Female genital tuberculosis – a disease seen again in Europe
Genitalna tuberkuloza žene – bolest koja se opet pojavljuje u Evropi

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Abstract

Background. Dramatic worsening of epidemiological situation with tuberculosis (TB) in the world has made extra-pulmonary tuberculosis actual again. Female genital TB is very rare, but each case still remains a serious medical problem. Case report. A 23-year-old human immunodeficiency virus (HIV) seronegative woman with two-month duration amenorrhea underwent surgery due to lower abdominal mass simulating a left ovary carcinoma, suggested by ultrasound examinations. During sampling, we found a mass of round, up to 3 mm, necrotizing nodules, diffuse in the uterus, ovarian and tubarial surfaces, in cervical and endometrial mucosa, and even in myometrium and fat omental tissue. No tumor mass was found. Microscopically, the tissue samples from all reproductive organs and omentum contained numerous tuberculous cæsating granulomas. Mycobacteria were identified by Ziehl-Neelsen method. Anti-tuberculosis treatment had been completed. Conclusion. In the differential diagnosis of an ovarian tumor and ascites TB should always be considered. It should also be suspected in recent Mycobacterium tuberculosis infection in younger women with amenorrhea, either HIV-seropositive or not.

Key words: tuberculosis, female, genital; ovarian neoplasms; diagnosis, differential; amenorrhea; risk factors.

Introduction

Tuberculosis (TB) is a curable infectious disease caused by Mycobacterium tuberculosis complex (M. tuberculosis). It can affect people of any age and involve any site. The total of 8-10 million infected people, worldwide, develops TB per year, while at least two million people die from this disease. Approximately 80% of individuals affected by TB are in the most productive age. In 1993, WHO expressed its great concern due to the epidemiological situation and declared it a global problem.

Once infected by TB bacilli, immune compromised persons are more liable to develop TB as an active disease. Although TB usually affects lungs, bacilli can be spread through blood stream and involve other sites leading to extra-pulmonary TB (XPTB). This latter also happens more frequently in immune compromised patients.

The genital tract in female is usually infected by hematogenous spread from a distant focus, but transmission through a sexual intercourse is also possible. Female genital TB usually affects endometrium and fallopian tubes. Sometimes progression to an abscess formation of the fallopian tube happens, and sometimes followed by large abdominal masses. The diagnosis is often made as a result of routine investigation for infertility but not rarely remains undiagnosed out of that framework. Sometimes, it is even associated

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with elevated serum cancer antigen-125 (CA-125) levels, which is suggestive of ovarian malignancy.

Nowadays abdominal and genital TB are rare in western world, despite the increasing number of TB cases among human immunodeficiency virus (HIV)-seropositive persons and migrants from endemic areas. It is more frequent in developing countries and especially in TB high prevalence countries. Female genital TB is very rare. However, each case still remains a serious medical problem in all the countries. If not recognized and treated successfully, it may lead to an unfavorable disease outcome and the patient’s death.

We present a case of genital TB in a 23-year-old HIV-seronegative woman, inhabitant of a South East European country, who underwent surgery due to lower abdominal mass simulating an advanced ovarian malignant tumor. Durante operationem biopsy was not available.

Case report

A 23-year-old Caucasian female, a non-smoker, presented to her gynaecologist and complained of having amenorrhea of two months duration. She always had a regular period, except during her pregnancy. History taking revealed that two years prior to admission she delivered a boy who died two months later of unknown causes. The patient’s brother was newly diagnosed and treated for pulmonary TB at the end of her pregnancy.

She was poorly nourished and afebrile. The rest of physical examination was normal. Erythrocyte sedimentation rate, routine biochemistry analyses and complete blood count were within normal limits except for thrombocytosis of 601 × 10^9/l (normal range 130–400 × 10^9/l). Ultrasound examination revealed a mass of the left ovarium, 20 mm sized, and about 300 ml of ascites. After peritoneal paracenthesis, microscopically, smear of the effusion contained few reactive mesothelial cells with a mass of lymphocytes and erythrocytes. There was no evidence of malignant cells.

The suspicious left ovarian mass was confirmed on repeated ultrasound examination at the gynaecological hospital where she was admitted for a surgical intervention. Preoperatively, the patient was afebrile; lungs were clear to auscultation, heart rate 88/min, arterial blood pressure 120/80 mmHg. Chest x-ray revealed bilateral shadows in both upper pulmonary lobes, which were regarded as possible inactive specific lesions rather than metastases.

During sampling, we found a mass of round, necrotising nodules, up to 3 mm, diffuse on uterus, ovarian, and tubarial surfaces as well as in cervical, and endometrial mucosa, and even in myometrium. The fat omental tissue contained the same nodules. All reproductive organs measured were regular sized. No tumor mass was found on the left ovary surface.

The tissue samples were fixed in 10% buffered formalin, dehydrated in upgrading alcohol and xylene and embedded in paraffin and haematoxylin-eosin stain. Microscopic finding was as follows: the tissue samples from all reproductive organs and omentum contained numerous tuberculous caseating granulomas (Figures 1–3). Mycobacteria were confirmed by identification of acid-fast bacilli (AFB) by Ziehl-Neelsen method (Figure 4). Thus the histological diagnosis of TB of all reproductive organs with tuberculous peritonitis was established without evidence of the left ovary tumor.

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Fig. 1 – Tuberculous granulomas on the surface of the left ovary, H&E × 10

Fig. 2 – Tuberculous granulomas in the left Fallopain tube, H&E × 10

Fig. 3 – Tuberculous granulomas in endometrial layer of uterus, H&E × 10

Fig. 4 – Numerous acid-fast bacilli are visible in tuberculous granulomas, Ziehl-Neelsen × 10
Further examination at the pulmonary ward showed that the patient was Bacillus Calmette-Guerin (BCG) vaccinated at birth. Sputum smears were negative for AFB and culture was also negative for \textit{M. tuberculosis}. Tuberculin skin test, purified protein derivative (PPD-P) was positive (+12 mm) two weeks after the surgery, i.e. prior to a short course antituberculosis treatment, which was completed without adverse effects. Platelets count normalized at the end of the treatment.

**Discussion**

In 1972 German authors still believed that occurrence of female genital TB and genital tumors were common problems of differential diagnosis \(^8\). Twenty-five years later, during 1990s, after constant decline of TB incidence in America and Europe (including eastern European countries), sudden worsening of epidemiological situation occurred. Synchronically with flourishing of HIV pandemic, XPTB became actual again but it is still rare in western countries. Although XPTB in total is more frequent in developing countries, and especially in TB endemic areas, genital TB in females is even there very rare \(^2\). The other rare reports predominantly come from endemic countries but Japanese authors, however, have reported two cases of genital TB in 84-year and 77-year old women presented with metrorrhagia due to specific endometritis and three cases have been described in Australia \(^1\), \(^2\), \(^9\), \(^10\). American clinicians found it necessary to include TB into differential diagnosis of a pelvic mass on the occasion of a case \(^6\). When it comes to Europe, after a case report, and statement that genital TB in women in Europe still is not only of interest in medical history, more than 10 years passed by before the latest reports of Turkish cases appeared \(^6\). A Danish case is a migrant woman from Somalia, TB high prevalent African country and Italian authors reported a case of a menopausal woman with menometrorrhagia as a sign of endometrial TB \(^11\). Reviewing these reported cases of female genital TB for tumor mimicking, we found them, too, but some of them without bacteriological evidence of \textit{Mycobacteria} on histological examination or positive culturing for \textit{M. tuberculosis}, without either history of close contact with a TB patient or without any data about a patient’s HIV status.

We presented the first case of TB of female reproductive organs established during the last 10-year period at a referral facility of an intermediate TB incidence European country. The low HIV prevalence country, since 2003 is classified to intermediate one \(^1\). The last decade in regional settings was characterized by economic crisis with low incomes and increasing unemployment in disintegrated country, the war and mass migration of population from the war affected regions. This lead both to prolonged emotional stress and malnutrition of population as risk factors for developing TB in infected persons, as well as an increased risk of being infected.

Immunodeficiency caused by HIV infection is a major risk factor for developing TB in an infected person. Although HIV-seronegative, our patient may be a good example of those immune compromised hosts that are an excellent milieu for disseminated hematogenous forms of TB, and thus developing genital TB as well. Even in TB low incidence countries the presence of such coincidences especially in migrant population, should provoke any clinician to have possible TB in mind.

Thus, this case report of genital TB in a young HIV-seronegative woman may serve as an illustration that the other risk factors may also influence human immunity and lead to a development of active genital TB mimicking ovarian malignancy. Apart from being unemployed and malnourished, under prolonged emotional stress of an internally displaced person and a mother who had lost her first born baby, our young aged patient had, most probably, a major factor for developing TB: a recent contact with an infectious pulmonary TB patient – her brother. According to the medical data obtained, the brother was diagnosed active AFB positive pulmonary TB at the end of the patient’s pregnancy, i.e. there was a possible contact of the patient, and even newborn baby, with the above mentioned TB case. Although without any evidence of precise source of infection deoxyribonucleic acid (DNA fingerprinting test was not available), we may suppose that the patient’s brother was the source. It has been proved that the possibility of developing TB is the highest during two years after being infected. Stress and malnutrition are also proved risk factors for developing TB (given that the infection by \textit{M. tuberculosis} had occurred).

Females with active genital TB are frequently presented with metrorrhagia and when the peritoneum is affected show a variety of complaints \(^10\). In the Malaysian 15-year analysis \(^2\), authors described nine cases of genital TB, and seven of them presented with asites, vague abdominal distension, and weight loss. None had amenorrhea as a chief complaint, which was the only complaint of our patient.

Bacteriological diagnosis is the gold standard in TB, but it cannot be successful without special staining and culturing of specimens. When it comes to XPTB, histological examination is a frequently used diagnostic tool. A pathologist, who finds specific granulomatous tissue, should make additional effort and perform a special staining to make \textit{Mycobacteria} visible. However, only tissue specimens positive culture in Löwenstein-Jensen medium is the proof of infection by \textit{M. tuberculosis}. Unfortunately, in routine clinical practice, if TB is not in the clinician’s mind, proper culturing is disabled by formalin fixation of the tissue delivered for histological examination. Thus, in the case of TB suspicion the specimens should be saved unfixed until the proper sampling and culturing. In our case report of female genital TB, diagnosis was established by histological examination and \textit{Mycobacteria} were visible after special staining. Nowadays some other diagnostic methods may also lead to a diagnosis of genital TB such as polymerase chain reaction.

When it comes to tuberculin skin test as a possible TB diagnostic tool, in countries where BCG vaccination is mandatory at birth, this test in TB diagnosis is of limited value since a vaccinated person is supposed to be tuberculin positive. Tuberculin skin testing in our patient was per-
formed by PPD 3 two weeks after the surgery according to World Health Organization/International Union against Tuberculosis and Lung Disease guidelines and read positive (+12 mm). Tuberculin skin test may be negative in an active TB patient if testing is performed in a post-operative period of a large surgical intervention.

With regard to prognosis, as for survival, owing to an adequate conservative treatment, disease outcome of genital TB is favourable. Although future fertility is doubtful in these patients, in Karachi University study 3/40 patients had successful pregnancies.

Female genital TB may simulate advanced ovarian malignancy and even when an extremely experienced surgeon performs the operation, a biopsy should be taken before or during the operation. Immediate undertaking a drastic life changing operation like hysterectomy with total adnexectomy, especially in young women, without prior proper diagnostic procedures, may lead to unrepairable consequences as definite infertility. This is the message, which is of enormous value in all the settings where **durante operationem** biopsy is still not a routine practice for any reason.

Clinicians should always consider TB as a differential diagnosis when encountering clinical presentations of an ovarian tumor and ascites, also having in mind that, although extremely rarely, synchronous appearance of genital TB and malignancy may be present 12.

**Conclusion**

Increasing health care workers’ consciousness on epidemiological situation with TB in the world and in their local settings and continual education referring to risk factors for developing TB may be of crucial importance in early detection of XPTB. It may accelerate the diagnostic decision-making process, prevent exposure to unnecessary surgery and allow early initiation of anti-tuberculosis treatment.

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**REFERENCES**


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