

Female genital system tuberculosis: a retrospective clinicopathological study of 1,548 cases in Turkish women

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Abstract

Purpose The incidence of tuberculosis (TB) has increased worldwide in the past decade and it still remains an important global public health problem.

Method A retrospective clinicopathological study of 1,548 cases of female genital tuberculosis between 1940 and 2011 was conducted.

Results The mean age of the cases was 29.49 years. Involvement of the endometrium was noted in 1,073, fallopian tubes in 164, cervix in 157, and 154 had multiple organ involvement. Clinically, 115 cases (7.4%) were diagnosed as having primary infertility and 12 cases (0.8%) as having secondary infertility. There was a coexistent

carcinoma in 1.5% of the cases. Peritoneal tuberculosis in 21 cases and tuberculous lymphadenitis in 7 cases were seen as well.

Conclusion The clinicopathological criteria of female genital tuberculosis in the different organs are described, and special attention is paid to infertility associated with tuberculous lesion, and awareness of the fact that the disease is still with us is thus particularly important.

Keywords Tuberculosis · Female genital · Female genital tract · Infertility · Epidemiology

Introduction

Tuberculosis (TB) is one of the most common worldwide cause of mortality from infectious diseases with approximately 95% of cases occurring in developing countries [1]. In 2010, there were 8.8 million incident cases of TB, 1.1 million deaths from TB among HIV-negative people and an additional 0.35 million deaths from HIV-associated TB worldwide and one-third of the world's population is estimated to be infected with *Mycobacterium tuberculosis* [2]. In Turkey, a total of 17,402 tuberculosis patients have been registered at tuberculosis dispensaries in 2009 [3]. However, extrapulmonary tuberculosis (EPTB) is less frequently found than pulmonary tuberculosis. The frequency of genital tuberculosis (GTB) is reported as 1–9% in different series [4–6]. Turkey statistics report a involvement of 5.7% of female genitourinary system involvement in 2009 [3].

Female genital tract TB is an important chronic pelvic disease and etiology of infertility. The fallopian tube is the most common site of tuberculous pelvic infection, which spreads to the uterine endometrium in 60% of the cases.

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Less frequently organisms may be identified in the ovary, cervix, vagina, and vulva. Spread of the infection is usually through the blood stream, but direct spread from other abdominal organs and the peritoneum is also possible [2, 4, 6–16].

Diagnosis is made with the isolation of *M. tuberculosis* from the genital tract by culture; but apart from this the demonstration of granulomas with or without langerhans giant cells by histopathology is universally accepted as adequate for female genital tuberculosis (FGTB) diagnosis, because the non-tuberculous causes of granulomas are usually ruled out without much difficulty [4, 6, 7, 17, 18].

Most patients with genital tuberculosis present with infertility, abdominopelvic pain, or menstrual irregularity [4, 7, 8, 19]. One-fifth of these are entirely normal on clinical examination, and awareness of the fact that the disease is still with us is thus particularly important.

Methods

The patient data were documented using the archives of pathology and obstetrics and gynecology departments between 1940 and 2011, except for 1970–1973 which we could not reach. The paraffin blocks of the cases were available from 1985 and were evaluated for the histopathological findings. The relation of the clinicopathological parameters was searched.

Results

This case series included totally 1,548 patients. The age of the cases were changing between 15 and 80 with the mean age 29.49 years, and the median age was 27 years. The clinical diagnosis was recorded in 166 of the patients, and these were infertility in 127 cases (76.5%), menstrual irregularity in 20 cases (12.1%), whereas 12 cases (7.2%) had leiomyoma, 1 case (0.6%) had ectopic pregnancy, and 6 cases (3.6%) had lung TB. Of the 127 cases of infertility, 115 cases (90%) had primary infertility and 12 cases (10%) had secondary infertility. Evaluation of the association of the lesion distribution between these complaints revealed that the incidence of endometrial TB was more in patients having menstrual irregularity and leiomyoma. In the patients having infertility complaint, 103 had endometrial TB, 11 cases were diagnosed as cervical TB, 9 cases as tubal TB, and 4 as ovarian TB in our study group. Besides, 18 patients of whom were operated for a malignancy GTB had been detected. The diagnosis was cervical in 2 of them, 4 cases had endometrial, 11 cases had adnexal, and 1 case had rectal coexistent carcinoma operation.

The biopsy material was incisional biopsy as probe curettage (PC) or cervical biopsy in 1,214 cases (78.6%), excisional biopsy as tubal or ovarian excision in 155 cases (10%), or resection in 176 cases (11.4%) as total abdominal hysterectomy.

The distribution of TB according to the organs was as follows: 1,073 cases (69.3%) endometrium, 164 cases (10.7%) fallopian tubes, and 157 cases (10.1%) cervix. Among these cases, there were also multiple organ involvements and they are summarized in Table 1. Tuberculous peritonitis was seen in 21 (1.3%) cases, and TB lymphadenitis was seen in 7 (0.4%) cases. The cases having TB peritonitis, had tubal involvement in 9 cases (0.58%), endometrial involvement in 1 case (0.06%), ovarian involvement in 2 cases (0.013%), and tubal and ovarian involvement in 1 case (0.06%). In TB lymphadenitis cases, 1 patient has FGTB in fallopian tubes, endometrium, cervix, and ovary as well.

The histopathological diagnosis was made by the presence of granulomatous inflammatory reaction, and caseating and noncaseating granulomas containing langerhans type giant cells (Figs. 1, 2).

The properties of the patients are summarized in Table 1 and the yearly distribution of the cases is given in Fig. 3.

Discussion

The actual incidence of genital tuberculosis cannot be determined accurately in any population, since some of patients are asymptomatic, symptoms of the patients are not typical and especially in the well-developed countries, it is thought to be eradicated and the disease is discovered incidentally [8]. Prevalence of FGTB as a cause for infertility is reported in a range from different parts of the world and in different time periods (changing from less than 1% in USA to nearly 18% in India) [4–7, 9, 18].

The reproductive period is thought to be the most risky time to be infected by genital tuberculosis. According to Sutherland, the mean age was 28.2 years in a time period from 1970 to 1980. Falk's series in Sweden also gave similar results [1, 8]. Similar to these results in Saudi Arabia between 1979 and 1983, Chadtopadhyay et al. [10] noticed the mean age to be 24.8 years. The age distribution is ranging from 20–40 to postmenopausal ages [4, 7, 19, 20]. In the presented series, the mean age was 29.49 years. The difference in age distribution between countries is not clarified but it is proposed to be related to the early marriage and childbearing in developing countries [4].

GTB has three main symptoms: infertility, pelvic pain, and menstrual changes. The most frequently observed symptoms are infertility with an incidence of 43–74%, lower abdominal intermittent chronic pain with an

Table 1 The properties of the patients

Property	Number of cases	Percentage
Biopsy type		
Excision (Salpingectomy-ooforectomy)	155	10
Incision (PC, Cx, Bx)	1,214	78.6
Resection (TAH)	176	11.4
Organ involvements		
Cervix	157	10.1
Endometrium	1,073	69.3
Tuba	164	10.7
Cervix + tuba	14	0.9
Cervix + ovary	6	0.3
Endometrium + tuba	57	3.7
Endometrium + ovary	14	0.9
Tuba + ovary	34	2.2
Cervix + ovary + endometrium	6	0.3
Cervix + ovary + tuba	3	0.2
Tuba + ovary + endometrium	7	0.5
Cervix + tuba + endometrium	13	0.9
Clinical finding		
Infertility	127	76.5
Menstrual irregularity	20	12.1
Pelvic mass (leiomyoma)	12	7.2
Ectopic pregnancy	1	0.6
Lung TB	6	3.6
Total	166	100
Concomitant tumor		
Cervical carcinoma	2	11
Endometrial carcinoma	4	22
Adnexal tumor	11	61
Rectal carcinoma	1	6
Total	18	100
Infertility		
Primary infertility	115	90
Secondary infertility	12	10
Total	127	100
Infertility and organ distribution		
Cervix	11	9
Endometrium	103	81
Tuba	9	7
Over	4	3
Total	127	100

incidence of 40–50% [4, 9, 11, 12, 17] followed by oligomenorrhea (54%), menorrhagia (19%), dysmenorrhea (12–30%), amenorrhea (14%), and dyspareunia (5–12%) [4, 17, 18]. The clinical setting in developed countries is often an incidental diagnosis during the workup for infertility, but in developing countries, GTB is a relatively

common condition with 39–58% reported [4, 5, 7, 18, 20]. GTB not only causes tubal obstruction, but also impairs implantation due to endometrial involvement and ovulatory failure from ovarian involvement or synechiae of the uterine cavity can be the cause of infertility [4, 7, 19]. The reported incidence of infertility among women with FG TB is 58–87% [4]. In the series of Nezar et al. [18], among 420 infertility patients 24 had GTB. In our cases complaining of infertility, the great majority (81%) had endometrial involvement and only a small group had tubal involvement (7%) indicating that their problem most probably had resulted from impairment of endometrial implantation. Although patients with genital tuberculosis are usually young women during workup for infertility postmenopausal bleeding can also be seen in the setting of endometrial TB [15], it is responsible for only 1% of postmenopausal bleeding. The low incidence in the postmenopausal age group is not fully understood. It is thought that atrophic endometrium offers a poor milieu for the growth of mycobacterium [4, 18, 21]. Pelvic pain can present so exquisite that the clinical picture can be like acute appendicitis [13], with 32–57% reported incidence [4]. Aboufalah et al. [19] reported it as the most common complaint in their series of 28 cases.

Constitutional symptoms are fever, night sweating, abdominal swelling, anorexia, and weight loss [16]. Abdominal symptoms are seen in the 9 months period of the diagnosis. A study from Pakistan [12] reported that the majority of the cases were between 25 and 45 years, the most common presenting symptom group following infertility and abdominal pain. In our cases, the most common complaint was primary infertility, followed by menstrual irregularity in the second line. Besides, leiomyoma, ectopic pregnancy, and lung TB were the other diagnoses, of which FG TB was found in the issue of diagnostic research.

In the studies of FG TB, the tubal involvement was seen in 95–100% and endometrial involvement in 50–99.5% of the cases [6, 13, 14, 18–20, 22]. The vagina and vulva are almost never involved. Other sites have shown variable rates of involvement (ovaries 20–62.5%, cervix 1–81.5%) [6, 13, 14, 20]. Tuberculous endometritis is reported to be almost invariably associated with tuberculous salpingitis except in the postmenopausal women, in whom there may be no tubal disease [21]. Parallel to these findings, the most common localizations were endometrium and fallopian tubes in our study group. There were multiple genital organ involvements in some of our cases. Similarly, Lamba et al. [23.] reported that the tubal lumina were obliterated in 50% of the endometrial diseases. Among these, myometrial involvement was seen in 2.5%, and cervical involvement was seen in 5–24% of the cases. TB peritonitis was seen in combination with GTB in 45–50% patients with GTB [7]. Multiple involvements were seen with TB peritonitis in 13

Fig. 1 Tuberculous endometritis: granulomatous reaction beside the endometrial glands. Granulomas (*thick arrow*) have epithelioid histiocytes and langerhans type giant cells (*thin arrows*) (H&E; $\times 200$, $\times 400$)

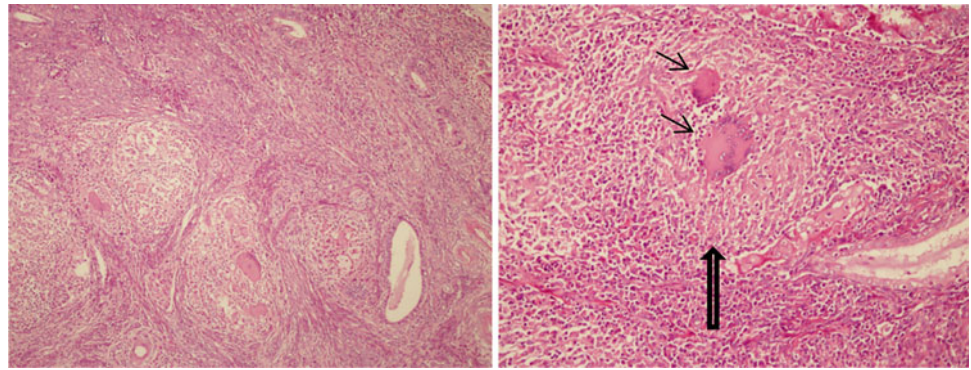


Fig. 2 Tuberculous salpingitis: granulomatous reaction beneath the tubal epithelium. (H&E; $\times 100$, $\times 200$)

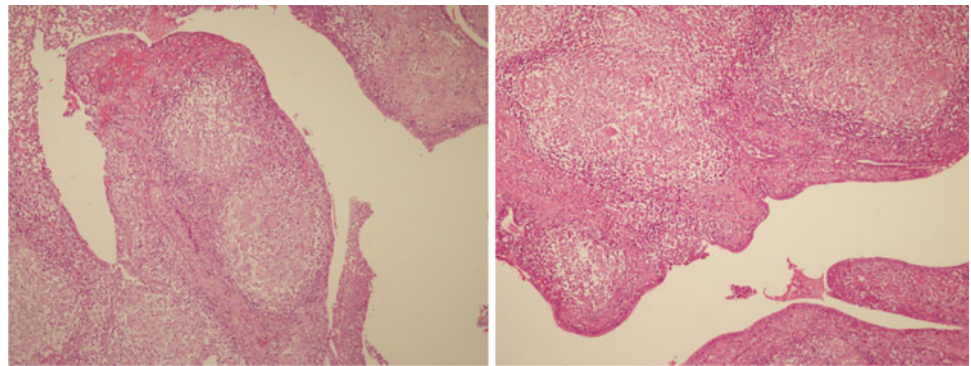
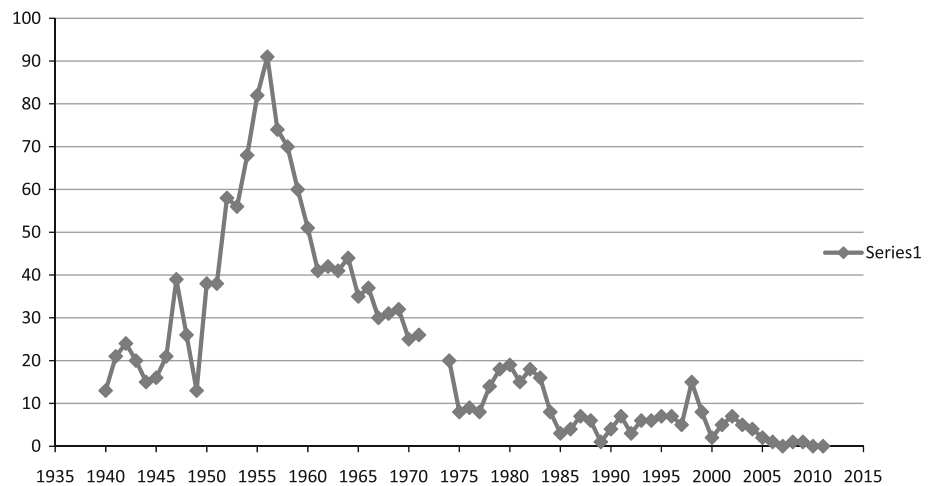


Fig. 3 The yearly distribution of the cases



cases, and with TB lymphadenitis in 1 case in our study group.

Tuberculosis bacilli reach female genital tract by three routes: (1) Hematogenous route (primary focus can be lungs, lymph nodes, urinary system, bone, or joints), (2) descending route (there is direct or lymphatic spread from intraabdominal organs), and (3) ascending route (vulva, vagina, or cervix play a role as the primary focus). Furthermore, the disease can reach the abdomen via peritoneal dialysis [6, 9, 24].

In our case series GTB was demonstrated to be associated with pulmonary TB only in 6 cases (3.6%). However, isolated cervical involvement was present in 157 cases (10.1%). Forty-two additional cases displaying multiple organ involvement including cervix, increase the ratio of cervical involvement up to 12.8%, suggesting that the ascending route might be an important way of distribution of FGTB in Turkish women population.

Tumor–TB coexistence is reported mostly as case reports in the literature [25, 26]. The differential diagnosis

between malignancy and peritoneal TB can be problematic since abdomino-pelvic TB usually masquerades as ovarian cancer. From Turkey, in the series of Koc et al. [27] among the 1,826 women suspected of ovarian cancer, 22 (1.2%) were found to have peritoneal TB and differential diagnosis with peritoneal carcinomatosis should be made [4, 28]. In our series, 18 patients having FG TB were operated for cervical, endometrial, tubal, and rectal coexistent carcinoma.

Although TB after the Second World War has been almost eradicated in the well-developed countries due to vaccination, early diagnosis, proper antibiotics, and increase in the life standards [8, 26], it still seems one of the major problems in the underdeveloped countries and also in the developing countries such as Turkey. Because of immigration, both from one country to another and also to cities, it seems that genital tuberculosis will be reborn in many countries and areas where it is thought to be eradicated [29, 30]. In our study it has been observed that the prevalence of TB cases decreased in the time period of 2–3 years after the Second World War and increased in the time period of 1950–1956, when the immigration was highest.

Genital tuberculosis is generally observed more frequently in rural areas where the hygienic and economical status is lower, and vaccination cannot completely be performed [8]. The eradication of TB, especially in the rural areas is closely related to the preventive medicine studies. Although it is thought to be a problem of underdeveloped areas, it is the problem of the whole world. Recent increases in the total number of TB cases observed in some developed countries reflect the growing proportion of foreign-born patients presenting with this condition [7, 28, 31] as well World Health Organization reported that tuberculosis was a global emergency in the early 1990s due to the increased number of HIV-infected patients, increased number of immigrants to the industrialized countries from developing countries, and various social problems such as poverty and homelessness [4, 6, 21].

In conclusion, we believe that genital tuberculosis should be kept in mind, especially in infertile cases even in the countries where it is thought to be eradicated.

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Conflict of interest None.

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