A RARE CAUSE OF PRIMARY AMENORRHEA

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• 22 years old Ms X attended SRM hospital OPD with the C/O not attained menarche
• No H/O cyclical lower abdominal pain, bladder/bowel disturbances
• H/O normal breast, axillary & pubic hair development
• No H/O headache, visual disturbances, discharge from nipple
• No H/O excessive weight gain/increased hair growth
- **Past History**: H/O antituberculous treatment for 2 month duration for chronic cough 6 years back. Defaulted after 2 mon. No proper follow up.
- No H/O surgeries in childhood, radiation / trauma
- **Family history**: Born of non consanguinious marriage. Has a younger sister 16 yrs old who attained menarche 2 yrs back.
- **Milestones**: normal
- **Treatment history**: progesterone challenge and estrogen + progestogens for 1 mon but with no withdrawal bleed.
EXAMINATION

- Ht- 158 cm  Wt- 56 kgs. BMI- 22.4 kgs
- Mod built & nourished
- Breasts-Tanner stage IV
- No thyromegaly
- Axillary hair-present
- Vitals -Normal
- CVS,RS,CNS- NAD
- P/A-soft
EXAMINATION

- L/E- vulva normal
- Pubic hair-Tanner stage IV
- Vagina present
- P/R-uterus felt
INVESTIGATIONS

- Hb-12.6 g %  PCV-36%
- RBS-87mg%
- PRL-14 ng/ml
- FSH-12.7miu/ml
- LH-4.8miu/ml
- TSH-2.2miu/ml
- Mantoux-negative
INVESTIGATIONS

- **USG Pelvis** - normal sized uterus with linear echogenicity in body of uterus between the ant and post wall.
- **Karyotyping** - 46 XX
- **Chest X ray** - cavitary lesion R upper lobe, Suggested CT Chest
- **Sputum AFB** - negative
CT Chest-Bil Apical pleural thickening, cystic bronchiectasis apical, ant RUL, ? Isolated cavitary lesion-post RUL, no lymphadenopathy
Hysteroscopy-

- **Vagina**-normal, **cervix**-healthy
- **Int os**- cicatrised, dilated with difficulty
- **Cervical canal**-N
- **uterine cavity**-N
- **EM**-Thin and pale, both **ostia** could not be visualized
- **EM** sampling done
Diagnostic Laparoscopy

- Curtain like adhesions b/w the omentum and ant abd wall
- Uterus-normal size, bladder drawn up
- Both sides tubal take off seen.
- TO mass R-4× 2.5cm, TO mass L-4× 5 cm
- Both fimbria not visualised
- Adnexal adhesions released
- Peritoneal fluid C/S, adhesions for HPE, EM for HPE, culture and PCR sent
PATHOLOGY REPORTS

- EM HPE- blood clot
- Adhesions- fibro collagenous tissue
- PCR of Endometrial sampling for mycobacterium- positive
Pt was put on Cat I ATT and she is in the third month of treatment.

Also on cyclical estrogen+ progesterone.

No withdrawal bleed as of yet.
Tuberculosis (TB) has become a global epidemic again with emergence of HIV/AIDS and multi-drug resistant strains of TB.

Female genital tuberculosis is typically a disease of young women.

Amongst the genital disorders, genital TB is the most baffling especially because of its various presentations. So genital TB is notorious for evading diagnosis.
• Genital TB almost always occurs secondary to pulmonary (commonest) or extrapulmonary TB (commonly abdominal).

• Fallopian tubes are involved in almost all cases of FGTB followed by the endometrium in 50-80%.

• Initially no macroscopic disease in endometrium, but caseation and ulceration occur later with the progression of TB.
MENSTRUAL IRREGULARITY IN CASES OF GENITAL TUBERCULOSIS

(1) Normal------------11.8%
(2) Oligomenorrhoea---36%
(3) Menorrhagia--------10%
(4) Amenorrhoea--------41%

primary(5.5%) secondary(35.5%)

Arch Gynecol Obstet 2008 277:37-41
When the endometrial tuberculosis is extensive, the endometrium is destroyed and replaced by hyalanised connective tissue, thereby obliterating the cavity.

Most of these patients are ammenorrheic due to end organ failure.
Though tuberculosis can be diagnosed on FNAC by detection of acid fast bacilli or caseating granulomas in smears the only source of material generally available and studied from genital tract is endometrium, involved only in 50-60% of female genital TB and limits the definite diagnosis. Further a single endometrial biopsy may miss the focal pathology.
Value of Endometrial Biopsy

Absence of signs of tuberculous endometritis in any one biopsy, is not a proof of absence of the disease.

Positive results follow one or more negative results.

Kistner used progesterone drugs to create a pseudo pregnancy, for 2 to 3 months and then did E.B. with good results for tuberculous endometritis.
Negative E.B. is however not an indication for discontinuing treatment of ATT particularly as histological examination of endometrium does not necessarily reflect the state of the fallopian tubes.
So a high degree of suspicion aided by intensive investigations may be required for the diagnosis of genital TB.
Laparoscopy is now a well-recognized procedure in the diagnosis of tuberculosis in infertile women. It can reveal presence of miliary granulomas, whitish yellow or opaque plaques surrounded by hyperemic areas over the fallopian tubes and uterus in acute stages. In chronic stages, the tubes show nodular salpingitis, patchy salpingitis, hydrosalpinx, caseosalpinx, or adhesions.
GENITAL TUBERCULOSIS - A DIAGNOSTIC DILEMMA*

- Varied clinical presentations
- Diverse results on imaging and laparoscopy
- Mixed lab tests
- Pelvic ultrasound - initial screening test
  - Ascites / loculated fluid (100%)
  - Adnexal mass (93%)
  - Peritoneal thickening (69%)
  - Omental thickening (61%)
  - Endometrial involvement (83%)
  - Peritoneal tubercles and adhesions

- MRI, hysterosalpingography, and endoscopy

- Diagnosed on the collective evidence from imaging techniques, endoscopy, histopathology and microbiology

*J Obstet Gynaecol India 2006; Vol. 56, No. 3: 203-204
• Chest radiographs, urine, and sputum cultures are not specific for FGTB
• But, helpful to rule out dissemination to other organs

Infertile women with a positive mantoux-
early laparoscopy
direct visualisation of fallopian tubes
collection of specimens for histopathology and microbiology
• LTBI - QFTG, T spot TB

• NAA
  - Amplicor MTB test (Roche, PCR)
  - Amplified MTD (Gen-Probe, TMA)
  - ProbeTec ET (BD, SDA)
  - High specificity / PPV; low sensitivity / NPV
  - To be used in conjunction with conventional tests and clinical data

• Rapid detection of drug resistance
  - Molecular beacons - Rif / INH
  - Line probe assays - INNO-LiPA Rif TB kit
  - Phage based assays - FASTPlaque TB, FASTPlaque TB MDRi kit, FASTPlaque TB-Response

Proc Am Thorac Soc 2006; Vol 3: 103-10
Diagnostic role of a positive Mantoux is controversial

Almost 45% of infertile women with strong indirect evidence of pelvic TB, such as laparoscopic findings (thickened tubes, areas of caseation, etc) - negative Mantoux

In 27 infertile women with a positive Mantoux, only 11 had clear laparoscopic findings suggestive of FGTB

Mantoux test in women with laparoscopically diagnosed tuberculosis
  - sensitivity - 55%
  - specificity - 80%

*Int J Gynaecol Obstet 2001, 72:165-169*
Fresh heparinised whole blood from sensitised persons incubated with mixtures of synthetic peptides (two proteins present in *M. tuberculosis*)
- ESAT-6 (early secretory antigenic target-6)
- CFP-10 (culture filtrate protein-10)

Lymphocytes in blood of TB patients recognize these mycobacterial antigens - generation and secretion of interferon-γ (IFN-γ)

Detection and subsequent quantification of IFN-γ by ELISA
- Rapid results (within 24 hours)
- No booster response (measured by subsequent tests - which can happen with Mantoux)
- No reader bias (cf Mantoux)
- ST: 80-95% (Mantoux 75-90%)
- SP: 95-100% (Mantoux 70-95%)
All patients with laparoscopy suggestive of tuberculosis 60% of those with a probable diagnosis and 33% of those with incidental findings, were positive by PCR. 1 EA sample from an infertile patient with normal laparoscopy was also positive.

Multiple sampling from different sites and amplification of the mpt64 gene segment by PCR offered increased sensitivity in determining tuberculous aetiology in female infertility.
Genital TB is categorised as serously ill extra pulmonary disease under cat I.

2 HRZE

INH-600 mg
Rifampicin-450 mg
Pyrazinamide-1500 mg
Ethambutol-1200 mg

4 HR

RNTCP DOTS GUIDELINES 2010
Prognosis for endometrial regeneration is very poor making these pts poor responders in infertility treatment

Int J of Gynecology & Obstetrics, 1999 :64, 193-194
Genital TB is now undergoing a worrying recrudescence. We need to have an indepth knowledge of the pathology, the diagnostic means with which to discover it early and the correct therapeutic instruments to overcome. Research for early establishment of diagnosis, effective medical and surgical therapies with preservation of reproductive capability of the affected must continue.
DOTS—sure cure for TB.
THANK YOU