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An Atypical Ovarian and Peritoneal Pelvic Tuberculosis Complicated by Toxidermia

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Abstract

Background: Ovarian tuberculosis is a rare form of tuberculosis. Its clinical presentation mimics an ovarian tumor, leading to misdiagnosis. Proper treatment with anti-tuberculosis drugs can lead to a cure for the disease but can sometimes cause adverse effects that compromise therapeutic management. **Observation:** We report a 71-year-old female Senegalese patient who presented with a chronic abdominopelvic mass with an elevated Cancer Antigen 125 (CA125) level, raising the suspicion of an ovarian tumor. She underwent an exploratory laparotomy and the anatomopathological study confirmed the diagnosis of ovarian and peritoneal tuberculosis. After starting treatment with anti-tuberculosis drugs, she developed toxidermia in the form of generalized urticaria. Discontinuation of the four-drug therapy and separate reintroduction of anti-tuberculosis drugs led to the incrimination of rifampicin. Progress was then favorable on Isoniazid (H) pyrazinamide (Z) and Ethambutol (E). **Conclusion:** Ovarian tuberculosis should be suspected in the presence of an abdominopelvic mass in a woman living in an endemic area. The occurrence of adverse reactions to anti-tuberculosis treatment is not uncommon, hence the importance of regular monitoring.

Keywords

Ovarian, Peritoneal, Tuberculosis, Toxidermia, Senegalese

1. Introduction

Tuberculosis, a bacterial infection caused by *Mycobacterium tuberculosis* (MT) complex, remains a public health problem in developing countries where it is

endemic. Pelvic tuberculosis accounts for 6% - 10% of cases, with tubal involvement being the most common. Ovarian localization remains rare, representing 20% of genital tuberculosis and presents clinical, radiological, and biological symptoms similar to those of an ovarian tumor, which can lead to a misdiagnosis [1] [2].

First described in 1843, peritoneal tuberculosis is one of the most frequent extrapulmonary localizations, representing approximately 58% of abdominal localizations. Its diagnosis may be challenging because of the variability of its presentation [3] [4].

The treatment of tuberculosis is based on anti-tuberculosis chemotherapy which, when correctly administered, generally leads to a cure. However, anti-tuberculosis drugs are sometimes responsible for serious side effects, which can compromise compliance and therapeutic efficacy [5].

We report a case of pelvic tuberculosis in an ovarian and peritoneal localization, complicated by toxidermia after initiation of anti-tuberculosis treatment. Through a review of the literature, we discuss the clinical and diagnostic particularities of this entity, as well as the different aspects of toxidermia due to anti-tuberculosis drugs and the appropriate treatment.

2. Observation

This was 71 years old female Senegalese patient, living in an urban area, with 7 gestures, 6 pares, and 1 abortion. She had no pathological history. She was admitted for an abdomino-pelvic mass that had been present for 4 months. She reported a deterioration in her general condition, with intense physical asthenia, anorexia and weight loss (not quantified), which had occurred approximately one year before the appearance of the abdominal mass. Examination on admission revealed a painless, firm mass in the left iliac fossa, with no tenderness. Abdominopelvic ultrasound showed a mixed fluid and tissue mass, with the tissue portion located in the left flank and measuring 155 cm on the long axis. Complementary CT scans showed a mixed tumor process and predominantly cystic, extending over the left ovary and measuring 144 mm long (**Figure 1** and **Figure 2**). CA125 was increased (146.2 IU/ml and 155.9 IU/ml). Retroviral serology was negative and fasting blood glucose was normal. In view of the high suspicion of an ovarian tumor, an exploratory laparotomy was performed and revealed a tumor lesion in the left ovary, indurated, friable, approximately 5 cm in size, with peritoneal carcinosis. Biopsies of the ovary and peritoneum were taken, and pathological examination showed connective tissue with homogeneous foci of eosinophilic necrosis surrounded by epithelioid and gigantocellular granuloma. There was no evidence of malignant proliferation. The diagnosis of ovarian and peritoneal tuberculosis was retained. No other localizations were found. The tuberculine intradermal reaction (TIDR) was phlyctenular.

Anti-tuberculosis treatment was started in accordance with Senegalese protocol: 2 months of Rifampicin (R), Isoniazid (H) Pyrazinamide (Z) and Ethambutol (E) and 4 months of RH. On day 2 of antituberculosis therapy, the patient

noticed the onset of itch over the whole body but sparing the face, associated with erythematous papular lesions. She consulted a dermatologist 2 days later because the itch had worsened and become unbearable. Dermatological examination revealed oedematous, highly pruritic maculopapular lesions, predominantly on the front of the legs and the back of the feet. The diagnosis of toxidermia due to anti-tuberculosis drugs was raised and the four-drug anti- tuberculosis treatment was discontinued. The patient was then started oral antihistamines (Mequitazine) and injectable corticosteroids (Betamethasone), and the cutaneous symptoms regressed, with disappearance of itch and urticaria and the appearance of scarlatiniform squamous lesions (Figure 3).

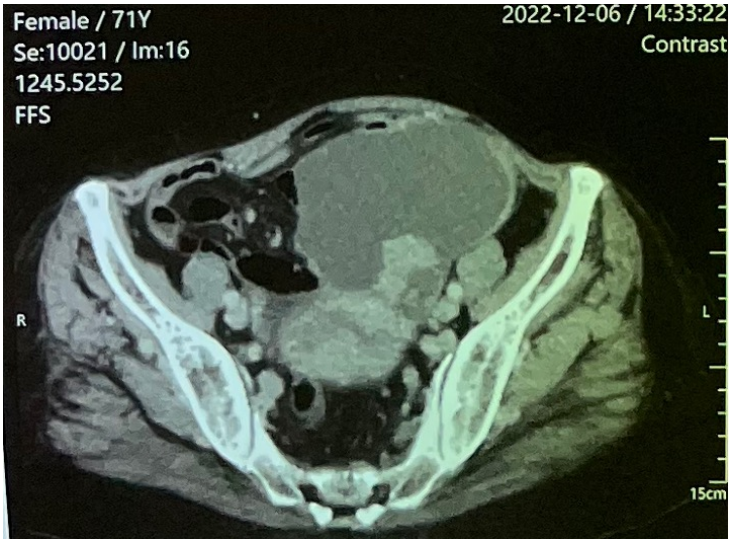

Figure 1. Abdominopelvic CT scan in axial section: mixed formation with predominantly multiwall cystic disease, with contrast of the solid portion and the partitions.

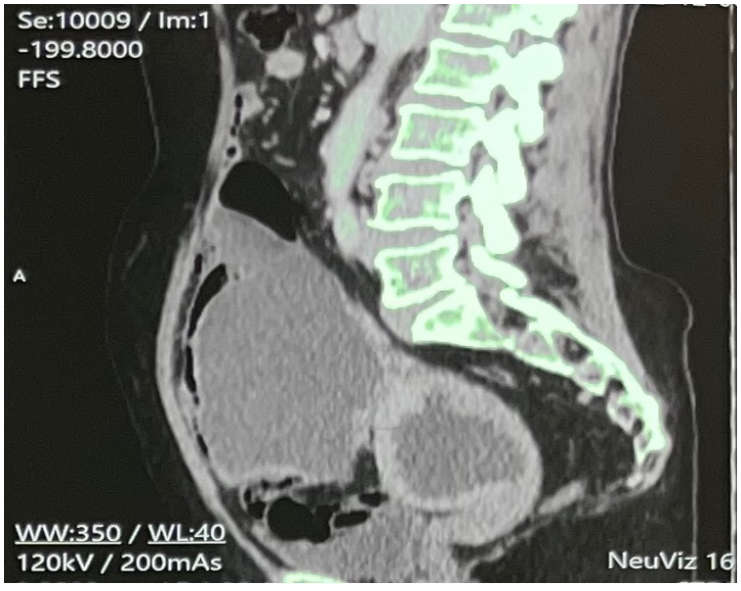

Figure 2. Abdominopelvic CT scan in sagittal section: mixed formation with predominantly multiwall cystic disease, with contrast of the solid portion and the partitions.

A gradual reintroduction of anti-tuberculosis drugs was then initiated, with Isoniazid alone for 2 days, followed by Isoniazid and Pyrazinamide for the next 2 days. Rifampicin was reintroduced on day 5, and on the same day, itch and erythematous papules reappeared. Rifampicin was then permanently discontinued, and the patient was put on HZE-based triple therapy. The course of the disease was marked by a regression of symptoms. The other potential adverse effects of anti-tuberculosis treatment were not observed (transaminases and uricemia were normal on day 6 of treatment).

Treatment was continued on 3 HZE/6HZ. On day 18 of treatment, the patient reported no complaints; there was a reduction in the abdominopelvic mass and complete disappearance of the maculo-papular lesions (**Figure 4**). However, a few squamous lesions on the soles of the feet remained. At one month of antituberculosis treatment, transaminases were normal. Uricemia was increased to 103.5 mg, but without any associated symptoms. A CA125 test was scheduled at M2 and a follow-up CT scan at month 6 of antituberculosis therapy.

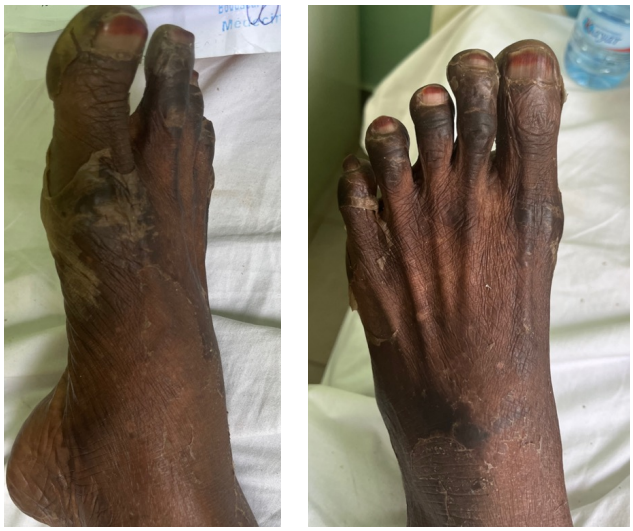

Figure 3. Scarlatiniform squamous lesions on day 2 after stopping RHZE treatment.

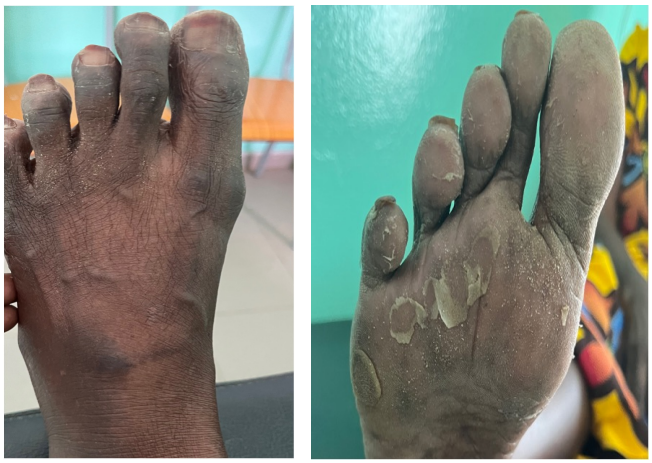

Figure 4. Progression of dermatological lesions on day 18 of HZE treatment.

3. Discussion

Tuberculosis remains a worldwide public health problem. Lung involvement is the most common and is most often the starting point for the spread to other organs. However, it is not uncommon to find other sites without pulmonary involvement [5].

Ovarian localization of the infection is rare, and contamination occurs via the hematogenous route, mainly from primary pulmonary infection. It can occur at any age but is more common in women aged between 20 and 30 who live in endemic areas [6] [7]. Peritoneal tuberculosis is slightly more common and the peritoneum can be infected by hematogenous spread of bacilli from a primary pulmonary site, or by localizations in adjacent organs such as intestine or fallopian tubes [3] [4]. In our case, our patient was 71 years old and presented with ovarian and peritoneal tuberculosis, probably from a primary pulmonary site that had gone unnoticed [6] [7].

The clinical presentation of ovarian tuberculosis is similar to an ovarian tumor, with polymorphic symptoms including pelvic pain, abdomino-pelvic masses, ascites, weight loss, etc [8] [9]. These nonspecific clinical symptoms often lead to misdiagnosis and excessive radical surgical treatment. In a study made by Oge *et al.*, out of 612 patients operated on for suspected ovarian cancer, 20 cases (3.2%) had peritoneal tuberculosis confirmed postoperatively [10]. The presence of other signs such as menstrual disorders, infertility, digestive and urinary signs can sometimes point to a diagnosis of tuberculosis. Also, an association with other localizations, particularly pulmonary or digestive, should be sought, but their absence does not rule out the diagnosis of tuberculosis [1] [10].

Imaging techniques such as ultrasound and CT scan are useful, but do not appear to be specifically helpful in differentiating a benign or malignant tumor from ovarian tuberculosis [11]. In our patient, the abdominopelvic CT scan suggested a tumor process developed at the expense of the ovary.

CA125 is a marker that is elevated in over 80% of ovarian cancers. However, its level can rise under normal conditions (pregnancy, menstruation), during chronic inflammatory conditions (endometriosis, pancreatitis, hepatitis, etc.) and in the post-operative period [12]. In our patient, the highest CA125 level was 155 IU/ml. Its measurement is therefore not a decisive factor in differentiating ovarian tuberculosis from ovarian cancer. However, its value lies mainly in monitoring patients undergoing anti-tuberculosis treatment [8] [9].

Recourse to surgical exploration is often necessary, reinforced by the suspicion of ovarian cancer. The approach may be either laparotomy or laparoscopy, supplemented by biopsy sampling. Histological studies can help to correct the diagnosis by demonstrating gigantocellular granulomas with caseous necrosis specific for tuberculosis [13] [14]. In our case, the patient's age was suggestive of a tumoral cause and it was the exploratory laparotomy and the anatomopathological study of the biopsy samples that led to the diagnosis of tuberculosis.

Treatment of pelvic tuberculosis is essentially medical. It is based on the daily

administration of a four-drug therapy combining Isoniazid (H), Rifampicin (R), Ethambutol (E) and Pyrazinamide (Z) for two months, followed by four months with a daily dual therapy combining Isoniazid and Rifampicin (RH) [1] [15]. This treatment allows the infection to be cured when properly administered. However, this therapeutic management can be compromised by the adverse effects of the treatment, the occurrence of which remains unpredictable. Among these adverse effects, skin involvements are frequent, representing 60% to 80% of cases of allergic reactions to anti-tuberculosis drugs [13] [16]. Most of these reactions are benign, involving hypersensitivity manifestations such as generalized urticaria, erythema multiforme, photosensitization, etc. They are sometimes more serious, leading to DRESS syndrome or Stevens-Johnson and Lyell syndrome. They often occur early, preferably within the first two months of treatment [17]. The mechanisms involved are varied and not fully understood. When they are genuinely linked to an allergy, immediate reactions are most often IgE-dependent. Non-immediate reactions, on the other hand, involve the activation of specific T lymphocytes and respond to several immunological mechanisms [18].

All anti-tuberculosis antibiotics may be implicated in the occurrence of adverse skin reactions, with varying degrees of frequency. Moreover, their combined use makes it difficult to identify the molecule responsible. Ethambutol appears to be the drug least likely to cause toxidermia, whereas pyrazinamide and rifampicin are the most frequent drugs implicated according to the series [13] [19]. Fekih *et al.* found 28% of allergy cases attributable to pyrazinamide in their study, compared with 23% for rifampicin [16]. Tan *et al.* reported 5.4% of cutaneous reactions due to anti-tuberculosis drugs, attributable to pyrazinamide in 2.4% of cases [20].

Certain risk factors have been incriminated in the genesis of allergy to anti-tuberculosis drugs. Some authors, such as Ormerod *et al.*, have also suggested that gender plays a favorable role, finding in their study significantly more frequent reactions in women than in men [21]. Other factors such as immunosuppression (the incidence of adverse events can be as high as 25% in people living with HIV), parenteral administration of treatment and treatment discontinuation also favor the occurrence of adverse events [13] [19] [22] [23].

In all cases, anti-tuberculosis chemotherapy must be stopped, with or without treatment with antihistamines and/or corticosteroids. Ideally, an allergy test should be carried out by a specialist to identify the causative drug. Tests should be carried out as soon as possible (as soon as the toxidermia has healed), after the corticosteroid therapy has been stopped [24]. However, this test is not always accessible and is not easily performed in routine practice, more often it is the separate reintroduction of antibiotics that enables the drug(s) responsible to be identified. This should be done sequentially, molecule by molecule, keeping the most suspected hypersensitivity reaction last. Strict clinical monitoring is essential [13] [18] [21] [25]. This was the approach adopted in our patient's case,

which led to the incrimination of rifampicin as the drug responsible for the toxidermia.

Once the causative drug has been identified, the course of action may vary depending on the context and recommendations. Some authors recommend definitive discontinuation of the drug, often with the need to extend the treatment regimen. In other cases, particularly when the allergy involves two major anti-tuberculosis drugs such as isoniazid and rifampicin, it may be advisable to introduce habituation to the anti-tuberculosis drugs. This involves introducing increasing doses of antituberculosis drugs to achieve temporary tolerance to the drug responsible for hypersensitivity. Success rates for desensitization to anti-tuberculosis drugs are generally acceptable, with success rates approaching 82% for rifampicin and 75% for isoniazid in some series [17] [26] [27]. In addition, regular monitoring of patients during treatment is essential, as is the identification and management of other potential adverse effects of anti-tuberculosis drugs. Therapeutic education is also necessary, as compliance with drug dosage and administration methods, and patients' knowledge of their side-effects, help to prevent these effects.

4. Conclusion

Pelvic tuberculosis in its ovarian form can sometimes simulate ovarian cancer. Although the clinical presentation, ultrasound and CT scan data and high CA125 levels may lead to a misdiagnosis, the diagnosis of tuberculosis must be raised, especially in endemic areas. The treatment strategy for tuberculosis is well codified, based on anti-tuberculosis drugs which are generally well tolerated. However, the undesirable effects of anti-tuberculosis treatment are sometimes serious, underlining the need for close monitoring of patients on anti- tuberculosis drugs.

Consent

The patient has signed an informed consent form, which is available.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

NAS and DT wrote the manuscript with input of KBMF and HDK. NAS collected and prepared the figures. LATD and SAD drafted and approved the final version to be published.

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