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Significance of diminished hormone expression in nulligravida woman presenting with triad of uterine pathologies

Seema Dayal[1], Adesh Kumar[2], Kalpana Kumari[3], Kritika Singh[1], Abhishek Sharma[1]

[1]*Uttar Pradesh University of Medical Sciences, Department of Pathology, Etawah, India*
[2]*Uttar Pradesh University of Medical Sciences, Department of Pulmonary Medicine, Etawah, India*
[3]*Uttar Pradesh University of Medical Sciences, Department of Obstetrics and Gynecology, Etawah, India*

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Corresponding Author:
Seema Dayal, Prof., Uttar Pradesh University of Medical Sciences, Department of Pathology, Etawah, India
seemadayal5@gmail.com

ORCID:
orcid.org/0000-0001-8282-2507

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ABSTRACT

Genital tract tuberculosis (TB) occurring together with adenomyosis and leiomyoma is rarely observed. A 40-year-old nulligravida woman was clinically diagnosed with the fibroid uterus. Histopathological examination revealed leiomyoma with adenomyosis and TB. Immunohistochemistry for oestrogen and progesterone receptors was performed to determine their expression, which was found to be moderate, although it was expected to be strongly positive. This case is being reported because of its rare coexistence of these conditions; moreover, it suggests that reduced hormone expression, particularly of oestrogen, may enhance the severity of TB, ultimately resulting in adverse reproductive outcomes.

Introduction

Female genital tract tuberculosis (TB) is a variant of extrapulmonary tuberculosis (EPTB) (1). It causes a negative impact on female fertility. TB's effects on female hormone alterations and menstrual cycles are overlooked. TB outcomes on hypothalamus, pituitary gland, and ovaries result in disordered menstruation. Simultaneously change in hormone profile and antigonadotrophic effects of *Mycobacterium* TB results in hypogonadism which accounts for infertility and menstrual irregularities. TB has been associated with lower serum oestrogen levels, and serum oestrogen levels are raised during TB treatment (2). It had been reported that in the TB patients, there were reduction in female sex hormone which leads to diminished ovarian function (3). This leads to

spontaneous abortions, which result in infertility. Leiomyoma is benign smooth muscle uterine tumour whereas adenomyosis is the presence of ectopic endometrial tissue in the myometrium. Both leiomyoma and adenomyosis are hormone-dependent tumors; that is, their size and activity increase with elevated of oestrogen and progesterone levels (4,5). The coexistence of genital TB with leiomyoma and adenomyosis is extremely rare. They also exhibit antagonistic hormone effects. This case is being reported because of its rare occurrence and to highlight the possible association between these pathologies.

Case Presentation

A 40-year-old nulligravida woman presented with complaints of pain and mass in the abdomen. She was also suffering from dysfunctional uterine bleeding, and her laboratory investigations revealed anemia, which represented her only clinical manifestation. Hormone levels could not be accessed earlier. A gynaecology examination was suggestive of fibroid uterus. The medications were not supportive in controlling dysfunctional uterine bleeding, so considering the dysfunctional uterine bleeding and the increased size of the fibroid uterus, hysterectomy was decided to be performed. Hysterectomy with bilateral (B/L) salpingo-oophorectomy was sent for histopathology examination. The specimen was measured 14 x 9 x 6 cm. Fibroids obliterated the endometrial cavity. It measured 8 cm and 4 cm in its largest and smallest diameters, respectively. On further sectioning, they were grey-white in colour with whirling.

The right-sided ovary measured 3 x 2 x 1 cm and the left-sized ovary measured 6 x 3 x 2 cm. Cut section of B/L ovaries showed solid and cystic areas.

The right-sided fallopian tube measured 3 cm in length, whereas left-sided fallopian tube measured 4 cm.

Tissues were stained with hematoxylin and eosin. Ziehl-Neelsen (ZN) stain was applied to confirm TB (6), simultaneously immunohistochemistry (IHC) for estrogen and progesterone was also applied.

Histopathology examination showed smooth muscle fibers with elongated blunt-ended nucleus and eosinophilic cytoplasm running at various angles with whirling. These finding confirmed leiomyoma.

Plenty of endometrial glands with stroma deep in myometrium (more than one low power field from endo myometrial junction) were appreciated. This histomorphology microscopic findings were suggestive of leiomyoma coexisting with adenomyosis and caseous necrosis [Figure 1 (a)].

These findings were accompanied by multiple epithelioid granulomas with caseous necrosis in myometrium [Figure 1 (b)]. ZN stain was also applied to isolate tubercular bacilli but could not be found contributory [Figure 1 (c)].

Based on these morphologies, the present case was reported as leiomyoma with adenomyosis and extra pulmonary TB. Tubercular features were also reported in other sections of the uterus.

IHC was applied for estrogen and progesterone receptors expression. Immunoreactive score (IRS) method was used. Nuclear positivity was confirmed. It was calculated as follows: IRS=staining intensity (SI) x percentage of positive (PP) stained cells (PP), where SI was the optical SI (graded as 0=no, 1=weak, 2=moderate, and 3=strong staining) and PP was the PP. The PP is mentioned as 0=no staining, 1=10%, 2=11-50%, 3=51-80% and 4=>80. The aggregation of these both finally result in IRS score categorization into negative, mild, moderate and strong expression.

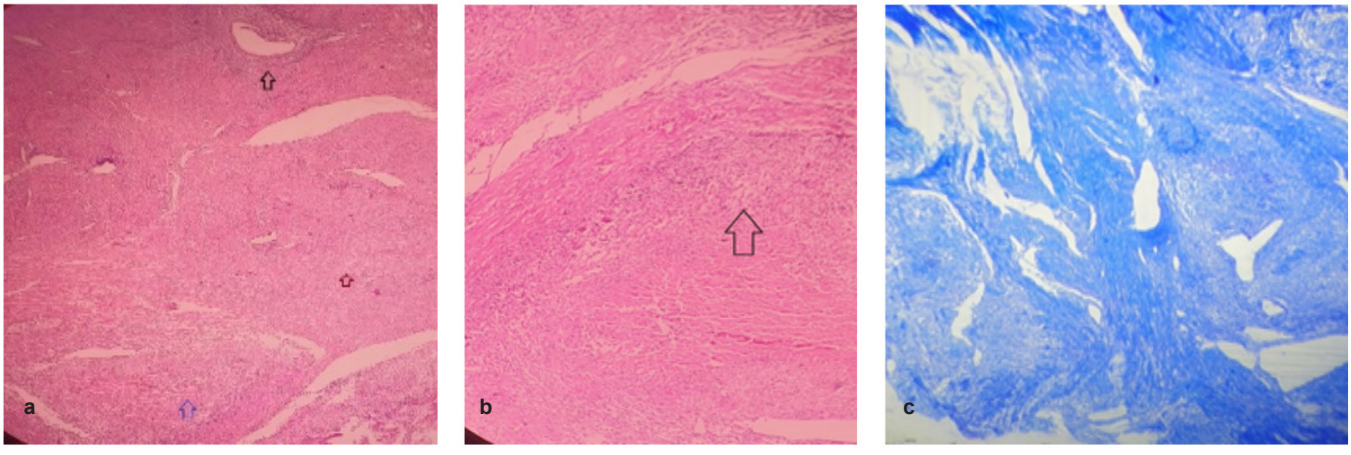

Figure 1. (a) H&E stained section showing adenomyosis (black arrow) leiomyoma (red) and caseous necrosis (blue). (b) H&E stained section showing caseous necrosis. (c) ZN stained section showing non-contributory staining
H&E: Hematoxylin and Eosin, ZN: Ziehl-Neelsen

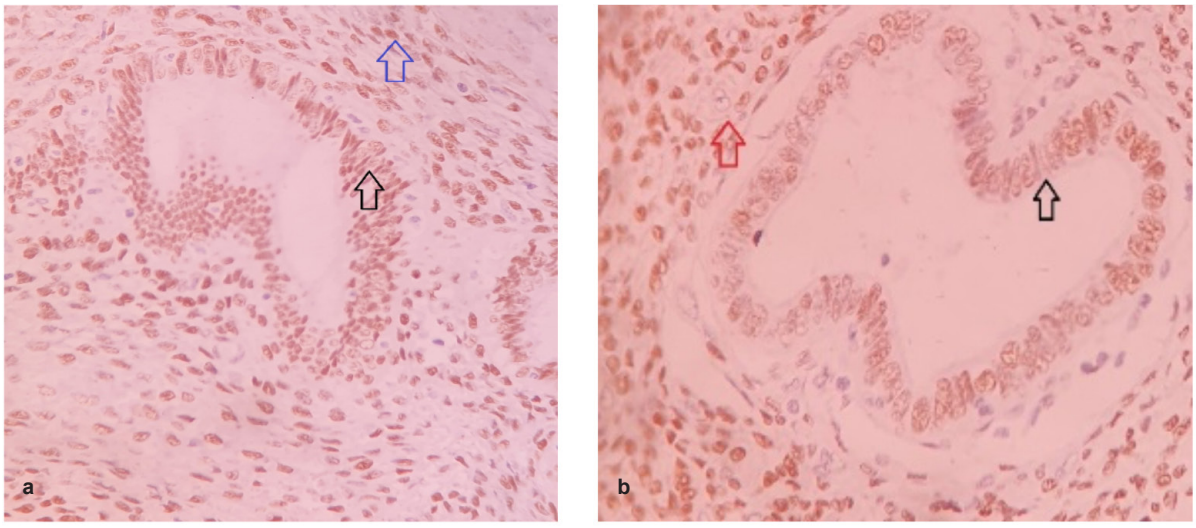

Figure 2. (a) Figure showing moderate positive immunoreactivity for estrogen receptor (black-gland, blue-stroma). (b) Figure showing moderate positive immunoreactivity for progesterone receptor (black-gland, red-stroma)

The results showed moderate immunoexpression of estrogen [Figure 2 (a)] and progesterone [Figure 2 (b)].

Informed consent was obtained from participants.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

This case presents a rare coexistence of leiomyoma, adenomyosis, and genital TB in a reproductive-age woman, highlighting the complex interaction between hormonal and infectious factors affecting the uterus.

Female genital tract TB causes adverse effect on reproduction. Tubercular bacilli infect the genital tract by four routes–haematogenous, descending direct spread, lymphatic, and sexual transmission. It may cause damage to fallopian tube leading to blockage or adhesions, reduced endometrial receptivity or ovarian damage. It is seen in patients of age range between 20 to 45 years. Clinically, it may be asymptomatic or present with symptoms diversity of symptoms like infertility and chronic pelvic inflammatory disease, dysfunctional uterine bleeding, pelvic pain and abnormal vaginal discharge (1) .These clinical features are not specific to female genital tract TB and may mimic other pathologies (6).

In current study, patient was 40-year-old nulligravida woman who presented with pain, mass in the abdomen and dysfunctional uterine bleeding.

The diagnosis of female genital tract TB are made on basis of culture positive specimen, or positive histopathology or strong clinical evidence consistent with active EPTB. Chest X-ray, complete blood count, erythrocyte sedimentation rate, and tuberculin test should be applied to rule out systemic spread. The two imaging techniques hysterosalpingography and sonography are also useful, as hysterosalpingography evaluates internal structure and tubal patency whereas ultrasonography carried out simultaneous evaluation of ovarian, uterine and extra pelvic involvement (1).

Radiology investigations such as ultrasonography shows thickened fallopian tubes with or without endometrial thickening, tubo-ovarian masses or adhesion. It is often may be misleading and mimic other intra uterine pathologies like leiomyoma specifically degenerated one, ovarian tumors etc (7). So, the awareness of sonographic changes associated with TB infection should be specifically known which may improve diagnostic accuracy and avoid clinical mismanagement and surgical explorations (8).

In the present case study, the ultrasonography findings were also suggestive of leiomyoma uteri.

On histopathology examination, TB is characterized by the presence of epithelioid cell granulomas along with caseous necrosis. The confirmation of TB is done by identification of *Mycobacterium* TB with ZN stain (7), but is difficult to diagnose the bacteria in the extrapulmonary sites because the organism are sparse in number at extra pulmonary locations (1).

In these cases, the ZN stain was also not contributory; however, the patient improved after antitubercular treatment.

Researches had already reported that ovarian steroids, oestradiol and progesterone promote leiomyoma growth (5). Intramural is the commonest variants (9). In present study, there were two intramural leiomyoma visualized obliterating the cavity. The symptoms depend on location, size of tumour and hormonal effect. Here, the patient was presented with mass, pain in abdomen and dysfunctional uterine bleed.

Leiomyoma on histopathology is characterised by spindle-shaped tumor cells with an elongated, blunt-ended nuclei and

eosinophilic cytoplasm forming bundles with whorls (9,10). We also found these features.

Adenomyosis is characterized by the presence of endometrial glands and stroma in the myometrium (11). We also observed these findings in our case.

Adenomyosis may coincide with leiomyoma, endometriosis, endometrial hyperplasia, endometrial polyp, and endometrial carcinoma, which occur due to unopposed estrogen (9,11). The present case consisted of adenomyosis with leiomyoma and myometrial TB.

Estrogen and progesterone receptors are the members of hormone receptor family of ligand dependent transcription factors. Hormone expression rises in leiomyoma and adenomyosis (4,5). Rosenthal et al. (12) mentioned that a lack of estrogen results in wide dissemination of TB. Ukibe et al. (13) assessed the hormonal changes in women suffering from TB and reported that progesterone and estrogen were found significantly low.

The benefit of the IRS score is that it includes both epithelial and stromal elements for expression (14). In the current study, the estrogen and progesterone receptor expression was found to be moderate.

Conclusion

The coexistence of leiomyoma with adenomyosis and TB is rare. Leiomyoma and adenomyosis depends on sex hormones for proliferation, whereas TB is associated with lower hormone expression. The reduced level of hormone expression, especially estrogen, increases the severity of TB and negatively affects reproduction. We emphasize that hormone receptor analysis should be included as a supplementary investigation in young and nulliparous or gravida tubercular patients.

Ethics

Informed Consent: Informed consent was obtained from participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., K.K., Concept: S.D., Design: S.D., Data Collection or Processing: K.S., Analysis or Interpretation: S.D., Literature Search: A.S., Writing: S.D.

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