A case of Genital Tuberculosis

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Abstract
Background: genital tuberculosis is a misleading health problem.
Methods: Laparoscopic surgery of a multiparous woman revealed a complex mass adhering to the pelvic floor. Collected samples were cultured for microbial infection. Polymerase Chain Reaction test was done for presence of Mycobacterium tuberculosis.
Results: Mantoux test and Polymerase Chain Reaction test were negative. Caseous necrosis on frozen section specimens were seen. Granulomatous inflammation composed of epithelial cells and multinucleated giant cells were found. Patient was cured with anti-tuberculosis treatment.
Conclusions: In the present case only histopathological investigation of the smear could detect the genital tuberculosis.
Keywords: Mycobacterium Tuberculosis; Tuberculosis; Tuberculosis, Female Genital; Infertility; Tuberculosis; Salpingitis; Diagnosis; Therapeutics; Female.

Introduction
Tuberculosis (Tb), a multifaceted disease, is an important public health problem worldwide [1, 2] with widespread morbidity and mortality [3]. About one third of the world’s population is infected. Of these, residents of Africa and Southeast Asia each accounted for about 3 million cases and the Western Pacific region for about 2 million cases. These regions accounted for 83 percent of total cases reported [4]. Tuberculosis, is divided into two clinical forms: pulmonary and extra-pulmonary [5]. The most common form is pulmonary tuberculosis, but the disease can affect almost any part of the body [1, 6]. In fact, it is well known that pulmonary tuberculosis patients develop extra-pulmonary tuberculosis. One such manifestation is the occurrence of female genital tuberculosis [3]. The spread of the pathogen to fallopian tubes, endometria and ovaries leads to a variety of clinical conditions [7, 8]. The fallopian tubes are the first and most commonly affected genital organs, followed by endometrium, ovary and cervix [2, 9]. Adhesions between tubes, ovaries, omentum, intestine, liver and diaphragm (the Fitz Hugh Curtis syndrome) are other common findings in tuberculosis [8-11]. Primary genital tuberculosis is an extremely rare genitral tract infection. Genital tuberculosis is almost always secondary to a focus elsewhere in the body [1, 12]. The Mycobacteria reach the genital tract through hematogenous spread in about 90% of patients with the primary foci being lungs, lymph nodes and skeletal system, direct spread via the lymphatic system or directly from the gastrointestinal tract, mesenteric nodes, or peritoneum and are rarely transmitted by sexual intercourse [2]. Genital tuberculosis often exists without any symptoms or clinical signs. The diagnosis of genital Tb can be achieved through high index of suspicion especially in patients at risk of the disease, in areas where it is common and with concurrent use of appropriate investigative techniques. High risk factors include previous pulmonary Tb or contact with one, resident in highly prevalent areas, low socioeconomic background, Human Immunodeficiency virus (HIV) positive, weight loss and presence of symptoms [13]. It may thus be considered for an at risk patient [14]. The usual laboratory procedure for clinical specimens involves microscopic examination for the presence of acid-fast bacilli, isolation of the organism by culture, identification and drug susceptibility testing of the recovered organism. As biochemical testing is slow, cumbersome and may yield ambiguous results, laboratories are increasingly using molecular methods [15]. Many molecular methods have been developed for direct detection, species identification and drug susceptibility testing of mycobacteria. These methods can potentially reduce the diagnostic time from weeks to days; are fast, reliable and sensitive [16]. Herein, we report a case of genital tuberculosis with misleading symptoms and with PCR negative result.

Method
A 34 year old multiparous, G2P2, Pakistani woman having two kids referred to the gynecology clinic of Imam Reza hospital-Tehran- Iran. Her Body Mass Index (BMI) was 18.4 kg/m². She complained of upper abdominal pain for the last one month along with nausea, vomiting and weight loss. Endoscopy revealed a normal esophagus, stomach and duodenum. Trans-abdominal and trans-vaginal ultrasound scanning showed a normal retroverted uterus, displaced to left due to a complex mass with 80 mm volume, thick septation and free fluid gathered in the posterior culde sac. These findings led her to gynecologist. Physical examination revealed normal vital signs, clear lungs and mild diffuse upper abdominal tenderness. On vaginal examination with speculum, cervicitis with yellow discharge and cervical motion tenderness was apparent. Pap smears were
also prepared. Urine culture, liver function tests, amylase, Erythrocyte Sedimentation rate (ESR), C-reactive protein (CRP), Human Chorionic Gonadotropin (β-HCG) and Mantoux test were requested for the patient. She received Clindamycin & Gentamycin with diagnosis of Pelvic Inflammatory Disease (PID). After one month she was readmitted with severe pain. Ultrasound scan showed right ovary surrounded by a complex mass. Laparoscopic surgery revealed a complex mass surrounding the right tube and ovary, adhering to the pelvic floor. Millet seeding less than 0.5 cm in pelvic organs were clear. Samples were collected for smear. Multiple biopsy specimens were collected from millet seeding in normal saline and in formalin for definitive diagnosis. Culturing of the collected samples was not done because at first, there was no suspicion of Tb. After receiving the pathological results, Polymerase Chain Reaction (PCR) test for identification of M. tuberculosis was requested. Right salpingophorectomy was done. 

Upon receiving the laboratory results, patient received anti-tuberculosis drugs using World Health Organization (WHO) recommended Directly Observed Treatment, Short-Course (DOTS) strategy [13]. The prescribed regimen was isoniazid, rifampicin, pyrazinamide and ethambutol for two months, followed by isoniazid and rifampicin alone for following four months [17]. After therapy was completed, patient was fully recovered but was followed up.

Result

Endoscopy of the patient, a 34 year old multiparous G2P2 Pakistani woman with BMI of 18.4 kg/m² revealed a normal esophagus, stomach and duodenum. The first trans-abdominal and trans-vaginal ultrasound scanning showed a normal uterus, complex mass with 80 mm volume with thick septation and free fluid in the posterior culde sac. The second ultrasound scanning also showed the complex mass surrounding the right tube and ovary. Microbiological study of the cervical discharge showed few polymorphonuclear leukocytes, gram staining was negative for pathogenic bacteria and culturing for common bacteria was negative after 72 hours incubation. Trichomonas was not observed. Collected samples were cultured for gonorrhea and Chlamydia which did not grow. Laboratory tests were negative for β-HCG, but CBC showed mild leukocytosis. Urine analysis and urine culture, liver function tests and amylase, ESR and CRP were normal. Mantoux test was negative. Pap smeared was negative for epithelial cell abnormality but showed moderate inflammation and reactive cellular changes. Right salpingophorectomy revealed necrotizing granulomatous salpingitis of both fallopian tubes, cystic follicles and corpus luteum of ovary. According to the pathological investigation, granulomatous inflammation composed of epithelial cells and multinucleated giant cells were found and chronic granulomatous salpingitis was suggestive of Tb. Caseous necrosis on frozen section specimen and culture of nodule was positive for M. tuberculosis. Foci of caseation were Seen (Figures 1& 2). Mantoux test and PCR were negative for mycobacterium tuberculosis. Treatment with standard anti-tuberculosis drugs was effective in treating the patient in expected period. No drug resistance was observed.

Discussions

Early diagnosis is crucial for treatment of the patient and prevention of further spread of the disease. Bacilli-positive Tb patients are the most potent sources of mycobacterium transmission in the community [18-20]. Genital tuberculosis must be taken into account in women of reproductive age who live in or are descendants of families from countries where Tb is endemic [5].

Systemic symptoms including weight loss, feeling unwell and night sweats may be present in genital Tb, as was observed in the present case. In the acute phase, the picture may resemble classical acute pelvic inflammatory disease [21]. In the present case, BMI of our 34 year old patient was low (18.4 kg/m²) with misleading signs mimicking gastric disorder. Later diagnosis was PID. In accordance to the radiological chest finding of the present case, Botha et al. stated that about 75% of cases with
active genital tuberculosis have normal chest X-ray [2]. Diagnosis of genital Tb is not easy because genital tuberculosis has a wide range of clinical and radiological manifestations with slow growing symptoms [22]. A proper diagnosis usually requires data derived from abdomino-pelvic ultrasonography, chest radiography, skin test, acid fast bacilli (AFB) staining, PCR analysis and histopathological evaluation [5, 15]. However, primarily due to the slow growth of the bacteria (4 to 8 weeks), these methods result in numerous missed or delayed diagnoses, thereby, adversely affecting patient care and tuberculosis control and allows for the spread of infection. Tb infection cannot be ruled out by negative results of these tests [16].

In the present case the vaginal mycobacterial infection was detected by two techniques i.e. PCR and histopathological examination of the sample. We obtained negative result by PCR. It was microscopic examination of the tissue that could reveal the vaginal tuberculosis. Despite our finding, many researchers believe that PCR is a reliable molecular diagnostic test as they could extract target DNA for diagnosis of extra-pulmonary Tb infection [23, 24]. They consider PCR as the most sensitive and specific method for the detection of tuberculosis [3, 15, 16]. However, according to some researchers, the overall accuracy of PCR approaches the results of conventional methods. Their results indicate that conventional biochemical tests are as sensitive as the PCR [25, 26]. According to some studies, PCR cannot replace Mycobacterium culture [3]. It is also to be noted that PCR techniques involve prohibitive expenditure in terms of instrumentation, expertise and reagents, putting them out of reach of many laboratories in developing countries [16, 26]. Sadeghian et al.( 2005) in their study compared three methods of culture, biochemical tests and PCR for identification of Mycobacterium tuberculosis. They concluded that there were no statistically significant differences between biochemical tests and PCR method [16]. Similar to our finding, Afzali et al's finding (2013) support this idea that in diagnosing genital tuberculosis, histopathology and demonstration of mycobacterium in the genital tract are useful tools for diagnosis [22]. We are also unisonous with Alcaide et al. and Domínguez et al. that histopathological investigation offers a promising scenario for extra-pulmonary Tb diagnosis [27, 28]. Contrary to our result, Abebe et al. (2004) concluded that the least sensitive technique was histopathological examination for granulomatous tissue reactions compatible with tuberculosis infection (2.4%) [7]. In the present case, despite the lack of direct microscopy and culture data, empiric Tb treatment with anti-mycobacterial therapy was initiated on the basis of granulomatous histopathology. The diagnosis was confirmed by the patient’s response to treatment and cure. This case confirmed the need for adopting effective diagnostic methodology for diagnosis of extra-pulmonary tuberculosis. Adequate anti-Tb chemotherapy for an appropriate period of time will result in almost 100% cure rate [28]. For this patient we also prescribed the recommended regimen which completely cured her [1, 2].

Conclusion

Accurate diagnosis followed by anti-tuberculosis treatment is the only way for control of the disease. A sensitive and specific diagnostic test for the rapid identification of patients with active Tb facilitates early treatment and prevention of transmission.

References