

Genital Tuberculosis Presenting as Primary Amenorrhoea

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Abstract

A 23-year-old married woman presented with primary amenorrhoea with well-developed 2ndary sex characteristics. She is chromosomally competent female (46xx) with average body built and had no problem in marital relationship. Clinical examinations and all relevant investigations including transvaginal ultrasound (TVS) showed uterus, adnexa normal size and volume. Progesterone challenge test was negative on 3 occasions. Laparoscopy showed distorted shape of fallopian tubes with beaded appearance. Biopsy

from it and endometrial samplings collected by aspiration showed granuloma with caseation necrosis, typical of tuberculosis (TB) though no AFB found on culture. PCR-RFLP also positive for TB. So, primary amenorrhoea with unresponsive endometrium with underlying Genital Tuberculosis was clinical diagnosis. She received 9 months treatments of 4 drugs regimens of anti-TB.

Key words: Tuberculosis (TB), Primary amenorrhoea.

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Introduction

Tuberculosis is the oldest infectious disease and is still the leading cause of maternal mortality and morbidity worldwide, 9% of women death due to TB, specially in reproductive age group. Tuberculosis of female genital tract (GTB) is common among all communities in all age groups where pulmonary or other forms of extra-genital TB are prevalent¹. It is an increasing major public health problem worldwide, with according to 2019 data showed 1.7 billion people infected, which constitute 23% of world population. It is 1 of the top 10 leading causes of infectious disease killer in the world with 1.4 million mortality/year². TB present in all countries and in all age groups where 95% infection in developing countries, 30 high TB burden countries accounted for 87% of all new infected cases including Bangladesh³. TB has plagued human being for millennia like a devastation. Today, despite advances in diagnosis and treatment, it is a global pandemic fuelled by spread of HIV/ Malaria (22 times higher risk), poverty and malnutrition (3 times higher risk), a lack of health services and the emergence of multi drug-resistant (MDR) strains of this bacterium⁴. The disease exists in mainly 2 forms- pulmonary and extra-pulmonary, GTB is one form of extra-pulmonary TB – nearly always 2ndary to a focus elsewhere in the

body specially in lungs. 5-13% of patients of pulmonary TB develop genital TB, also involves kidney, ureter, bladder, even the nervous system⁵. Clinical feature usually develops 10-15 years after primary infection and most of the times remains asymptomatic. So the true incidence and prevalence is difficult to estimate as a large number of patients remains asymptomatic with respect to genital tract and the disease is not looked for in an asymptomatic patient and so they remain undetected, undiscovered, undiagnosed and hence remain untreated⁶. Worldwide genital TB is found in 5-10% of women with infertility problems^{6,7}, with low rate in Australia (1%) and higher in India (19%). The incidence of genital TB has increased recently, partly contributed to HIV pandemic, in african countries 60-90% of patients with extra pulmonary TB are HIV positive –which contributes 45% of case fatality rate even with treatment⁸.

Case Report

A 23-year-old, factory worker, from a low socio economic class family was admitted to Dhaka Medical College Hospital on 17th February, 2018 with the complaints of non-establishment of menstruation till then. Her parents gave the history that she was an apparently healthy female since her birth and grew normally like other girls of her age. She attained her female 2ndary sexual characteristics at 13 years but all these events were not followed by normal sequence of menarche (1st establishment of menstruation). She gave no history of periodical lower abdominal pain, dysuria, frequency or retention of urine. There was no history of gross endocrine abnormality nor any significant weight gain

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or loss. She gave no history of visual disturbance or any headache, galactorrhoea, voice change, trauma or childhood encephalitis. There was no family history of primary amenorrhoea or constitutional delay in menarche, TB or diabetes. But in community there was an affected person of TB. She gave no significant drug, medical or surgical history. At 18 years, when consulted a local doctor, who prescribe her tablet progesterone, 5 mg 3 times daily for 5 days but this was not followed by withdraw bleeding. She was married for 2 years and never had any problem in sexual relationship. She was examined thoroughly, general parameters all were normal with well-developed feminine figure and voice. Distribution of classic female pattern of pubic hair, axillary hair normal and with long scalp hair. Visual field normal with normal colour vision, no anosmia and no bony abnormality noted. Thyroid glands normal and accessible lymph nodes were not palpable. Breast examination revealed nipple, areola and glandular structures well developed. Per abdominal examination revealed no palpable mass or abnormality. Vaginal examination- typical female external genitalia with normal length vagina and cervix, there was no vaginal discharge. Bimanual examination detected uterus normal size, anteverted, mobile, fornices were free and slight tenderness present. No palpable adnexal mass delineated through fornix. Per rectal examination same as that of per vaginal findings and no induration or tenderness elicited.

All relevant investigations done where total count was found slightly raised with lymphocytosis and ESR was 87. Mantoux test was borderline positive at 13 mm, sputum, urine no abnormal results, chest X-ray showed no focus of infection or radio opacity in lungs. Ultrasound revealed no abnormality of internal genital organs with homogenous echo texture of both endo and myometrium of uterus, ovaries were normal size and volume. Then special investigations like hormone assays done which showed levels of T3, T4, TSH, Prolactin, Oestrogen and Progesterone were within normal limit. The FSH and LH level were a bit higher like 29IU/L and 13 IU/L respectively. Progesterone challenge test was again negative. After proper counselling laparoscopy was done which showed uterus normal in size, anteverted, mobile, cervix and vaginal canal present and normal. Ovaries were of normal size but both the fallopian tubes were mildly distended and found beaded

appearance. Biopsy was taken from tubes and endometrial sampling was collected by aspiration, peritoneal fluid also collected. The histopathology report showed typical granuloma with central caseation surrounded by plenty of lymphocytes, epitheloid cells and Langerhan's type of giant cells. Then PCR was done, found positive (85-90% sensitive), PCR-RFLP assay done for molecular identification as no AFB found on Lowenstein Jensen (LJ) culture media. Biopsy material was also stained with Ehrlich-Ziehl-Nelsen (EZN) no AFB was found, but when cultured in Mycobacterium Growth Indicator Tube (MGIT) came positive after six (6) weeks which was again confirmed by seeing presence of mycobacteria from this positive culture when stained by EZN staining- the strain was identified as Mycobacterium TB Complex (MTC). So, she was finally diagnosed as primary amenorrhoea with unresponsive endometrium due to unusual or atypical presentation of genital TB.

Anti-TB susceptibility was performed and the strain was found sensitive to all first line Anti-TB drugs.

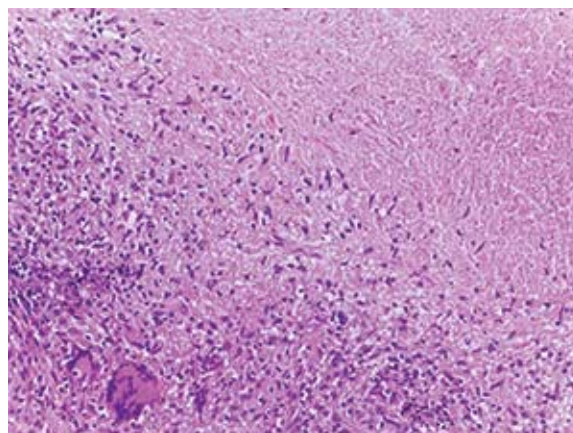


Fig.-1: *Histopathology: Caseation necrosis with Langerhans giant cell at the periphery*

She received first 2 months with 4 anti-TB drugs (Isoniazid, Rifampicin, Ethambutol and Pyrazinamide) and next 7 months with 2 anti TB drugs (Isoniazid and Rifampicin) along with pyridoxine. And was advised to come for follow up visit after 6 months. She attended follow up visits but it was not proceeded by any menstruation.

Discussion

Primary amenorrhoea is defined as when there is non establishment of menstruation and should be

investigated by 16 years of age in presence of 2ndary sex characteristics and by age of 14 when no 2ndary sex characteristics present⁹. For establishment of menarche the 5 criteria must be full filled as i). she must be chromosomally competent female (46XX) as testicular feminizing syndrome or superfemale can have feminine figure but not chromosomal competent female. Ii) Hypothalmo-pituitary –ovary-uterine axis must be intact and well- functioning, her uterus was not responding to this axis iii) Must have responsive endometrium-she is not complying with this iv) must have patent outflow tract-here she has patent vagina. v) active support from thyroid & adrenal gland-her both gland functions are alright.

Menstruation is the final result of series of events that results in sexual maturity with maturation of hypothalamus, pituitary and ovaries through several years of late childhood results in a cascade of events that finally results in establishment of normal menstrual cycle. Amenorrhoea will result when there is a defect or failure of function of any of these organs involved in this cascade^{10,11}.

Tuberculosis of female genital tract is common in that community where pulmonary or other forms of extra genital TB are prevalent. Mycobacterium TB, the acid fast bacilli is responsible for 90-95% cases of extragenital TB and M bovis to that of 5-10% cases. The TB bacilli reach the genital tract by any of the following mechanisms: a) blood stream- here primary focus is in lungs, lymph nodes, urinary tracts, bones or joints. b) ascending primary infection in vulva, vagina and cervix may result from direct inoculation at sexual coitus in adults or by children accidentally sitting unclothed where others have spit or coughed¹². Genital TB is always 2ndary to a focus elsewhere in the body. The spread may have taken place in very early stage of the disease usually in adolescence or early maturity. So by the time the genital lesion is found which can be of any age, the primary has often healed and is undetectable^{9,13}.

Any part of the genital tract may be affected but the common sites are fallopian tubes (90-95%) and endometrium (50-60%), ovaries (20-30%). Almost both the tubes are affected but the involvement is not always symmetrical. It begins in submucosa at outer ends – gradually progresses inwards bombarding endometrium with bacilli. The findings of endometrial TB always means

that tubes are infected as the tubal TB spreads the endometrium in half the cases^{9,14}. The genital disease may be acute and rapidly extending disease but mostly indolent. In majority cases it progresses slowly and remains asymptomatic like our patient. The involvement of cervix and vulva(1-2%) may have shallow superficial indolent ulcers with undermined edges. The involvement of uterus usually looks normal in naked eye. Extensive involvement may result in collection of caseous material to form a type of pyometra or may cause abscesses in myometrium- leading to adhesion and partial obliteration of cavity^{8,15}. And sometimes as in our patient extensive adhesion leads to Asherman's syndrome/intrauterine synechia-that is the exact reason of her primary amenorrhoea. Ordinarily TB endometritis can only be recognized by histological and bacteriological examination of tissue as in our case.

The appearance of TB tubes varies widely. Sometimes as endo-salpingitis with distortion of lumens and sometimes as exo-salpingitis with tubercle on surface. But sometimes tubes may look completely normal though majority of cases –it is found as thickened, shotty and beaded appearances like our patient's tubes were found. Sometimes there may be formation of hydro or pyosalpinx or a thick fibrous wall may become calcified/ ossified¹⁰. Ovaries are involved in 30% cases but not without tubal involvement.

TB is a silent disease, may be asymptomatic even when present 20 Or more years. The woman remaining in apparently excellent health, pelvic organs also feel normal on bimanual examination in 50% cases. As the women remains completely asymptomatic, the presence of pelvic TB most often revealed during investigation of infertility or amenorrhoea like our patient presented. In approximately 50% cases menstrual function found normal, oligomenorrhoea in 54% cases and amenorrhoea in 14.35% cases. It is explained by suppression of ovarian function, compensatory hyperactivity of anterior pituitary can result in raised excretion of gonadotropins. Endometrial damage result in amenorrhoea even though ovulation continues. 2ndary amenorrhoea is more common and menorrhagia found in 19% cases^{11,16}. Except in acute phase it is not associated with pain.

Conclusion:

TB is an important cause of infectious morbidity and mortality and has devastating impact in females of

developing countries as it can jeopardise the lives of women in various ways of menstrual problems, pregnancy loss and infertility- which is most pathetic as it is not amenable to easy diagnosis and treatment. Cure to restore fertility is uncommon. If the tubes are closed at the outset-permanent sterility is likely, and attempts at salpingostomy results in re-closure most of the time. If the tubes are open, pregnancy may be possible but because of residual infection or scarring and distortion of endosalpinx, tubal implantations are likely. Miscarriage of intra uterine pregnancy also common. Although the prognosis to cure is good but prospect for pregnancy is negligible. Some centres reported successful pregnancy with IVF, which would appear to be the only treatment if any possibility of success.

Incidence of female GTB is higher in Indo-Bangla-Pak subcontinent and incidence is on the rise mostly due to low socio economic conditions. Gynaecologists will be increasingly faced with these cases, so must consider genital TB as a possibility when women of reproductive age present with menstrual problems, chronic pelvic pain, unexplained infertility and or repeated miscarriage to avoid unnecessary and ineffective interventions.

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