

ENDOMETRIAL TUBERCULOSIS IN INFERTILITY: REPORT OF 2 CASES AND A REVIEW OF THE LITERATURE***OJO, B.A. ** AKANBI, LI ** SAMUEL, S.O ** ODIMAYO, M.S ***ADESIYUN, O.A.***** Pathology Department, College of Medicine, University of Ilorin, Ilorin, ** Microbiology and Parasitology Department, University of Ilorin Teaching Hospital, Ilorin, *** Radiology Department, College of Medicine, University of Ilorin, Ilorin, Kwara State, Nigeria.****Correspondence To: Dr. BA Ojo Phone: 08033918810 E mail: babarindeo@yahoo.com**

Tuberculosis is a chronic granulomatous disease affecting human and many other mammals. Most human diseases are caused by *M.tuberculosis* but some are due to *M.bovis*.(1).

Tuberculosis of the tubes and endometrium is intimately bound to the problem of sterility. Despite the decline in frequency of genital tuberculosis in industrialized world coupled with widespread use of antibiotics worldwide, it still remain a possible cause of female infertility especially in developing world.(2)

It was the commonest diagnosis among infertile population in India (3), Malaysia (4) and Saudi Arabia (5). Nigeria, U.S.A., and Pakistan have reported a low and infrequent findings (6,7,8).

Endometrial tuberculosis seems to occur when the ovaries and uterus are in a state of activity (9) and it derives its significance as a clinical entity because of its tendency in focusing on those in these reproductive age group.

Tuberculosis of the genital tract gives rise to few symptoms especially in its mild or moderate phase, its discovery is usually made unexpectedly but will render a large percentage of infected women sterile unless detected and treated adequately in its earliest phases. The cases presented below is to highlight its clinical presentation and to serve as a reminder that pelvic tuberculosis still exist and will not disappear unless tuberculosis is completely eradicated.

Case Reports

Case 1: Mrs I.T is a 26years old Nigeian nulliparous woman who presented on 13th of September 2002 with 3years history of inability to get pregnant despite adequate unprotected sexual contact with her husband, on and off colicky lower abdominal pain, irregular menses with menorrhagia in the 2years preceding presentation.. She had her menarche at the age of 15.

On physical examination, significantly physical findings were suprapubic tenderness on deep palpation, bulky uterus of 8weeks size and positive cervical excitation tenderness. The husband's semen analysis shows a count of 20million spermatozoa per ml and 70% motility. Her PCV

was 33%, White blood cell (WBC) count of $4.8 \times 10^9/l$, differentials: neutrophils (57%), lymphocytes (37%), monocyte/eosinophil (06%) and ESR of 30mm/hour. High vaginal and endocervical swabs for microcopy culture and sensitivity shows no significant growth, the urinalysis and electrolyte, urea and creatinine were essentially normal. Ultrasound scan showed sizeable amount of fluid in the pouch of Douglas with internal echo giving an impression of Pelvic inflammatory disease. Hysterosalpingiography (HSG) shows a dilated right fallopian tube in its outer half in keeping with right hydrosalpinx. The left fallopian tube was not demonstrated. Chest X Ray was normal. Histopathology report of endometrial biopsy showed granulomas with

multinucleated giant cells, mononuclear cell infiltration and dilated tubular gland. Ziehl Neelsen stains confirm acid-fast bacilli. A diagnosis of primary infertility secondary to tuberculous endometritis was made. Patient was subsequently referred to medicine department for anti tuberculous therapy.

Case 2

Mrs II, a 32years old para 1+0 housewife presented on the 23rd October 2003 with 2years history of inability to conceive despite regular unprotected intercourse, 6weeks history of abdominal pain and 2weeks of progressively increasing abdominal swelling and dysmenorrhea. The last childbirth was 7years earlier. There was no history of cough or contact with patient with chronic cough. No history of heat or cold intolerance and no weight loss. Patient had presented in a private hospital earlier where abdominal ultrasound and hysterosalpingography was done among other investigations. She is the second wife of the husband who had a child through the first wife 2years earlier.

On examination, there was a cystic, non-tender, non-mobile lower abdominal mass of 14weeks size. Uterus was deviated to the right but not enlarged. The PCV was 30%, abdominal ultrasound scan shows a huge multicystic left ovarian mass probably undergoing torsion. Hysterosalpingography revealed bilateral tubal blockage. An assessment of secondary infertility with ovarian cyst and bilateral tubal blockage was made and patient was admitted for exploratory laparotomy.

Intraoperative findings include abdominal mass of 16weeks size, completely matted pelvic organs with inability to identify any organ (frozen pelvis), adhesion involving omentum and gut with purulent/caseous exudates obtained from cul-de sac of the mass and haemorrhage with minimal ascites .

Minimal adhesiolysis was done to permit exploration and samples of ascitic fluid and purulent caseous exudates were taken for cytology, Acid-fast Bacilli and tissue biopsy. Her postoperative condition was uneventful and patient was discharged home on the 8th day. Sample taken for histology showed extensive area of necrosis and numerous granulomas comprising of macrophage, plasma cells and lymphocytes. There were also multinucleated giant cells of the foreign body and langhans type. A diagnosis of tuberculous endometritis was made and patient was commenced on antituberculous therapy. However she was lost to follow up.

Tuberculosis still remains a major disease in the developing countries (1). The prevalence of endometrial tuberculosis varies between countries. It is rare in the U.S.A., higher in Europe and much higher in developing countries (1,5,7,).

Pelvic tuberculosis is always secondary to tuberculosis elsewhere in the body and the primary lesion may remain silent for many years (10,11,12). Female genital tuberculosis usually begins from an hematogenous spread to the endosalpinx from where it may spread to the endometrium(50%),ovaries(30%),cervix(10%), and vagina(1%)(13). Nogales-Ortiz et al (14) showed involvement of the tube in 100% of the patients, endometrium (79%), myometrium (20%), uterine cervix (24%) and ovaries (11%).

Our two cases presented at ages 26 and 32 years. Tuberculous endometritis is commoner in the reproductive age group especially in developing countries where they are commonest in the 26-35 years age group (7, 15,16,17,18). Though rare, tuberculous endometritis has also been reported in postmenopausal women (10,19). The rarity is possible because of the decreased vascularity of the tissue, the lack of regular endometrial shedding in such patients, however means there is no barrier to

the establishment of the infection and to its progression (20).

The discovery of endometrial tuberculosis are usually unexpectedly mostly by endometrial biopsy in the course of investigative studies to explain infertility. The two cases were discovered while been investigated for infertility. According to Ojo (21), Schaefer(22), Chattopadhyay(5) and Klein(17) ,between 0.7-9.3% of infertile women are affected with endometrial tuberculosis.

Both patients here presented with lower abdominal pain. An intermittent chronic ache in the lower abdomen is observed in 20-30% of cases, in nearly 20%, the pain is mistaken for sub acute peritonitis (23). One of the two cases was managed for concomitant acute pelvic inflammatory disease. Pain in such patients may be due to secondary organisms invading the tube (24). Menstrual function may remain normal, menstrual abnormalities seen include oligomenorrhoea (54%), Menorrhagia (19%), amenorrhea (14.3%), postmenopausal bleeding (1.6%) and dysmenorrhoea (rare) (23,24).

Our patients show no constitutional symptoms at presentation. Malaise, loss of weight, night sweats and fever are seen only during unusually active phase of the disease (24).

The most likely explanation of failure to diagnose tuberculous pelvic infection correctly is the difficulty in distinguishing it from various forms of pelvic inflammation (24). Symptoms of chronic pelvic inflammatory disease in a virgin or in infertile woman with no past history of post abortal or venereal infection should be assumed to be tuberculosis until proven otherwise (23,24). Also one may suspect tuberculosis if the pelvic inflammatory process does not respond to antibiotic therapy one would expect if the principal abnormalities were due to gonococcus or streptococcus (24).

X-ray diagnosis is useful but not conclusive and could not alone provide a basis for definitive therapy (10,17). In the early stages, no evidence of endometrial infection may be present and hysterosalpingogram may be normal. As the process advances, confluence of the affected areas with caseation and ulcer develops; it then demonstrates variation from the normal. In more advance cases, the X-ray will reveal distortion of the endometrial cavity. In rare instances, the uterine cavity may be entirely obliterated so that no dye will enter and hysterosalpingogram may show a portion of the cervical canal (25) This is further exemplified by our two cases.

Final diagnosis depends on pathologic and bacteriological study of tissues or secretions. The diagnosis and confirmation of o

ur cases was by histology. Accurate diagnosis with biopsy depends on a biopsy taken late in the cycle (20,24). The finding of epitheloid clusters with giant cell is highly suggestive but not conclusive, unless tuberculous bacilli can also be demonstrated in special stained preparations. Traditional Ziehl-Neelson staining with basic fuschin is satisfactory. Modern laboratory processing use auramine-rhodamine staining and fluorescence microscopy. Part of endometrial tissues is sent for culture as well, otherwise endometrial tuberculosis may be missed in up to 50-75%cases (25). PCR can also be done on endometrial tissue. However, this may be positive even with dead bacilli and may not be reflective of an active disease. If endometrial sampling is not possible, the collection of first day menstrual discharge may reveal positive culture. Negative culture is not conclusive.

A chance of getting cured to restore fertility is uncommon (26). Some centers have reported pregnancy with IVF, which would appear to be the only treatment with any possibility of success (27).

Ectopic pregnancy following antituberculous drug therapy for pelvic tuberculosis is a recognized clinical syndrome (10,28,29).

With AIDS pandemic and increasing poverty in most developing countries, there may be a need to refocus on effective nationwide immunization against tuberculosis with health education campaign against AIDS. These are important factors in tuberculosis as pelvic tuberculosis will not disappear unless tuberculosis is completely eradicated.

REFERENCES

1. Waters M.F.R. Leprosy (Hansen's disease, hanseniasis). In: Weatherall & J. Ledingham J.G.G. Warrell D.A. (eds) Oxford Text book of Medicine, 3rd edn. Oxford University Press, 1995, 667-679.
2. Ajayi GO: Incidence of genital tuberculosis in infertile patients submitted to microbial tubal repair-Lagos University teaching 1987-1995. *Nig J Genito-urinary Med* 2:1-4, 2002.
3. Gauribazaz M, Mashewart B, Neera: Tuberculous endometritis: A clinicopathological study of 1000 cases. *Br J Obstet Gynecol* 90:84-86, 1983
4. Sivanesavatnam V, Lim BH, Sivanesan S and Manon A: Pelvic tuberculosis; an uncommon gynaecological problem in Malaysia. *J Trop Med and Hyg* 89:167-169, 1986.
5. Chattopadhyay Sk, Sengupta BS, Edrees TB and Al-Mesbari A: The pattern of female genital tuberculosis in Riyadh, Saudi Arabia. *Br. J. Obstet Gynecol* 93:367-371, 1986.
6. Mordi VPN, Adebisi-Akingba AO: Proceedings of an International conference organized by the society of Gynecology and Obstetrics of Nigeria, Ibadan-Nigeria. 16-23, p.531, Oct, 1977.
7. Isreal SL, Roitman HB, Clancy C: Infrequency of unsuspected endometrial tuberculosis. A histologic and bacteriologic study. *JAMA* 183:63-65, 1963.
8. Ayesha Y, Gohar Z, Nadra S: Frequency of endometrial tuberculosis in female infertility. *J Coll Physicians Surg Pak* 12(1):55-57, Jan 2002.
9. Aras S; Genital Tuberculosis Thesis, Ankara University, Ankara, 1960.
10. Batemann Bg, Nunley WC, Kitchin JD, Fechner RE: Genital tuberculosis in reproductive age women. *J Reprod Med* 31:287, 1986.
11. Falk V, Ludviksson K, Agren G: Genital tuberculosis in women. *Am J Obstet Gynecol* 138:947, 1980.
12. Francis WJA: Female genital tuberculosis. *J Obstet Gynaecology Br Commonwealth* 71:418, 1964.
13. Carter JR. Unusual presentation of genital tract tuberculosis. *Int J Gynecol Obstet.* 33:171-176, 1990.
14. Nogales-Ortiz F, Tarancon I, Nogales-Ortiz FF, Jr: The pathology of female genital tuberculosis. A 31 year study of 1436 cases. *Obstet Gynecol* 53:422, 1979.
15. Sutherland AM: Tuberculosis of endometrium. A report of 250 cases with the results of drug treatment. *Obstet Gynecol* 11:527-537, 1958.

16. Moyer DL: Endometrial diseases in Infertility, Progress in Infertility. Ed. Behram and Kistner RIV> Little Brown and Company Inc. p.158.1968.
17. Klein Ta, Richmond SA and Mishell DR: Pelvic Tuberculosis. *Obstet Gynecol* 43:99-104.1976.
18. Hutchins Cj: Tuberculosis of the genital tract. A changing picture. *Br. J. Obstet Gynecol* 84:534-538.1977.
19. Tang LCH: Postmenopausal tuberculous cervicitis. *Acta Obstet Gynecol Scan* 65:279.1986.
20. Fox H and Buckley CH: Inflammatory disease. In: *Pathology for gynaecologist*, 3rd edition. Edward Arnold. London. p.46-47, 1991.
21. Ojo OA, Onifade A and Bannermann RHO: The pattern of female genital tuberculosis in Ibadan. *Israel J Med Sci* 7:281-287,1971.
22. Schaefer G: Tuberculosis of the genital tract. *Clin. Obstet Gynecol* 9:968,1970.
23. Rajamaheswari N :Pelvic tuberculosis. Article available online at :SUNMED.org 2004.
24. Langdon P and Sheldon CS: Tuberculosis and other specific infections that produce pelvic inflammation. In: *Gynecology* 2nd edition, W.B.S Saunders company, Philadelphia. p881-895,1978.
25. David AM: Genital tuberculosis in females. *J Mt Sinai Hosp* @3:507-572,1956.
26. Schaefer G: Full term pregnancy following genital tuberculosis. *Obstet Gynecol Surv* 190:81,1964.
27. Gurgan T, Yarali H, Urman B, dagh Vand Dogan N: Uterine rupture following hysteroscopic lysis of synechiae due to tuberculosis and uterine perforation. *Hum Rep* 11:291-293,1996.
28. Halbrech I: Healed genital tuberculosis. *Obstet Gynecol* 10:73,1957.
29. Snaith LM, Barns T: Fertility by pelvic tuberculosis. *Lancet* I:712,1962.