

Female genital tuberculosis: About 6 cases

Authors

- 1) Asma Hmila, MD, Resident in Obstetrics and Gynecology, Department of Obstetrics and Gynecology, University hospital center Mohammed VI of Oujda, Morocco
- 2) Hafsa Taheri, MD, Assistant Professor of Medicine, University hospital center Mohammed VI of Oujda, Morocco
- 3) Saadi Hanane, MD, Associate Professor of Medicine, University hospital center Mohammed VI of Oujda, Morocco
- 4) Ahmed Mimouni, Professor of Medicine, University hospital center Mohammed VI of Oujda, Morocco

Corresponding Author: Dr. Asma Hmila, MD, Resident in Obstetrics and Gynecology, Department of Obstetrics and Gynecology, University hospital center Mohammed VI of Oujda, Morocco; Email : hmila_asma.tn@outlook.com

Manuscript submitted – 11th June 2020

Peer review completed – 2nd July 2020

Accepted for Epub – 5th July 2020

Distributed under Attribution-Non Commercial – Share Alike 4.0 International (CC BY-NC-SA 4.0)

Abstract:

Background: Genital tuberculosis in women is uncommon. Its clinical pictures and radiological aspects are nonspecific. The histological confirmation is necessary. Treatment is medical but infertility prognosis is often poor due to irreversible tubal damages. **Objective:** Our study aims to report the epidemiological characteristics of genital tuberculosis suffering women, their clinical pictures and the treatment undertaken. **Methods:** This is a retrospective study reporting six cases of confirmed genital tuberculosis operated in the Obstetrics and Gynecology Department of the Mohammed VI university hospital in Oujda between January 2015 and December 2018. **Results:** The profile of the woman carrying this disease in our study was that of the young woman in the period of genital activity with an age average of 36 years. Low socioeconomic level was found in all the patients. The major clinical signs were pelvic pain, abdominal distension, and weight loss. The radiological images found were essentially cystic with ascites. Exploration laparoscopy found pseudo-tumoral masses, whitish granulations, and adhesions. The confirmation of the diagnosis is histological represented by epithelio-gigantocellular follicles with or without caseous necrosis. Under a well-conducted antibacillary medical treatment for a sufficient duration, the evolution is favorable with a risk of sequels especially on the patient's fertility. **Conclusion:** The most important treatment of tuberculosis is preventive based on the BCG vaccine and the improvement of living conditions. Genital tuberculosis in women isn't frequent but has a poor prognosis especially the fertility one. Medical treatment is effective but tubal damages can be irreversible.

Keywords: Tuberculosis, genital tuberculosis, fertility.

Tuberculosis is a contagious, endemic-epidemic disease with essentially human-to-human transmission. Its most common site is pulmonary and it is the usual source of transmission. The germ responsible is Mycobacterium Tuberculosis or the Koch bacillus. It is a strict aerobic that is part of the alcohol-resistant mycobacteria. It can affect any women with a predominance of young ones aged between 20 and 30 years-old¹, few cases were declared in peri or post-menopausal. These forms are most often due to a long latency period of the disease, rarely late tuberculosis involvement. The pelvic contamination is mainly hematogenous.

Its clinical picture is often misleading simulating an ovarian or tubal tumor. The diagnosis of certainty is based on histology and bacteriology which is not always positive². Despite the means of investigation implemented, the diagnosis of genital tuberculosis remains late, threatening the fertility of women³. The prognosis is linked to tuboovarian infertility. Anti-tuberculosis chemotherapy has markedly transformed the prognosis of the disease despite the possibility of resistance to treatment⁴.

Methods

It is a retrospective study about six cases of genital tuberculosis reported in the Obstetrics and Gynecology department of the Mohammed VI University Hospital of Oujda, Morocco over 4 years, from January 2015 to December 2018.

Results

All of our patients come from an unfavorable socioeconomic background. We did not note a notion of tuberculosis contagion in our patients but one patient had a history of treated cervical lymph node tuberculosis. The average age of our patients was 36 years with predominance of the age group of 20 to 30 years old. 83% of the patients were complaining from chronic pelvic pain associated in most cases with other troubles: a pelvic mass in one patient (16%), abdominal distension in one patient (32%), urinary signs in two cases (32%), and digestive signs in one case (16%) and primary infertility in one case (16%). Deterioration of general condition were found in all patients with the association of asthenia, weight loss and night sweats in two cases (32%), isolated weight loss in two cases (66%) and isolated fever in one case (16%).

Pelvic ultrasound, performed on all patients, showed ovarian cysts in 3 patients (50%) (Figure 1) and ascites in 4 patients (66%) (Figure 2). Hysterosalpingography was performed in a single patient with primary infertility; it revealed an irregular bilateral distal tubal narrowing without peritoneal diffusion of the contrast product of the two tubes. Pelvic computed tomography was performed in 4 cases showing ascites in 50% of the cases, ovarian cysts in 32% (Figure 3), signs of peritoneal carcinosis and tuboovarian collections in 16% of the cases. Magnetic resonance imaging (MRI) was performed in two patients showing a suspicious tumoral process with signs of peritoneal carcinosis in one patient (16%) (Figure 4).



Figure 1 : Ultrasound image showing heterogeneous collections



Figure 2 : Ultrasound image showing ascites

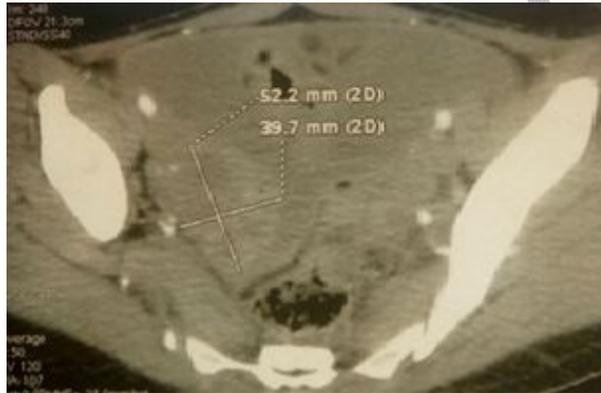


Figure 3: Pelvic CT scan showing a laterouterin mass



Figure 4 : Cross section abdominopelvic MRI: suspicious tumoral process with signs of peritoneal carcinosis

The biological assessment carried out in all the patients revealed a biological inflammatory syndrome in 3 patients (50%) and a high CA-125 level in 3 patients (50%). The intradermal reaction to tuberculin performed in 4 patients was positive in just one case (16%).

All of the patients had undergone laparoscopic surgical exploration. The aspects were suggestive of tuberculosis with milinary whitish granules scattered over the peritoneal cavity in 3 cases (50%) and adhesions in 5 cases (83%). Ascites was found in all patients. All patients underwent a peritoneal biopsy with the removal of ascites fluid. A right adnexectomy was performed in one patient. Cytological examination of the ascites fluid found a richly lymphocytic exudative fluid devoid of malignant cells in 4 patients, in 2 cases it was a transudative fluid. The anatomopathological examination revealed epitheliogigantocellular follicles with caseous necrosis in 4 cases (60%) and without caseous necrosis in 2 cases (40%).

All the patients were put on specific medical treatment based on anti-bacillary for six months, combining three anti bacillary for two months: Isoniazid (5mg/Kg/d), Rifampicin (10mg/ Kg/d) and Pyrazinamide (30mg/Kg/d); Then two anti-bacillary for the remaining four months: Isoniazid (5mg / Kg / d) and Rifampicin (10mg / Kg / d). In all cases, under good antibacillary treatment, the evolution was favorable marked by clinical and biological improvement. Regarding fertility, two patients still infertile (33%) and are considering in vitro fertilization.

Discussion

Genital tuberculosis is in the fifth site of tuberculosis in Morocco after pulmonary, lymph node, osteoarticular and digestive ones⁵. Its pelvic location represents 6 to 10% of the cases dominated by tubal, then cervical and endometrial involvement⁶. The socio-economic level plays an indisputable role in maintaining this problem. The genital form conventionally affects the disadvantaged socio-economic strata⁷. However, a sub-Saharan study reported 21% of genital tuberculosis diagnosed in infertile patients belonging to wealthy classes⁸. Regarding our series, we found that all patients came from an unfavorable socioeconomic level.

The presence of a personal and family history of pulmonary tuberculosis is a significant risk factor for genital tuberculosis in women. The notion of tuberculosis contagion or history is found in 30.6% of cases⁹. According to Rhanmi's study, tuberculosis history was in 50%¹⁰, Essabir 10.7%¹¹, Zayet 8.5%¹². In our study, the tuberculosis history is only 16%. In the study of El Mansouri⁵, the notion of tuberculous contagion is nonexistent in the majority of cases of genital tuberculosis. This absence of contagion doesn't eliminate the diagnosis.

Almost all cases of genital tuberculosis are reported among genitally active women aged between 20 and 35 years-old. However, they can be related to a distant infection that dates back to the post-pubertal period¹³. In the literature, the average age of patients varies between 17 and 40 years with a median of 25.6¹⁴. In fact, in developing countries, this pathology typically affects young women during the period of genital activity in 72% of cases, unlike in developed countries where genital tuberculosis becomes the prerogative of postmenopausal women in 62% of the cases¹⁵. According to Rhanmi's study, the average age was 33¹⁰, Essabir found it 32.4¹¹ and Zayet 42.2¹². In our study, the average age was 36 years.

The clinical signs are multiple and variable with no specific character, explaining the long evolution of the disease at the time of diagnosis. In decreasing order of frequency, according to the majority of studies, we encounter pelvic pain, infertility, and menstruation disorders. The tumoral forms of genital tuberculosis represents 15% of all pelvic localization of tuberculosis. It can be encountered at any age with a predilection in young women aged 20 to 30 years^{16,17}. The clinical expression of female genital tuberculosis has changed significantly. Indeed, currently, it is often discovered during a couple's infertility assessment^{18,19}. This diagnosis should be considered first and foremost in our country where tuberculosis is endemic. Indeed, the prevalence of genital tuberculosis in infertile populations in developing countries is between 5% and 20% and it is even higher in patients with tubal infertility (39% to 41%)²⁰. The clinical examination turns out to be very rich compared to the latent forms, but it remains most often misleading. It may show an abdominopelvic mass and/or a latero-uterine mass. This abdominal mass is sometimes painful; it is either isolated or associated with ascites¹⁶ which is of variable abundance and progressive constitution²².

Abdominopelvic ultrasound is the first line examination before any suspicion of genital tuberculosis. Indeed, it can highlight the signs suggestive of the diagnosis but it can be misleading and show tumor-suggesting images^{16,21}. The presence of a heterogeneous pelvic mass with thick wall and double component, associated with anarchic hypervascularisation and ascites², can suggest an ovarian tumor with peritoneal carcinosis; peritoneal nodules are visible on ultrasound when they are large, superficial (greater than 1cm) or when they are surrounded by ascites requiring high frequency probes²³. The abdominopelvic CT scan makes it possible to better analyze the ultrasound lesions, to carry out a diagnosis of presumption and to make the assessment of extension. It is however not very specific, its sensitivity is close to 70%²⁴. There are no suggestive or pathognomonic aspects of genital tuberculosis; several aspects are possible: ovarian abscess frequently confused with a malignant tumor of the ovary; cystic pelvic mass or formations often heterogeneous infiltrating the fat and the neighboring organs or fistulized in them, in particular the rectum, which highly suggestive of tuberculosis, but not specific²⁴; peritoneal nodules or thickening which can range from the simple densification of fat to the lump thickening leading in massive damage to real "peritoneal cakes". MRI has become increasingly used for the exploration of pelvic masses²⁶. It allows a better characterization compared to the CT scan, localizes the pelvic lesions and identifies their origins. In our study, MRI was performed in two patients showing ascites with an ovarian cyst and signs of peritoneal carcinosis.

Biological abnormalities are not specific for the diagnosis of genital tuberculosis; the blood count usually shows a hypochromic microcytic anemia of the inflammatory type, a moderate hyperleukocytosis with lymphocytosis and/or more rarely a leukopenia. However, a normal blood count does not rule out the diagnosis²³. The erythrocyte sedimentation rate, on the other hand, is accelerated in the majority of the cases, witnessing an inflammatory syndrome. However, its normal value does not eliminate tuberculosis, it, therefore, makes it possible to monitor the progress of this disease and the effectiveness of the treatment²⁷. The study of ascites fluid allows a diagnostic orientation by its appearance (generally citrine yellow, rarely cloudy or hematomas), its chemical study (an exudative liquid, a positive Rivalta test with a protein level higher than 25 g/l), its cytological study (clear lymphocyte predominance, rarely a liquid rich in neutrophils), and its bacteriological study. The exudative and lymphocytic character of the ascites fluid is suggestive of tuberculosis but not specific because it can be seen in other pathologies in particular peritoneal carcinosis. The serum CA-125 level is recommended as an indirect marker for the diagnosis and progression of genital tuberculosis. Indeed, his serum level drops rapidly after the institution of anti-tuberculosis treatment²⁸. Simsek et al.² showed that the decrease and normalization of serum CA-125 levels are correlated with the good evolution of the disease under anti bacillary treatment; they thus proposed the dosage of CA-125 as a marker for monitoring efficacy of treatment.

Laparoscopy is of major interest in the diagnosis, the extension and scalability assessment and fertility prognosis¹⁶. In addition to its aesthetic benefit, it shortens the length of hospital stay with a faster recovery compared to laparotomy, and leads to less pelvic adhesions, which is particularly important for women of reproductive age who wish to preserve their fertility. It allows both direct exploration of the peritoneal cavity and the realization of biopsies for histological study. Laparoscopy was offered for all patients with symptoms suggestive of genital tuberculosis or in favor of peritoneal carcinosis (Table 1). Most studies report an abdominal approach behind a strong suspicion of ovarian cancer. Laparotomy is urgently indicated in front of a pseudo-surgical table or the event of a laparoscopic digestive perforation.

Studies	Granulations(%)	Adhesions (%)	Peritoneal nodules (%)	Ascites (%)
Zayet ¹²	59.4	32.4	5.62	13.5
Essabir ¹¹	37.2	1.71	17.85	10.71
Rhanmi ¹⁰	60	60	00	00
Our study	50	84	32	100

The anatomopathological examination of the biopsies makes it possible to confirm the diagnosis by showing a tuberculoid or gigantocellular granuloma associated with caseous necrosis¹³. In our series, peritoneal biopsies and whitish formations showed an epitheliogigantocellular aspect with caseous necrosis in 4 patients, and without caseous necrosis in the 2 patients.

The treatment of genital tuberculosis is above all medical and possibly surgical, and like any tuberculous localization, it will only be undertaken after certainty diagnostic. It must be continuous, early, regular and

sufficiently prolonged²⁹. The scheme proposed by the national tuberculosis control program in Morocco includes the combination of 3 anti-tuberculosis drugs (Isoniazid, Rifampicin, and Pyrazinamide) for 2 months, 2 anti-tuberculosis drugs (Isoniazid and Rifampicin) for 4 months. Surgical treatment is indicated only behind complicated forms, in particular^{21,2}: persistence of adnexal mass despite medical treatment, in particular cold abscess, relapse of tuberculosis after one year of treatment, the compressive or fistulized masses, the fistulas which do not dry up and the persistence of pelvic pain after three months of treatment or when they have not completely disappeared after one year of treatment, persistent metrorrhagia after anatomical and clinical healing or surgical treatment of tuberculous synchiae. Different surgical procedures are proposed depending on the lesions observed, in particular²¹: a biopsy, drainage, flattening of an abscess, adhesiolysis, cystectomy, oophorectomy, and even an adnexectomy. Under well-managed, effective medical treatment, and for a sufficient duration, the evolution is generally favorable on the clinical and biological levels. Late complications can be observed especially when the diagnosis and treatment are delayed. They are dominated by fibrosis and peritoneal adhesions responsible for ureteral strictures, intestinal obstructions, ectopic pregnancy and infertility in women, genital tuberculosis is being responsible for tuboovarian infertility in more than 39% of cases²⁹.

Conclusion

The frequency of genital tuberculosis is very different according to the studies and the countries; this is first of all due to the various criteria used for the establishment of the diagnosis. In our country, the frequency remains stable over the years despite the generalization of vaccination. Its incidence is increasing with the HIV pandemic, even in developed countries. It is a pathology of young women, rarely occurring in postmenopausal women. We must emphasize the importance and the need to strengthen the preventive fight for the eradication of this pathology, by the generalization of correct BCG vaccination, the possibility of screening and systematic treatment of any primary tuberculosis infection and the improvement of living conditions. It is only at this price that we can hope to see disappear this affection, which weighs heavily on the genital and reproductive function of the woman.

References

1. Amouri A, Boudabbous M, Mnif L, Tahri N. Profil actuel de la tuberculose péritonéale: étude d'une série tunisienne de 42 cas et revue de la littérature. *La Revue de médecine interne*. 2009; 30(3): 215-20.
2. Taleb AL, Bouchetara K, Boutteville C. La tuberculose génitale de la femme. *Encycl MédChir (Paris-France), Gynécologie. EncyclMédChir. Gynécologie*. 1989; 490: A10-7.
3. El Mansouri A, Moumen M. Les formestumorales de la tuberculose génitale de la femme: à propos de huit cas. *La Semaine des hôpitaux de Paris*. 1993; 69(30): 899-903.
4. Che D, Campese C, Decludt B. Les cas de tuberculose déclarés en France en 2002. [Cases of tuberculosis reported in France in 2002.]. *Bull Epidemiol Hebdo*. 2004;4:13-16.
5. Lrhorfi, MH, Tazi K, Hachimi M, Lakrissa A. Urogenital tuberculosis. Experience in 10 years. *Progres en urologie: journal de l'Association française d'urologie et de la Société française d'urologie*. 2001; 11(1): 62-7.
6. Nebhani M, Boumzgou K., Brams S, Laghzaoui M, El Attar H, Bouhya S, et al. Tuberculose pelvienne simulant une tumeur ovarienne bilatérale: À propos d'un cas. *Journal de gynécologie obstétrique et biologie de la reproduction*. 2004; 33(2): 145-7.
7. World Health Organization. *Treatment of tuberculosis: guidelines*. Geneva: World Health Organization: 2010.
8. Guillet-Caruba C, Martinez V, Doucet-Populaire F. Les nouveaux outils de diagnostic microbiologique de la tuberculose maladie. *La Revue de médecine interne*. 2014 ; 35(12) : 794-800.

9. Tripathy SN, Tripathy SN. Infertility and pregnancy outcome in female genital tuberculosis. *International Journal of Gynecology & Obstetrics*. 2002; 76(2): 159-63.
10. Rhanmi A. La tuberculose pévi-génitale pseudo-tumorale simulant un cancer ovarien, à propos de dix cas et revue de la littérature (Doctoral dissertation). 2016.
11. Essabir S, Aboufalah A, Abbassi H. Aspects anatomo-cliniques de la tuberculose génitale féminine. Les aspects anatomo-cliniques de la tuberculose génitale féminine. 2010.
12. Zayet S, Berriche A, Ammari L, Razgallah M, Abdelmalek R, Khrouf M, et al. Caractéristiques épidémiocliniques de la tuberculose génitale chez la femme tunisienne: une série de 47 cas. *The Pan African Medical Journal*. 2018; 30: 71.
13. Kashyap B, Srivastava N, Kaur IR, Jhamb R, Singh DK. Diagnostic dilemma in female genital tuberculosis-staining techniques revisited. *Iranian journal of reproductive medicine*. 2013;11(7): 545.
14. Mondal SK., Dutta TK. A ten year clinicopathological study of female genital tuberculosis and impact on fertility. *Journal of Nepal Medical Association*. 2008; 48(173): 52-7.
15. Akka L, Khalil H, Cherif IdrissiGannouni N, Jalal H, Samlani Z. La tuberculose ovarienne pseudotumorale: à propos de quatre cas. *Imagerie de la femme (Imprime)*. 2009 ; 19(4) : 251-4.
16. Boujoual M, Zazi A, Elhassani ME, Kouach J, Allaoui M, Oukabli M, et al. Tuberculosepéritonéale pseudo tumoralemimant un cancer ovarien/[Pseudo tumoral peritoneal tuberculosis mimicking advanced ovarian carcinoma]. *International Journal of Innovation and Applied Studies*. 2014; 9(3): 1354
17. Zergeroğlu S, Aydoğdu T, Mollamahmutoğlu L, Demirtürk F, MocanKuzey G. An uncommon adnexal mass: Ovarian tuberculosis. *Journal of Obstetrics and Gynaecology*. 2008; 28(7): 755-6.
18. Bhanothu V, Theophilus JP, Reddy PK, Rozati R. Occurrence of female genital tuberculosis among infertile women: a study from a tertiary maternal health care research centre in South India. *European journal of clinica lmicrobiology & infectious diseases*. 2014 ; 33(11) : 1937-49.
19. Sfar E, Ouarda C, Kharouf M. Female genital tuberculosis in Tunisia. Apropos of 118 cases at the Rabta Neonatology and Maternity Center in Tunis (January 1984-December 1988). *Revue française de gynécologieetd' obstétrique*. 1990; 85(6): 359-63.
20. Botha MH, Van der Merwe FH. Female genital tuberculosis. *South African Family Practice*. 2008; 50(5): 12-6.
21. Hasanzadeh M, Naderi HR, Hoshyar AH, Shabane S, Shahidsales S. Female genital tract tuberculosis presenting as ovarian cancer. *Journal of research in medical sciences*. 2014; 19(2): 184.
22. Abdallah M, Larbi T, Hamzaoui S, Mezlini E, Harmel A, Ennafaa M, et al. Tuberculose abdominale: étude rétrospective de 90 cas. *La Revue de médecine interne*. 2011; 32(4) : 212-7.
23. Tongsong T, Sukpan K, Wanapirak C, Sirichotiyakul S, Tongprasert F. Sonographic features of female pelvic tuberculous peritonitis. *Journal of ultrasound in medicine*. 2007; 26(1): 77-82.
24. Thoreau N, Fain O, Babinet P, Lortholary O, Robineau M, Valeyre D, et al. Tuberculose péritonéale: 27 cas dans la banlieue nord-est de Paris. *The International Journal of Tuberculosis and Lung Disease*. 2002 ; 6(3) : 253-8.
25. Lantheaume S, Soler S, Issartel B, Isch JF, Lacassin F, Rougier Y, et al. Peritoneal tuberculosis simulating advanced ovarian carcinoma: a case report. *Gynécologie, obstétrique & fertilité*. 2003; 31(7-8): 624-6.

26. Kim SH, Kim SH, Yang DM, Kim KA. Unusual causes of tubo-ovarian abscess: CT and MR imaging findings. *Radiographics*. 2004; 24(6): 1575-89.
27. Vardareli E, Kebapçı M, Sarıcam T, Pasaoglu Ö, Acıkalın M. Tuberculous peritonitis of the wet ascitic type: clinical features and diagnostic value of image-guided peritoneal biopsy. *Digestive and Liver Disease*. 2004; 36(3): 199-204
28. Sharma JB, Karmakar D, Kumar R, Shamim SA, Kumar S, Singh N, et al. Comparison of PET/CT with other imaging modalities in women with genital tuberculosis. *International Journal of Gynecology & Obstetrics*. 2012; 118(2): 123-8.
29. Caliskan E, Cakiroglu Y, Sofuoglu K, Doger E, Akar ME, Ozkan SO. Effects of salpingectomy and antituberculosis treatments on fertility results in patients with genital tuberculosis. *Journal of Obstetrics and Gynaecology Research*. 2014; 40(10): 2104-9.

Conflict of interest: None. **Disclaimer:** Nil.

Epub Ahead of Print