due to its asymptomatic period. The value of ultrasound and other imaging studies are limited, compared to histopathologic diagnosis.

CASE REPORTS

Case A

A 39 year-old G2P2 (2002) came in due to post coital spotting of 4 months' duration, associated with copious non-foul smelling vaginal secretions. She denies hypogastric pain, night sweats, chronic cough, weight loss or anorexia. Previous pap smears were normal. She had no previous surgery or exposure to radiation. There was no history of malignancy in the family. Patient recounts exposure to pulmonary TB 3 years prior, as primary caregiver to her 6 year-old son. The patient was regularly menstruating and denies intermenstrual spotting or prolonged vaginal bleeding. Two pregnancies were carried to term and delivered vaginally with no complications. There was no period of infertility recounted. The patient had her coitarche at 24 years old with one lifetime sexual partner. She had been married for 12 years to a 47 year-old seaman and claims to have oral contraceptive pill intake for 3 years. The patient is a non-smoker and a non-alcoholic beverage drinker. On physical examination, BMI was 24. There were no palpable preauricular and supraclavicular lymph nodes. No neck masses noted. Chest and abdomen were unremarkable, no enlarged or palpable inguinal lymph nodes. On pelvic examination, there was a nodular hyperaemic periurethral mass measuring 1x1cm, which does not bleed easily. The cervix was converted to a nodular friable mass measuring 4x6cm with extension to the fornix from 1 o'clock to 7 o' clock position. On rectovaginal examination, both parametria were nodular but free. Patient underwent cervical biopsy with a primary consideration of cervical carcinoma stage IIB. Upon histopathologic confirmation, caseous necrosis and Langhan giant cells were noted, supporting the diagnosis

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of tuberculosis. Further work ups were done, revealing multiple ill-defined densities with nodular configuration in both upper lungs in chest radiographic studies. Sputum was positive for AFB at 9-10/100hpf. Urine and stool were negative for AFB. Transvaginal ultrasound revealed a hyperechoic cervical lesion with some hypoechoicities looking like moth-eaten structures. The endometrium was thin with probable calcifications. The ovaries were normal. She was started on quadruple anti-Koch's therapy and responded well to treatment. Upon follow up after 8 months of medication, the patient reports general improvement of well-being, with resolution of postcoital vaginal bleeding and vaginal discharge. There was likewise a decrease in size of the cervical and periurethral masses. She was advised continuation of treatment for 9 months, with interval repeat chest x-rays, pelvic examination, transvaginal ultrasound, as well as colposcopic examination to monitor response and effectivity of treatment.

Case B

A 28 year-old nulligravid came in due to yellowish discharge of two years duration however no consult done until one year prior when an increase in the amount of discharge, now foul smelling with associated post coital spotting was noted. Initial consult at a private clinic revealed unremarkable pelvic findings. Ultrasound revealed normal anteverted uterus with proliferative endometrium of bilateral ovaries not delineated with note of two masses, both with complex echoes tender to probe manipulation and with irregular shape and bordered by fluid. The left mass measured 7.31x6.37x3.78cm while the right mass measured 7.59x7.90x5.96cm. A cystic anechoic thick walled mass with cogwheel pattern at the superior pole of the right pelvoabdominal mass measuring 2.82x2.74x2.34cm. Antibiotics for PID was started. Repeat TVS yielded same results hence a primary consideration of cervical carcinoma with metastasis was inferred: She was referred to a gynecologic oncologist, however, was lost to follow up. Six months prior, consult at our institution due to persistence of copious foul smelling discharge, now with associated increasing abdominal girth and post coital spotting. No exposure to tuberculosis was noted on family members or partner. Coitarche was at 22 years old with 2 sexual partners. No menstrual irregularities noted. On examination, BMI was 24, no anterior neck masses seen. A firm moveable infraumbilical mass measuring 10x7cm was noted. The a note of nodular fungating mass at the ectocervix; internal examination revealed that the cervix was converted to a 2x2cm nodular fungating mass with smooth fornices noted. Rectovaginal examination noted the left parametria was smooth, shortened but free while the right parametria was smooth and pliable. Repeat TVS revealed a normal sized uterus with rich color flow, thin endometrium of 0.29cm, a pelvoabdominal mass measuring 8.96x4.10x8.79cm with 1.58cm cystic anechoic thin walled area at the posterior end, within the mass is seemingly normal ovarian tissue. Cervical biopsy was done and a referral to a gyne-oncologist was made. Plans of trachelorrhapy was disclosed. Histopathology then revealed chronic granulomatous inflammation consistent with tuberculosis. Slide review was concurrent with previous reading: acute on chronic granulomatous endocervicitis with microglandular hyperplasia and focal langhan's giant cells favour a tuberculous process. Chest Xray, as well as urine, stool and sputum AFB were unremarkable. Patient was referred to infectious disease specialist where quadruple therapy was started. Monthly pelvic examination revealed gradual resolution of the fungating mass as well as the vaginal discharge. She now claims to whitish non foul smelling discharge. Continuation of treatment was advised and partner work up was recommended. Patient is desirous of pregnancy and was advised TVS after 6 months of medications to monitor effectivity of treatment, confirm the possibility of conceiving, and predict the probability of ectopic pregnancy. TVS showed a normal sized uterus with secretory endometrium, normal right ovary with corpus luteum, normal left ovary, left adnexal mass 6.68x3.24x5.86cm and right adnexal mass 8.71x3.53x8.62cm, both with low to medium level echoes within. She was then advised to delay pregnancy until complete resolution of symptoms and further work ups be made. Future plans include diagnostic laparoscopy for persistent disease or hysteroscopy once complete resolution was noted.

Case C

A 37 year-old G3P3 (3003) consulted the outpatient department for amenorrhea of 5 years duration. The patient sought initial consult at a tertiary hospital where she was given Progesterone pills however no response was noted. Two months prior, clear watery, non-foul smelling discharge was noted. She denies weight loss or loss of appetite, no vaginal spotting, no dyspareunia or post coital bleeding. The patient noted copious yellowish, foul smelling discharge one month prior, using 2 fully soaked panty liners per day. No consult done until one day prior when post coital spotting was noted. All pregnancies were carried to term and delivered vaginally without complications by a traditional birth attendant at home. On physical examination, BMI was equivalent to 18.2. No neck masses or palpable lymphnodes noted. Chest, lung, and abdomen examinations were unremarkable. Pelvic exam revealed the cervix was friable with a 3x2cm fungating mass that easily bleeds with purulent yellowish

discharge. On internal examination the cervix was parous and nodular, the uterus was asymmetrically enlarged to 12 weeks size and adnexa were unremarkable. Cervical carcinoma stage IIb was considered, the patient was advised of a series of medical and surgical management. Transvaginal sonography revealed unremarkable cervix, uterus and adnexa. Cervical biopsy was submitted: note of necrotic tissue with acute and chronic inflammation, no malignancy was described. Histopathologic diagnosis was non-caseating granulomatous inflammation, consider tuberculosis as primary cause. Patient was advised further work up however was lost to follow up.

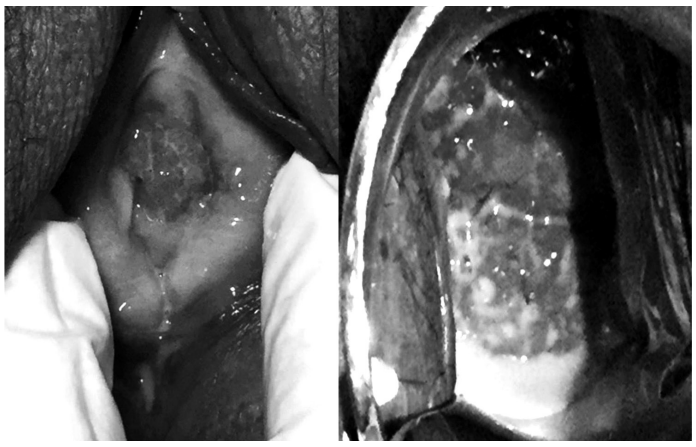


Figure 1. Pre-treatment (A) Periurethral mass (B) Cervical lesion of Case A

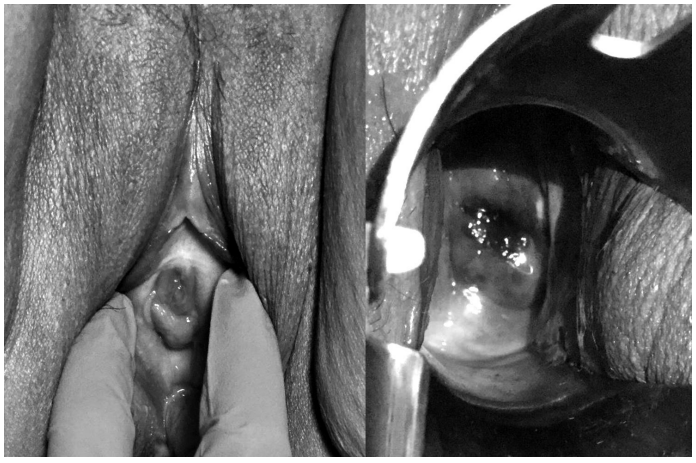


Figure 1. And Post-treatment of quadruple anti-Koch's medications for 8 months (C) Periurethral mass (D) Cervix

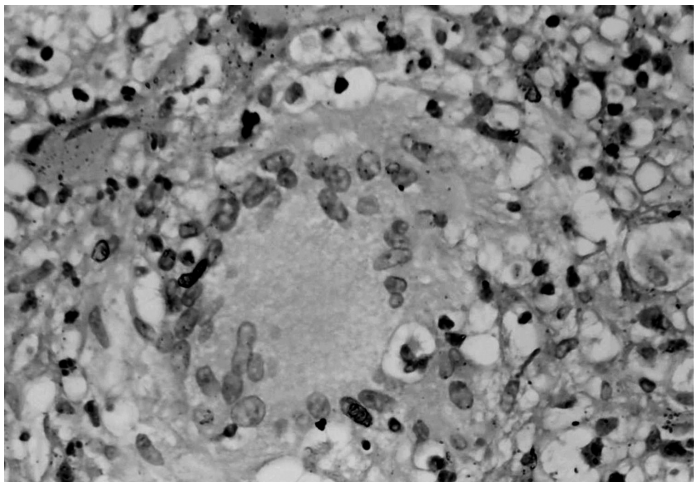


Figure 2. Langhan's Giant Cell, a walling-off response to avoid metastasis with spindle cells and fibroblasts

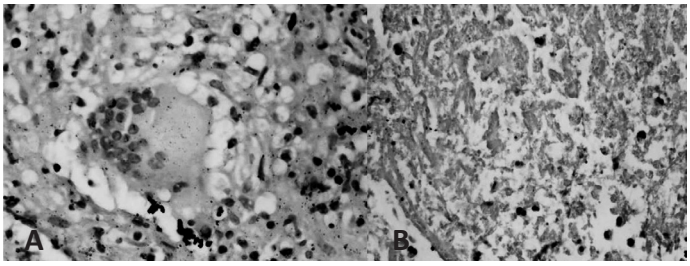
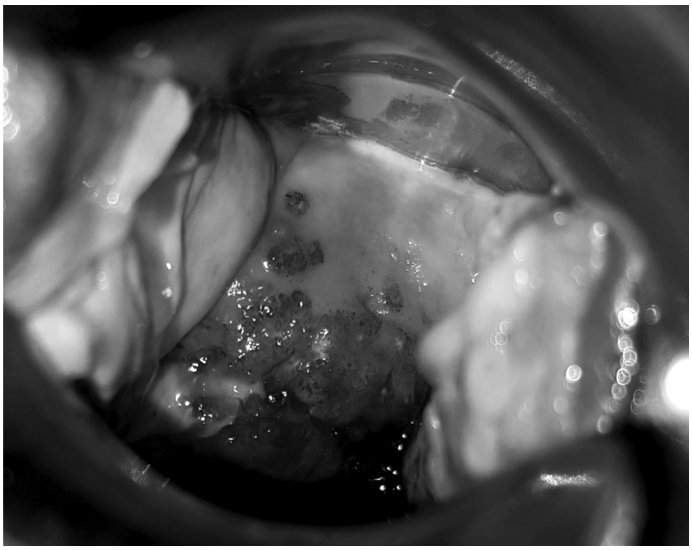


Figure 3. (A) Epitheloid Cells, Histologic Hallmark for tuberculosis and (B) Caseous Necrosis



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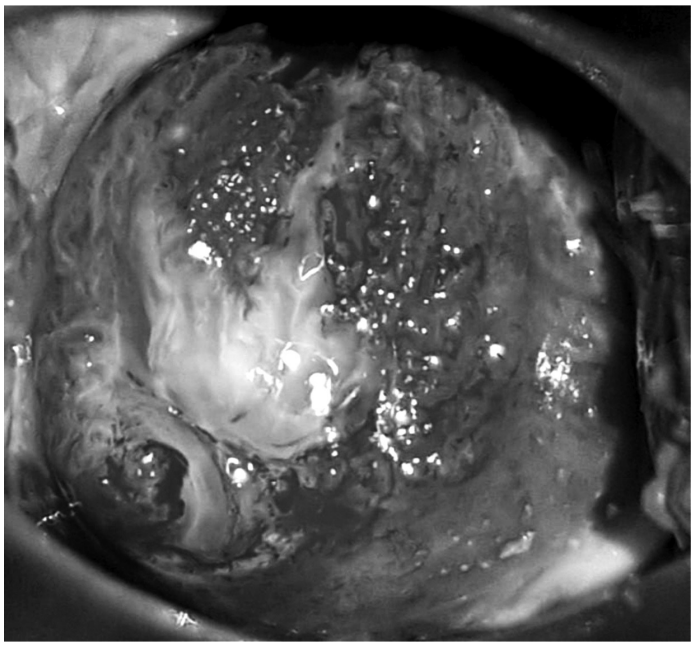

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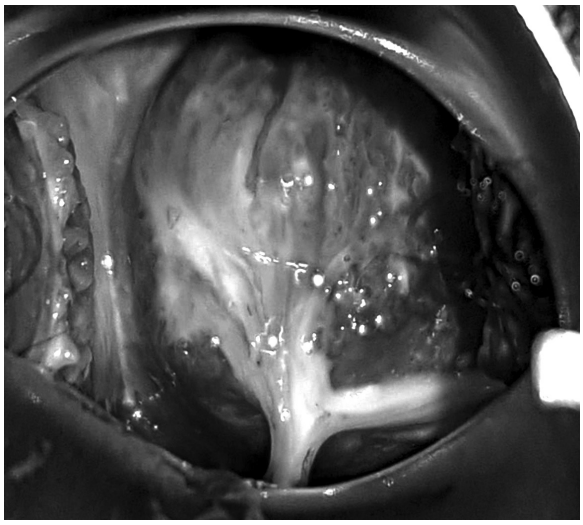

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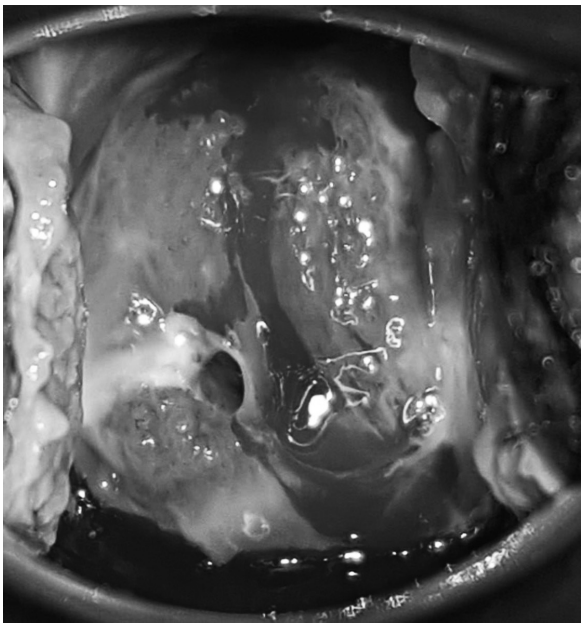

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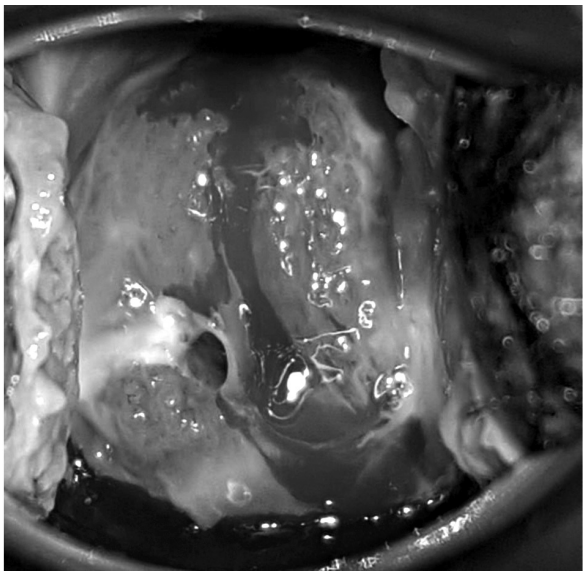

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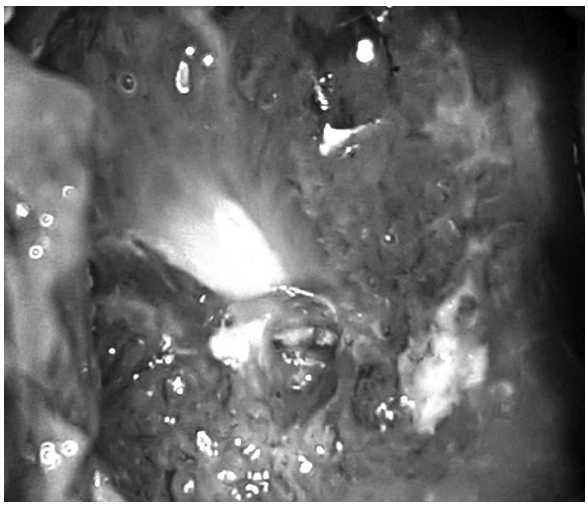

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Figure 4. Cervical lesions of Case B from (A) diagnosis, (B) 1st month of treatment, (C) 2nd month, (D) 3rd month, (E) 4th month, (F) 5th month

Figure 5. Cervical lesion of Case C, showing nodular fungating mass with copious yellow discharge

DISCUSSION

Three cases of cervical masses in women in the 3rd to 4th decade of life were described. Usual symptoms were postcoital vaginal spotting, increased vaginal discharge of months duration and amenorrhea. Initial impression of carcinoma was highly entertained. According to Domingo and Dy Echo, cervical cancer is the second most common malignancy and is the most common cancer-related mortality among Filipino women.[1] Cervical vaccines, colposcopic examinations, Pap Smears and contraceptives have been advocated, yet detection and development of the disease remains to be insurgent. The nature of the cervical malignancy remains elusive. Reported new cases of cervical cancer last 2005 was 7,277, with reported deaths of 3,807.[1] The census for cervical cancer steadily increases with a high mortality rate attributed to its late detection, and the treatment being inaccessible, unavailable, or unaffordable.[1] Most cases are diagnosed at stages III or IV. Risk factors for cervical malignancy include:

smoking, oral contraceptive use, fertility, early coitarche, and socioeconomic status. In order to diagnose cervical cancer, a tissue biopsy is required and is the first step. All three cases were advised of possible results and has been counselled of the economic burden of what lies ahead.

Histopathology results revealed chronic granulomatous inflammation suggestive of tuberculous infection. Because of the rarity of a cervical TB, the difference in management between TB and malignancy, and the huge impact of a misdiagnosis of cervical carcinoma, slide reviews were requested. Slide review of the gynecologic oncologist was in concurrence with the primary interpretation, chronic granulomatous inflammation with surface ulcerations, suppuration, caseation necrosis and focal Langhan's giant cells, findings which favour a tuberculous process. Microsections revealed inflamed vascularized fibrous tissue fragments with surface ulcerations. The tissue sections contain considerable number of inflammatory cells, predominantly chronic type admixed with neutrophils towards the surface and along the areas of necrosis. Occasional Epitheloid histiocytes were appreciated as well as multinucleated giant Langhan's cells.

The detection of typical granulomata is sufficient for diagnosis if the other causes of granulomatous cervicitis, such as amoebiasis, schistomiasis, brucellosis, tularemia, sarcoidosis, and foreign body reaction, have been excluded.[4] Other typical features of tuberculosis on histology are epitheloid cell granulomas with or without Langhan's giant cells. Caseating necrosis is rare in specimens from the genital tract[5] however, tissues obtained from all patients exhibited caseous necrosis alongside the pathognomonic Epitheloid histiocytes.

Further investigation were done to case A and B to determine the presence of pulmonary and other extrapulmonary sites of tuberculosis. Findings for Case A: Chest x-ray revealed multiple ill-defined densities in both upper lungs, sputum AFB revealed 1-9 AFB/ 100 visual fields, urine and stool were negative.

Case B had inconspicuous results.

Pelvic tuberculosis is a frequent cause of chronic pelvic inflammation and infertility.[1] The macroscopic appearance of tuberculous cervicitis mimics cervical cancer.[4] The discovery and the pestilence of the disease remains elusive.

It has been estimated that 5-13% of the cases of pulmonary TB develop a genital infection. The fallopian tubes are affected most commonly (90%), followed by the endometrium (50%), and the ovaries (10-30%). The cervix is rarely involved and accounts for 5-24% of cases of genital tract tuberculosis.[4] Tuberculosis of the cervix accounts 0.1-0.65% of all cases of tuberculosis, and 5-24% of all genital tract TB.[6] In the Philippines, there are only 4 reported cases of genital tract tuberculosis. As previously mentioned, TB is endemic in the Philippines, and it is said that the prevalence of genital tuberculosis is directly proportional to the incidence of pulmonary tuberculosis in an area.[5] The infrequency of reported cases may be attributed to the low detection rates due to the relatively asymptomatic or non-specific signs and symptoms of the extrapulmonary disease.

Of the two cases with further work up, only case A appears to have disseminated tuberculosis. Symptomatic genital TB usually presents with menstrual irregularities, abnormal vaginal bleeding, and abdominal pain. However, some cases are asymptomatic and are discovered accidentally during investigations of infertility.[4] There are postulations of hormone dependence of the disease as to the discovery is mostly among females of reproductive age.[7]

The genital organs are usually infected from the primary chest lesion by hematogenous spread.[4] Mycobacterium tuberculosis is a slow growing bacterium and only doubles its population every 18-24 hours. This slow doubling time partly explains the chronic nature of the disease and may allow dissemination before acute symptoms develop.[5]

Having presented with nonspecific symptoms of postcoital vaginal spotting and increased vaginal discharge, in a patient with a cervical mass, the patients were initially assessed to have cervical carcinoma stage IIB. As tuberculosis of the cervix will be mistaken for carcinoma far more frequently than it will be confused with any other disease, the necessity for immediate differentiation is apparent.[2]

According to Danforth, 4 types of tuberculous invasion are distinguished: the ulcerative, the miliary, the papillary, and the interstitial. The ulcerative type is usually characterized by a single lesion, the edges of which are rather well defined. The ulcer bleeds easily on contact but less so in instances of carcinoma. The papillary type may be confused with carcinoma which it may resemble closely. In the miliary variety, the cervix is enlarged and small miliary tubercles may be visible on the surface. The interstitial type appears first in the substance of the cervix, forming a nodule which may become necrotic. The necrotic material may be discharged, leaving a cavity.[2] In all three cases, the appearance of the cervix may be classified as papillary due to its nodularity and immediate bleeding upon manipulation or contact, thus explaining symptoms. During primary infection, organisms may spread systemically and at a later stage, may be activated at a genital stage. The most common mode of transmission to the genital tract is through hematogenous spread from pulmonary or other sites of tuberculosis.[4]

Until the advent of anti-Koch's therapy, hysterectomy with bilateral salpingooophorectomy had been the practice.

Cervical tuberculosis generally responds to standard anti-tuberculous treatment. A four drug regimen consisting of isoniazid, ethambutol, rifampicin and pyrazinamide is used for the first two months, followed by triple or dual therapy, with its dosing computed in relation to the body mass index. The total duration of treatment should be six months to a year. Excellent cure rates are reported for all of the standard treatment regimens.[5]

A lesion on the cervix provides a marker to assess response to therapy. Serial colposcopic observation and histopathological examination by punch specimens can confirm therapeutic response.[8,10] Case A had visible decrease in the periurethral mass as well as clearing of the cervix and improvement of discharge. Case B had improvement in the discharge as well as clearing of the cervix. Hysterosalpingography is an important diagnostic tool especially for patients who are in the child bearing age. This may be particular for Case B, on the other hand, Case A is not desirous of pregnancy hence no future plans for hysterosalpingography is contemplated.

The immediate differentiation of tuberculosis and carcinoma is beneficial and prudent as to plan for treatment. Irradiation of a tuberculous cervix is a therapeutic error, as the insertion of radium preceded by the necessary dilatation of the cervix predisposes to the spreading of the disease.[2] There is rarely any need of surgery except in cases resistant to medical treatment. Indications for surgical intervention include: (1) persistence of or progression of the disease despite adequate medical treatment; (2) suggested residual large tubo-ovarian abscess; (3) positive endometrial culture/ histology and recurrence of pain or bleeding after 9 months of medical treatment; and (4) fistulas that fail to heal. Surgical therapy usually consists of total abdominal hysterectomy and bilateral salpingooophorectomy and should be performed at least 6 weeks after initiation of antituberculous therapy, because antimicrobial treatment facilitates the surgical procedure and reduces the risk of perioperative complications.[8]

This case series emphasizes that though uncommon, tuberculosis is an important differential diagnosis for cervical lesions with nonspecific signs and symptoms, especially in countries with high prevalence of the disease.

SUMMARY

Tuberculosis is a pervasive disease yet symptoms remain vague and nonspecific. Cervical tuberculosis represents a minority of cases; its rarity is an important differential diagnosis with patients who presents with suspicious looking cervix and nonspecific symptoms. Mainstay treatment remains to be anti-Koch's medications. ■

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