Pelvic Tuberculosis

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"The student who dates his knowledge of tuberculosis from Koch may have a very correct but a very incomplete appreciation of the subject" SIR WILLIAM OSLER, 1892.

"1999- The gynaecologist who dates his knowledge of tuberculosis before the advent of hysteroscopy and laparoscopy may have a correct but a very incomplete appreciation of the subject"

Introduction

The first reported case of female genital tuberculosis was described by Morgagni in 1744. On a post mortem examination of a 20 year old woman, he found the uterus and the fallopian tubes filled with caseous material.

Almost invariably tuberculosis of the genital tract is secondary to a primary lesion elsewhere in the body and the primary lesion is usually quiescent by the time pelvic disease is diagnosed. Almost 80% of the patients will have evidence of such a lesion in the form of X-ray appearances of past or present, infection, or pleurisy, or presence of Mycobacterium tuberculi in the urine, or evidence of calcified abdominal glands.

Pathogenesis

Generally the infection reaches the genital tract, primarily the tubes in majority of cases, through the blood stream, usually from a pulmonary lesion. From the tubes the infection reaches the endometrium, in a retrograde spread or the pelvic and abdominal mesothelium in an antegrade spread. In a minority of cases the tubes, ovaries, and uterine serosa are involved secondary to an abdominal lesion. Primary infection of the female genital tract is extremely rare unless the husband has active genito-urinary tuberculosis.

About 5-13% of cases with pulmonary tuberculosis develop genital tuberculosis. [Tripathy, 1981] The infecting mycobacterium is the human type in a vast majority of the cases, though rarely a bovine strain may be responsible for the disease, through intestinal infection.

Pathology

Tuberculosis of the genital tract may produce no signs or symptoms apart from infertility; or there may be signs of pelvic infection, more often simulating chronic rather than acute pyogenic infection; or there may be evidence of tubo-ovarian masses. It is probable that the fallopian tubes are affected in all cases, the endometrium in 40-50%, the ovaries in 20%, the cervix in about 10%, and the vulva and the vagina in less than 0.5-1%. [Schaefer, 1956]

The fallopian tubes are invariably the site where the infection first reaches the genital tract. Bilateral tubal involvement is the rule in all cases. Infection begins in the mucosa and then spreads through the tubal wall to the peritoneal surface. The macroscopic appearances are similar to those of non-tuberculous chronic salpingitis with tubal thickening, fibrosis and adhesions. The end of the tube is generally closed or phimosed leading to hydrosalpinx or pyosalpinx. This gives the inverted retort shaped or the 'Tobacco Pouch' appearance to the tubes on hysterosalpingography. In some cases the fimbrial end of the tube is open and everted, with fimbrial agglutination. Although the tube may be anatomically patent in such cases, the mucosal folds have flattened, following the loss of muco-ciliary apparatus, the muscularis is replaced by fibrous tissue, and the tube becomes rigid, narrow and non-functional. This collaborates with the lead-pipe appearance of the tube seen on hysterosapingography. All these tubal changes cause a spatial anatomical and functional alteration of the tube leading to tubal factor infertility in the majority

of affected patients.

The ovaries may be involved, with adhesions to the ovarian fossa, or adhesions to the terminal segment of the tube forming a tubo-ovarian mass. Rarely the ovaries may harbour a cold abscess presenting with insidious symptoms and as a pelvic mass on clinical bimanual examination or pelvic ultrasound.

Endometrial infection occurs in 80% of cases, but this probably is an underestimate, since the endometrium sheds cyclically and reinfection may not occur in every cycle. In advanced cases there is complete destruction of the endometrium including the basal layer, resulting in complete obliteration of the cavity with Ashermann's syndrome and secondary amenorrhoea, or resulting in the formation of a caseous pyometra.

The uterine size varies from normal to atrophic in most of the cases, though rarely myometrial scarring and hypertrophy may result in an increased uterine size and volume. Rarely tuberculous pyometra may be associated with uterine enlargement.

Tuberculous cervicits is uncommon, but may present as an ulcer resembling ectropion, or a proliferative lesion resembling carcinoma, tempting the gynaecologist to perform a Radical Wertheim Hysterectomy, without tissue biopsy or histopathology.

Histological examination reveals typical tubercles with giant cells, epitheloid cell and round cells. Caeseation is prominent in advanced cases, with pyosalpinx or tubo-ovarian abscesses. The presence of acid fast bacilli is not sought invariably in the stained sections.

Clinical Features

Symptoms vary considerably with the severity and stage of the disease; from silent or enigmatic surprise to frank ascites with miliary tuberculosis. At one extreme there are many patients with no signs and symptoms, and the diagnosis is made during evaluation for infertility. At the other end of the spectrum the patients may present with anaemia, weight loss, cachexia, anorexia, night sweats, fever, excessive vaginal discharge, chronic pelvic pain, and abdomino-pelvic masses.

Menstrual disturbances such as shortened irregular cycles, with heavy bleeding is usual in case there is ovarian involvement. Sometimes however in case of severe endometritis there may be scanty periods or even complete amenorrhoea following incomplete or complete obliteration of the uterine cavity. The incidence of primary or secondary amenorrhoea is much higher in the Indian and Asian population, compared to the western population. This is possible due to more severe form of disease in the lower socio-economic strata, leading to extensive scarring and amenorrhoea.

In a series of 711 cases of gynaecological tuberculosis [Sutherland, 1985], the presenting symptoms are as shows in Table I.

Table 1
Presenting symptoms in 7 11 patients with Pelvic Tuberculosis

Infertility	314(44.16%)
Pelvic Pain	179(25.17%)
Menstrual Disturbances	127(17.86%)
Amenorrhoea	36(5.06%)
Vaginal Discharge	27(3.79%)
Postmenopausal Bleeding	16(2.25%)
Miscellaneous	12(1.68%)

In a very large series of 1380 cases Wagh, [1977] reports amenorrhoea in over 60% of the cases. This is grossly different than the incidence reported by Sutherland in Table. 1. This difference is attributed to a more severe form of disease in our country, with delayed diagnosis leading to dense scarring and fibrosis of the cavity. The menstrual disturbances in Wagh's series are as shown in Table II.

Diagnosis

Pelvic tuberculosis is difficult to diagnose. Culture and histopathology can be inaccurate, although a positive culture and histopathology clinches the diagnosis, the diagnosis often depends on a high index of suspicion

history, especially past history of tuberculosis or a family history of tuberculosis, old scars of cervical lymphadenitis, clinical and laparoscopic data, and response to empirical therapeutic drug treatment.

Table II:
Menstrual Pattern in Tuberculous Endometritis
With Primary Infertility

Menstrual Cycle	Number of Cases	Percentage
Primary Amenorrhoea	170	12.3
Secondary Amenorrhoea	580	42.0
Amenorrhoea of 2-6 months	90	6.5
Oligomenorrhoea	140	10.2
Normal Menstrual Cycle	170	12.2
Meno-metrorrhagia	150	9.5
Polymenorrhoea	100	7.3

General Examination

The aim is to uncover an extragenital lesion, especially in the lungs. The same may exist in the spine or in long standing cases even the kidneys may be involved. References to blood changes are scanty. Anaemia is only a feature in advanced cases. There is a mild to moderate leukocytosis with preponderance of monocytes, with a decrease in lymphocytes, in the acute stage. As the acute stage subsides the monocytes fall and the lymphocytes increase. The sedimentation rate (ESR) is usually elevated, although that is not very specific for diagnosis, but a gradual reduction is used as a marker for therapeautic response.

Hysterosalpingography

The following radiological features are fairly typical of tuberculosis.
- Bilateral cornual block with intravasation of the contrast.
- Irregular cavity with filling defects.
- Rigid pipe-stem narrowing of the isthmus, punctate opacification of crypts and diverticuli in the lumen of this part of the tube.
- A clubbed ampulla with retort shaped hydrosalpinges.
- Calcification in the tubes and ovaries.

Laparoscopy

Ascities and tuberculous peritonitis were once thought to be relative and absolute contraindications to laparoscopy respectively [Philips, 1977]. Although it was rarely used in Europe and North America, for diagnosing or managing ascites of unknown etiology, it has been used extensively in India, but more so by general surgeons rather than the gynaecologists. In a series of 2500 peritoneoscopies Udwadia [1986] reported 178 case of abdominal or pelvic tuberculosis with ascities. He also found that demonstration and culture of acid fast bacilli was rare, thus making histological diagnosis essential. Laparoscopy is fairly accurate in diagnosing pelvic tuberculosis. Invariably when done as an investigation for infertility, evidence of past affliction is seen in the from of thickened tubes, with intraluminal ceseation and terminal hydrosalpinx with retort shaped tubes. Tubo-ovarian masses either unilateral or bilateral are fairly common, with the terminal portion of the tube completely plastered to the ipsilateral ovary embedded in muco-filmy pseudo-membranous adhesions. Adhesions in the pouch of Douglas is another common finding of old pelvic Kochs. Very typically old Kochs leaves behind bowel and omental adhesions to the parietes, unlike post operative adhesions; which are restricted to the site of he previous scar on the parietal wall. Another common findings is perihepatic muco-fibrous adhesions commonly more extensive to the right than to the left.

There are times when the pelvic appearance is highly suggestive of old Kochs, but without any tissue evidence. We strongly feel that in such cases if multiple sections of the tube were possible the diagnosis would be definitely forthcoming.

In the presence of acute infection, miliary tubercles with peritoneal congestion and straw coloured ascitic fluid may be seen. Frank caeseation may be found in some. Rarely the whole appearance may be difficult to distinguish from that of ovarian malignancy with necrotic tissue all over. In a study by Sheth [1989] 70 women with ascites of unknown origin were subject to laparoscopic examination. In 56 of the patients visual diagnosis, aided by biopsy was made. Malignancy was diagnosed in 32

cases, tuberculosis in 20 cases and cirrhosis of the liver in 4 cases. Out of the 20 cases with tuberculosis, it was suspected in 18 cases by visual aid. The other 2 cases were initially suspected to be malignancy at first. The appearance varied from widespread miliary tuberces, a few tuberces with areas of caseation, calcification, large matted lesions and widespread adhesions. Of the 20 cases with tuberculosis, the disease affected pelvic structures in 16, of whom 12 also showed extensive abdominal disease. In all 20 women the diagnosis was confirmed by histology, but of the 16 cultures for acid fast bacilli only 8 (50%) were positive, and all 12 guinea pig inoculations were negative.

The morphological appearance of fallopian tubes and surrounding tissues of 1120 cases with proven tubal infertility were observed under laparoscopy by Yang et al [Yang et al 1996]. Hydrotubation was performed at the same time in each case. Tubal infertility diagnosed by laparoscopy accounted for 32.8% of infertile patients. Among them, pelvic tuberculosis accounted for 63.6%, while nonspecific inflammatory disease (NSID) 36.4%. 44.8% of the tuberculosis and 62.2% of NSID group had negative findings during pelvic examinaticn. Four types of tuberculosis lesions were demonstrated; miliary ascites (9.4%), adherent mass (35.8%), adhesion and calcification (43.1%) and nodular sclerosis (11.7%). In the NSID group, simple tubal obstruction accounted for 29.9%, the remaining were mild adhesions or hydrosalpinx. Complete tubal occlusion occupied 81.2% in tuberculosis group and 70.7% in NSID cases. In the tuberculosis group the positive rate of pelvic lesion biopsy and endometrial biopsy was only 59.1% and 20.5 respectively.

Hysteroscopy with Endometrial Biopsy

Hysteroscopic visualization of the uterine cavity is not very specific for diagnosing tuberculous infection, but some of the common findings are:

- A normal cavity with obliterated fibrosed tubal ostiae.
- Intracavitary adhesions, more commonly dense fibrous or fibro-muscular.
- Fibrosed tubular cavity, with complete absence of endometrial proliferation.
- Complete obliteration of the cavity.

Endometrial curettings are examined macroscopically for tubercles, but diagnosis is based on the microscopic identification of Mycobacterium Tuberculi, by acid fast Ziehl-Neilsen staining.

Guinea pig inoculation and culture is no longer used to aid in the diagnosis. In a series of 20 patients with a macroscopic and histological diagnosis of abdominal or pelvic tuberculosis, Sheth [1990] reported a negative guinea pig inoculation test in all 12 (100%) patients in whom it was tested. This may be possible due to the tissues failing to evoke a response, or that the animals may have acquired immunity from tuberculosis in the environment.

Polymerase Chain Reaction (PCR)

In 1994, Hashimoto et al [1994] used polymerase chain reaction on the endometrial tissue for detection of Mycobacterium Tuberculosis. The endometrial culture was also positive for Mycobacterium Tuberculosis. The pelvic CT scan and hysterosalpingography showed slightly expanded uterus and irregularity of the endometrium. Since these data established a diagnosis of early primary endometrial tuberculosis, the combined therapy of three antituberculous agents was commenced. Menstrual smear, culture and PCR for M. tuberculosis were examined monthly through the therapy. The mycobacterial cultures become negative soon after the start of therapy, followed by a negative PCR result 3 months later, thus concluding that PCR is useful for the rapid detection of M. tuberculosis not only in pulmonary but also in endometrial tuberculosis. Mirlina et al [1998] reported polymerase chain reaction (PCR) for diagnosing genital tuberculosis in females. PCR was used to examine endometrial curettage specimens in 44 patients with different nosological entities. It showed a high sensitivity (80%) and a high specificity in the diagnosis of genital tuberculosis.

CA 125

CA 125 is a gynaecological tumour marker developed using monoclonal antibody, and it helps to screen and distinguish between benign and malignant adnexal

masses. [Sophen et al 1990] The specificity of this marker is 80-90% in postmenopausal women, but in premenopausal women, the same may be elevated in pregnancy, endometriosis [Barbieri et al 1986] uterine fibroids, pelvic inflammatory disease [Hailila et al 1986] or menstruation.

Sheth [1996] reported a raised CA-125 in 3 cases with advanced pelvic or abdominal tuberculosis. The levels ranged from 275 U to 545 U. Subsequently Nistal et al [1996] reported three cases of women with abdominal pathology in which an elevated serum CA-125 tumor marker could have led to an erroneous diagnosis of ovarian carcinoma. However, after peritoneal biopsies were taken, tuberculosis was diagnosed. Furthermore, specific tuberculostatic treatment normalized serum CA-125 levels.

This leads us to recommend that in the developing world all premenopausal women with pelvic masses with or without ascities and raised CA-125 may benefit from a diagnostic laparoscopy and tissue biopsy, to rule out tuberculosis. Normal values however do not rule out ovarian malignancy, endometriosis or tuberculosis.

Ultrasound Guided Fine Needle Aspiration

A retrospective analysis was done of 37 ultrasonically guided fine needle aspirations (US-FNAs) from retropertoneal, abdominal and pelvic lymph nodes.[Al-Mofleh, 1992] The cytologic examination diagnosed 15 cases of malignant and 13 of tuberculous lymphadenopathy. The aspirate was normal in the remaining nine patients. On further workup of the last group, five patients turned out to have false-negative cytology. Of them, two had neoplasms, another two had tuberculosis, and one had sarcoidosis. The neoplastic disorders consisted of 7 lymphomas, 5 secondary carcinomas, 2 seminomas and 1 carcinoid tumor. The diagnostic specificity was 100% and the sensitivity 85%. Neither major nor minor complications were encountered in these patients. US-FNA is safe, highly specific and sensitive in diagnosing malignant and tuberculous lymphadenopathy.

Transvaginal Trucut Biopsy

The first author carried out a transvaginal trucut biopsy in his office in 5 cases of abdomino-pelvic masses. [Sheth, 1995] The biopsy gave a clear diagnosis of ovarian cancer in 2 cases, non tubercular inflammation in 2 cases and tuberculosis in 1 case. In the developing world, transvaginal trucut biopsy is an important method for diagnosis of pelvic masses as an office procedure. The same could replace the need for laparoscopy, in patients who have a contraindication to the procedure. It can also be used in patients with multiple previous abdominal surgeries, where there is a potential for bowel or vessel injury during laparoscopy.

Imaging

There is no typical ultrasound appearance to make a definitive diagnosis of pelvic tuberculosis. The finding of a large amount of loculated fluid containing septations and debris on ultrasound along with bilateral hydropic fallopian tubes is frequently suggestive of pelvic tuberculosis. [Crowley et al 1997]. A study [Rodriguez & Pombo, 1996] in which CT scans were retrospectively reviewed in 19 patients known to have "peritoneal tuberculosis" (PT) and compared with scans in 19 patients know to have "peritoneal carcinomatosis (PC). Computerised tomography (CT) images were evaluated for thickening (smooth versus irregular), enhancement, presence of nodules, and site of involvement on the parietal peritoneum. Ascites was presents in all cases of PT and PC, loculated in 10 cases (PT=4, PC=6), and located in the greater peritoneal sac (PT=15.PC=10) or in the greater and lesser sacs (PT=4, PC=9). Slight smooth thickening and pronounced enhancement of the parietal peritoneum were seen in 15 of 19 PT patients and in 5 of 19 PT patients (p<0.001), whereas irregular thickening was found in only 9 of 19 PC patients (p<0.001). Peritoneal nodules were present exclusively in PC (7/19) (p<0.01). The sites of the parietal peritoneum involvement were the pelvic (PT=9, PC=3) (p<0.001), and perihepatic (PT=6, PC=8) regions. Omental cakes were found in 4 of 19 PT patients. The most useful CT findings for distinguishing PT from PC were observed in the parietal peritoneum. The presence

Table III
Dosages and Toxicities Of First-And Second-Line Agents

Drugs	Daily dose children	Daily dose adults	Max Daily Dose	Adverse Reactions.
First-line Agents				
Isoniazid	10-20mg/kg PO, IM, IV	5 mg/kg PO,IM,IV	300mg	Hepatitis, peripheral neuropathy, hypersensitivity
Rifampin	10-20 mg/kg PO,	IV	600mg	Orange discoloration of secretion and urine, hep...... fever, purpura (rare), rash
Pyrazinamide	15-30 mg/kg PO	15-30 mg/kg PO	2 g	Hepatitis, hyperuricemia
Streptomycin	20-40 mg/kg IM	15 kg/mg IM	1 g	Vestibular and renal (rare) toxicity
Ethambutol	15-25 mg/kg PO	15-25 mg/kg PO	-	Optic neuritis,rash
Second-line agents				
Capreomycin	15-30 mg/kg IM	15-30 mg/kg IM	1 g	Auditory, Vestibular, and renal toxicity
Kanamycin	15-30 mg/kg IM	15-30 mg/kg IM	1 g	Auditory, Vestibular, and renal toxicity
Ethionamide	15-20 mg/kg PO	15-30 mg/kg PO	1 g	Hepatitis, hypersensitivity
Para-aminosalicyclic acid	150 mg/kg PO	150 mg/kg PO	12 g	GI disturbance, hypersensitivity, hepatitis, sodium load
Cycloserine	15-20 mg/kg PO	15-20 mg/kg PO	1 g	Psychosis, personality changes, convulsions, rash

of a smooth peritoneum with minimal thickening and pronounced enhancement suggests PT. Whereas nodular implants and irregular peritoneal thickening suggest PC.

Treatment

Medical

Beside rest and nutrition, medical treatment with anti-tubercular drugs forms the first line of treatment. It is vital that the medication is correctly prescribed with the right counselling and sometimes coaxing to continue the therapy conscientiously for the required and prescribed duration.

Medications are commonly divided into first-line and second-line agents. The first-line agents are typically more effective and less toxic than second-line drugs. A third category of drugs consists of medications that have both in vitro and in vivo activity but for which there are few to no clinical trails demonstrating their effectiveness. The recommended dosages and common drug-related toxicity's of the antituberculous medications are listed in Table III.

The goal of selecting a treatment regimen is to maximize efficacy, minimize toxicity, and ensure completion of therapy. In cases caused by highly resistant organisms, this may be difficult to do. In known or suspected drug-resistant case the initial regimen should include at least three drugs to which the isolate is susceptible and, preferably, which the patient has never before taken. The regimen may subsequently by tailored based on the results of susceptibility tests and the clinical course.

Beginning in 1986, the American Thoracic society (ATS) and the Centers for Disease Control and Prevention (CDC) recommended an initial three drug regimen, including isoniazid, rifampin, and pyrazinamide. [American Thoracic Society, 1986]

As drug-resistant strains of M. Tuberculosis become more prevalent in the United States, this recommendation was modified by American Thoracic Society [American Thoracic Society, 1994] to include ethambutol (or streptomycin) in addition to isoniazid, rifampin and pyrazinamide in all tuberculosis suspects who reside in areas with greater than 4% resistance to isoniazid Ethambutol (or streptomycin) should be continued unti' drug susceptibility results are available. In the instance of a fully susceptible isolate, ethambutol (or streptomycin) should be discontinued, as its inclusion in the regimen does not improve efficacy but carries a risk of drug toxicity. Pyrazinamide should be discontinued after the inital 2 months and isoniazid and rifampin should be continued for an additional 4 months, with the total duration of therapy being 6 months.

Our current practice is to initiate all patients on a 4 drug regime that includes Isoniazid, Rifampicin, Ethambutol and pyrazinamide, along with high dose Pyridoxine to prevent peripheral neuropathy. There are convenient kits containing the daily requirement. [Wokex 4 - tian of Rifampicin 450 mg plus Isoniazid 300 mg plus vitamin B - 6 10 mg, 2 tabs. of Pyrazinamide 750 mg each, 1 tab. of Ethambutol 800mg. 1 kit costs Rs. 16/-] This combination is used for 2 months followed by omission of Pyrazinamide and continuation of the other drugs for a further period of 6 months. [Wokex: 3 - 1 tab of Rifampicin 450 mg plus Isoniazid 300 mg plus vitamin B - 6 10 mg, 1 tab. of Ethambutol 800mg. 1 kit costs Rs. 9/-] The patient's response is monitored by clinical improvement, ESR and 6 weekly liver function tests are performed to watch for toxicity.

In case of lack of clinical response, the Streptomycin injection 1gm/day IM, is initiated, for a duration of 30 to 60 days. Any further use of alternative chemotherapy is done in conjunction with a physician well versed in the management of drug resistant tuberculosis.

MDR Tuberculosis

The global tuberculosis epidemic will result in an estimated 90 million new cases and 30 million deaths during the current decade. Programmatic control of this devastating epidemic and clinical management of individual cases has been complicated in recent years by the widespread emergence of drug-resistant Mycobacterium tuberculosis. Rates of infection caused by multidrug-resistant (MDR) organisms, defined as resistance to at least isoniazid and rifampin, have reached critical levels in many areas of the United States and the world. [Cohn et al 1997]

Patients with MDR tuberculosis, defined as resistance to least isoniazid and rifampin, should always be treated with a minimum of at least three to four drugs to which the isolate is susceptible, and the duration of therapy will depend on the agents used and the extent of disease. Some authorities recommend hospitalization at the time of initiation of therapy to monitor for drug toxicity and intolerance. [Iseman, 1993]

At the National Jewish Center, treatment is initiated with small doses that are gradually increased to the target dose over 3 to 10 days. Serum drug concentrations are determined to optimize therapy, as the pharmacokinetics of many of the antituberculous medications are not uniformly predictable. This is particularly important in the setting of HIV infection because of the increased risk of drug malabsorption. With the loss of isoniazid and rifampin, the two most important drugs, efficacy is decreased and prolonged therapy is necessary. In this setting, most authorities recommend a four-drug regimen, including an injectable agent. The oral medication should consist of any first-line agent that is available, plus a fluoroquinolone and other second-line agents. Ethambutol, when used as a primary agent in the treatment of tuberculosis, should be given at doses of 25 mg/kg instead of 15 mg/kg. Treatment should be 18 to 24 months beyond the time of culture conversion. The injectable agent should be continued for 4 to 6 months or until toxicity occurs or the maximum dose is reached. Surgical resection should be considered if culture conversion has not occurred by 6 months, particularly in patients with resistance to all first line agents.

New Antituberculosis Agents

Quinolones, Rifamycins, Clofazamine, Thiacetazone, Ampicillin/ Clavulanate, Imipenem, and Amikacin are all being tried as newer anti-tuberculosis drugs.

The fluoroquinolones have been used widely in the treatment of MDR tuberculosis, although there are few clinical studies available to guide clinicians. [Kennedy et al 1996]

In a randomized controlled trial of 200 patients with sputum smear-positive tuberculosis in Tanzania, patients received either a regimen containing isoniazid, rifampin, and ciprofloxacin or one consisting of isoniazid, rifampin, pyrazinamide, and ethambutol. The time to conversion to smear negativity was longer and the relapse rate higher for the ciprofloxacin-containing regimen than for the standard regimen, although these differences were mainly in the HIV-1 infected patients. Thus, the sterilizing activity of ciprofloxacin appears to be less than that of

the combination of pyrazinamide and ethambutol; however, when substituted for ethambutol in a regimen containing isoniazid and rifampin, ofloxacin appeared to be of equal efficacy. The fluoroquinolones remain a welcome addition to the treatment regimen in cases of MDR tuberculosis, but further studies are necessary to better define their role. Two other rifamycin agents, rifabutin and rifapentine, have excellent MICs against M. tuberculosis, but cross-resistance among these agents and rifampin is common. It is important to note, however, that roughly 30% of M. tuberculosis strains resistant to rifampion remain susceptible to rifabutin. In these instances, rifabutin may be useful addition to the treatment regimen. All mycobacterial species have at least one beta-lactamase, hence, use of beta-lactam agents is usually not therapeutically effective; however, beta-lactam agents in combination with beta-lactamase inhibitors are bactericidal for M. tuberculosis, and preliminary date suggest they may have a role in the treatment of extremely drug-resistant isolates.

Surgery in Pelvic Tuberculosis

Prior to the advent of anti-tuberculosis drug therapy treatment of gynaecological tuberculosis was very unsatisfactory. The choice lay between surgery and conservative management. Laparotomy and pelvic clearance was the usual procedure. There was a high incidence of post-operative bowel fistulae and death[Jedberg, 1950]

Currently pelvic clearance is occasionally called for. Indications include persistent active or recurrent disease following adequate treatment, persistent pelvic pain, severe menorrhagia, pelvic masses, the occasional coexistence of an ovarian cyst or fibroid, or suspicion of malignancy.

In the current perspective of assisted reproduction, it would be worth conserving the uterus even if adnexectomy is indicated in infertile patients, thus permitting the possibility of Oocyte donation in the future.

In a large series of 85 patients operated by Sutherland (1989), where technically feasible, total hysterectomy with removal of both tubes and ovaries was carried out by the abdominal route irrespective of the patient. All patients previously received anti-tuberculous drugs and the operation was carried out under further drug cover, with treatment continuing for 6-9 months postoperative. In this series no patient developed a fistula nor were any deaths reported.

The indications for surgery in the patients is listed below in Table IV.

Table IV.
Indications for surgery in 85 patients with gynaecological tuberculosis.

Abdominal Pain with Adnexal Masses	38
Uterine Fibromyomata	14
Recurrence of Endometrial Tuberculosis	10
Adnexal Masses without Pain	9
Excessive Uterine Bleeding	6
Ovarian Cysts	6
Carcinoma of Corpus Uteri	1
Suspicion of Endometrial Neoplasia at Follow-up	1

The senior author had on one occasion explored a patient for ovarian malignancy, the diagnosis being based on CT findings and a raised CA 125. The findings revealed normal ovaries with large omental caking. Frozen section from the omental masses revealed tuberculous pathology. Abdomen was closed and anti-tuberculous drugs were initiated. Review laparoscopy done 6 months later, revealed complete dissolution of the omental masses, and normal pelvic viscerae. Hence we feel it is prudent to resort to a frozen section for diagnosis in a doubtful case and treat medically rather than attempt a pelvic clearance in the mistaken diagmosis of carcinoma ovary.

Genital tuberculosis and HIV

The incidence of HIV-associated tuberculosis is increasing worldwide, especially in developing countries. HIV infected patients rapidly develop clinically significant disease, respond poorly to complete treatment and present with extrapulmonary tuberculosis. Although a relative increase of genital tuberculosis would be expected, this has not been reported. Probably,

tuberculous systemic disease is diagnosed earlier, before genital tuberculosis occur. Giannacopoulos et al [1998] report a- case of a young African female patient, who was admitted with symptoms of acute pelvic inflammatory disease due to genital tuberculosis and proved to be HIV infected. The patient was managed by intravenous antibiotic administration, but since no clinical or laboratory improvement was achieved, a laparotomy and salpingo-oophrectomy was performed. Histopathology revealed tuberculosis and after that the patient proved to be HIV infected. Further investigation did not reveal pulmonary or other extragenital manifestation of tuberculosis. The only manifestation of HIV infection and genital tuberculosis was the symptoms of an acute pelvic inflammatory disease, which is extremely rare.

It is recommended to test for HIV in all patients of genital and extra-genital tuberculosis and conversely all patients with HIV should have a high index of suspicion for tuberculous infection.

Conclusion

The incidence of genital tuberculos may be higher than one might imagine, based on the lack of reports in the literature, and may account for a significant amount of female infertility. Tuberculosis, a chronic infectious disease, is one of the major etiologic factors of female tubal infertility, especially on the Indian subcontinent. Laparoscopic examination is a valuable procedure for the etiological diagnosis of tubal infertility, along with histopathological and AFB staining of tissue biopsy.

Women with genital tuberculosis appear to represent a less favorable subset within other tubal factor patients when treated with IVF-ET. Although IVF represents a useful treatment and improves the chances of fertility, in what was considered a desperate situation. The cases of multidrug-resistant tuberculosis are associated with significantly higher rates of morbidity and mortality, and successful treatment typically necessitates prolonged courses of chemotherapy, measures to ensure patient compliance and considerations of resectional surgery.

Unfortunately it is not possible to completely go by the available literature, since most of the studies are from areas of low endemic incidence. Countries with rampant tuberculosis do not have the finance for requisite research. Hence it would be essential to understand that one may have to base ones diagnosis and management on the acquired experience and sometimes initiate empirical treatment in spite of the absence of diagnostic proof.

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