

ABDOMINAL TUBERCULOSIS SIMULATING ADVANCED OVARIAN CANCER: A DIAGNOSTIC DILEMMA

ABSTRACT

Background: The rate of preoperative misdiagnosis between abdominal tuberculosis and ovarian cancer is high because the symptoms are non-specific, examinations can be misleading, and biomarkers commonly linked with other diseases also make appropriate diagnosis difficult.

Objective: To evaluate the clinical and diagnostic features in women with abdominal tuberculosis that simulated advanced ovarian malignancy.

Material and Methods: A retrospective review of 11 cases of abdominal tuberculosis managed at the Gynaecologic Oncology unit of the University of Port Harcourt Teaching Hospital with suspected advanced ovarian cancer between January 1, 2016, and December 31, 2021. Clinical characteristics, laboratory results, including serum tumour markers, radiological findings, and ascitic fluid evaluation were extracted from theatre records and case notes and entered into a proforma. SPSS 25 was used for data analysis, and the results are displayed as frequency tables.

Results: More than half 6 (55%) of abdominal TB was found in patients aged 20 to 40 years, with many patients 8 (82%) being nulliparous. Abdominal distension, Abdominal pain, and weight loss were the most common presenting symptoms. All patients had clinical evidence of ascites, along with thickening or ill-defined nodularities in the Douglas pouch and/or in the adnexal areas on a pelvic examination. CA-125 levels were elevated in all 11 patients (100%), with a mean value of 327.8 U/mL. Pleural effusion and increased infiltration were seen in 5 (45.5%) patients. Ultrasound scan and computed tomography studies showed pelvic ascites in all 11 (100%) patients. Debritic ascites with peritoneum thickening, and mesenteric and omental

stranding were observed in all 11 patients (100%), and all 11 (100%) patients had laparotomy. All patients received standard antitubercular therapy.

Conclusion: In relatively young females with nonspecific symptoms, a diagnosis of abdominal TB should be considered. Ultrasound-guided biopsy, laparoscopy, or a mini-laparotomy may be the most direct and least-invasive approach for a diagnosis, avoiding unnecessary extended surgery in these patients.

Keywords: Abdominal tuberculosis, Extrapulmonary tuberculosis, Ovarian cancer, Port Harcourt

1. INTRODUCTION

“Ovarian cancer is the seventh most common cancer in women and the fifth leading cause of cancer-related deaths” [1]. “These cancers typically present in advanced stages with a poor prognosis. Their presentation is sometimes nonspecific, with vague symptoms, and multiple tests are performed before a confirmatory diagnosis is made. Ascites from abdominal tuberculosis (TB) can mimic disseminated ovarian cancer and should be considered in the differential diagnosis” [2].

“TB is a major public health problem in Nigeria, which is ranked sixth among the 30 high TB burden countries in the world and first in Africa. Nigeria is also one of 14 countries that are on all three WHO Global high-burden country lists for tuberculosis, tuberculosis/HIV, and multidrug-resistant tuberculosis, with an estimated incident rate of 219 per 100,000 population and mortality rate (excluding HIV+) of 64/100,000” [1]. “Furthermore, Nigeria is one of the eight countries that accounted for two-thirds of the global TB burden, accounting for 4% of the total global burden” [3].

“Extrapulmonary TB refers to tuberculosis that occurs in locations other than the lungs. Although mycobacteria are spread throughout the body by blood during the initial infection, primary extrapulmonary disease is uncommon except in immunocompromised hosts. Extrapulmonary TB has become more common since the discovery of human HIV infection and may be seen in endemic regions such as Nigeria”. [4]

“Abdominal TB, which is not as common as pulmonary TB, can be a source of significant morbidity and mortality and is usually diagnosed late due to its vague clinical presentation. Abdominal TB usually occurs in four forms: lymph nodal TB, peritoneal TB, gastrointestinal TB, and visceral TB involving the solid organs” [5]. “It accounts for 11% of all cases of extrapulmonary TB. TB peritonitis, the most common type of abdominal TB, accounts for 1-2% of all TB cases” [6,7].

“Serum CA-125 can be elevated in both ovarian cancer and abdominal TB” [8]. “Similar clinical and imaging findings make diagnosing and distinguishing these two disease entities difficult. A high index of suspicion combined with good clinical acumen can aid in making an earlier diagnosis. More importantly, it is extremely valuable to be able to rule out malignancy as soon as possible and relieve the patient's anxiety” [8].

“Though TB affects people of all ages, adults over the age of 15 account for more than 90% of cases. People living with HIV made up 9% of TB patients (72% in Africa), with two-thirds living in eight countries: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (5%), Nigeria (4%), Bangladesh (4%) and South Africa (3%)” [3]. “Males account for most cases and deaths (64%), but females (36%) are also affected significantly” [3]. “Extrapulmonary infections accounted for 14% of the 6.4 million incident cases reported in 2017, ranging from 8% in the WHO Western Pacific Region to 24% in the WHO Eastern Mediterranean Region” [3].

“However, extrapulmonary tuberculosis was said to be underreported” [9]. The objective of this study was to evaluate the clinical and diagnostic features in women with abdominal tuberculosis that simulated advanced ovarian malignancy, who were referred to the Gynaecologic Oncology unit.

2. MATERIAL AND METHODS

2.1 Study Area

This study was conducted at the gynaecologic oncology unit of the University of Port Harcourt Teaching Hospital (UPTH). The University of Port Harcourt Teaching Hospital is a 988-bed hospital in Alakahia, in Obio-Akpor Local Government Area of Rivers state. It is a tertiary hospital that serves as a referral centre for all levels of healthcare in Rivers state and other neighbouring states including Bayelsa, Imo and Abia. Every week, the gynaecology clinic is open from Monday to Friday, and each clinic session is led by a team of consultants. Patients are evaluated in the clinic before they are admitted into the gynaecological ward for surgery.

2.2 Methods

We reviewed the medical records of patients with abdominal TB that mimicked advanced ovarian cancer who were managed at the Gynaecologic oncology unit of the Obstetrics and Gynecology department of the University of Port Harcourt Teaching, Nigeria, over a period of 6 years between January 1, 2016, and December 31, 2021. According to histopathology reports, 11 patients were diagnosed with abdominal TB after exhibiting symptoms and signs similar to advanced ovarian cancer.

We examined the clinical presentations, laboratory results, radiological findings, diagnostic modalities, treatment, and outcomes. Laboratory data included complete blood count, serum CA-125, CA19-9, and carcinoembryonic antigen (CEA) levels. Radiological examination included

chest radiograph; ultrasound scan and contrast-enhanced computed tomography (CECT) scan of the thorax, abdomen, and pelvis.

Pauslian et al [6] advocated that “the diagnosis be confirmed by at least one of the following criteria: (1) histological evidence of caseating granulomatous inflammation in tissue specimens or ascitic fluid; (2) acid-fast bacilli identified in tissue specimens or ascitic fluid; (3) tissue or ascitic fluid culture yielding *M tuberculosis*; or (4) a good therapeutic response to anti-TB agents in patients with clinical evidence of abdominal TB”. All patients received standard tuberculosis treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol for a duration of 9 months.

Information was obtained from patients' case files and histopathology reports. Each patient's proforma was checked for accuracy before being entered into a spreadsheet and analysed.

2.3 Statistical Analysis

The data was analyzed using the Statistical Package for Social Sciences version 25. For categorical variables, frequency and percentages were calculated; for continuous variables, mean SD was reported. Frequency tables were used to summarize descriptive statistics.

3. RESULTS

During the study period, 11 patients with a documented diagnosis of abdominal tuberculosis mimicking advanced ovarian cancer were identified from institutional records. More than half 6 (55%) of the abdominal TB was found in patients aged 20 to 40 years, with many patients 8 (82%) being nulliparous and only 3 (27.3%) being multiparous.

Abdominal distension, Abdominal pain and weight loss appeared to be the most common presenting symptoms among the 11 patients, and two of them (18.2%) also reported fever and night sweats. All patients had clinical evidence of ascites, along with thickening or ill-defined nodularities in the Douglas pouch and/or in the adnexal areas on a pelvic examination, but only

two (18.2%) had the suggestion of an adnexal mass. Only three patients (27.3%) were suspected of having abdominal tuberculosis at the time of presentation. This is shown in Table 1.

Mild normochromic, normocytic anaemia with a mean haemoglobin level of 7.8 g/dL was observed in haematological indices. CA-125 levels were elevated in all 11 patients (100%), with a mean value of 327.8 U/mL (range, 14-698 U/mL). Other serum tumour markers like CEA and CA19.9 were obtained in some patients because they were referred with a provisional diagnosis of ovarian malignancy. The mean CEA level was 1.9 (range: 0.4-10) ng/mL, and the mean serum CA 19.9 level was 16.5 (range: 0-289) U/mL. This is displayed in Table 2.

Abnormal chest X-ray signs, such as pleural effusion and increased infiltration, were seen in 5 (45.5%) patients but were specific for pulmonary TB in only two patients (18.2%). Chest tube insertion was done by the cardio-thoracic unit to drain the effusion. However, the sputum specimens in these two patients were negative for acid-fast stain for M tuberculosis (Table 3).

Transabdominal and transvaginal ultrasound and computed tomography studies showed pelvic ascites in all 11 (100%) and a tubo-ovarian mass in 3 (27.3%). Debritic ascites with peritoneum thickening and mesenteric and omental stranding were demonstrated in all 11 patients (100%), and retroperitoneal lymphadenopathy in 4 patients (36.4%, Table 3).

Abdominal paracentesis was performed on five patients whose findings were deemed most inconclusive for an ovarian cancer diagnosis; this revealed a clear exudative fluid with benign lymphocytic cells being predominant (in a range of around 60-70%). In these five cases, acid-fast bacilli staining (Ziehl-Neelsen) and TB culture from ascitic fluid were performed, and both yielded negative results.

Diagnostic procedures

All 11 (100%) patients had an exploratory laparotomy and underwent extended surgery, which included a total hysterectomy and bilateral salpingo-oophorectomy. All patients had a pathognomonic picture of miliary tuberculosis with peritoneal thickening, omental cake formation, and adhesion throughout the peritoneal cavity. All patients had TB confirmed by the final pathological examination, and all had acid-fast staining (Table 1).

Treatment and outcomes

Postoperatively, all patients had uneventful courses, and all received quadruple anti-TB therapy for at least 6 months. Every two months, serum CA-125, a clinical examination, and an ultrasound were performed. During the anti-TB treatment, serum CA-125 levels gradually returned to a normal range (0-35 U/mL) and remained such after the course was completed.

Table 1: Clinical Features

Variables	Frequency (n= 11)	Percent (%)
Abdominal distension	11	100

Abdominal pain	11	100
Weight loss	11	100
Ascites	11	100
Fever	2	18.2
Adnexal mass	2	18.2

Table 2: Laboratory Findings

Variables	Mean
Haemoglobin	7.9 g/dl
Serum CA-125	327.8 U/mL (range: 14-698 U/mL)
Mean CA 19.9	16.5 (range: 0-289) U/mL
Mean CEA	1.9 (range: 0.4-10) ng/mL

*CA=cancer antigen, CEA = carcinoembryonic antigen

Table 3: Radiological Findings

Features	Frequency (n=11)	Percent (%)
Chest X ray	5	45.5
Omental caking	11	100
Peritoneal thickening	11	100
Ascites	11	100
Retroperitoneal lymphadenopathy	4	36.4
Tubo-ovarian mass	3	27.3

4. DISCUSSION

“One of the most common sites of extrapulmonary involvement is abdominal tuberculosis” [2].

“The diverse clinical manifestations and complications of abdominal tuberculosis continue to challenge the diagnostic acumen and therapeutic capabilities of all physicians” [2,4].

“The symptoms and signs of both abdominal TB and advanced ovarian cancer are often nonspecific including abdominal distension, discomfort, or pain, breathlessness, weight loss, presence of ascites, and abdomino-pelvic mass. Some studies have suggested that younger age at presentation (median 20-40 years) in patients with abdominal TB could be a differentiating feature from malignancy (median age 50-70 years)” [10]. Abdominal TB can occur at any age, but most common in young women but preoperative differentiation between advanced ovarian carcinoma and abdominal tuberculosis may be difficult. In our study, we observed a similar age range.

“CA 125 serum levels are typically regarded as highly suspicious for epithelial ovarian malignant tumours, particularly in postmenopausal women, and can reach extremely high levels in patients with widespread peritoneal dissemination” [11]. “However, it is a nonspecific marker that may increase in a variety of benign gynaecological and non-gynecological conditions such as endometriosis, pelvic infection, peritonitis, pancreatitis, hepatitis, and nephrotic syndrome, as well as non-gynecological cancers with intraperitoneal metastases. The mean CA 125 level in the current study was 327.8 U/mL, mimicking a malignant ovarian disease. Hence, this study reinforces the nonspecific nature of elevated serum CA-125 as reported by previous authors” [12, 13].

“Abdominal imaging in abdominal TB often mimics ovarian malignancy and has been reported to have limited diagnostic accuracy” [14]. “Ascites, peritoneal and omental disease, pelvic mass,

and enlarged retroperitoneal lymph nodes are common in both tuberculosis and advanced ovarian malignancy” [7]. However, certain radiological features may favour tubercular pathology over malignancy and an experienced radiologist may be able to provide a differential diagnosis.

“On abdominal ultrasound, ascites with fine fibrous strands and lymphadenopathy with hypoechoic cores suggestive of caseation indicate a higher probability of tuberculosis. An abdominal contrast CT scan showing septate or particulate ascites; omental fat stranding; ill-defined adnexal masses; smooth, strongly enhancing peritoneal thickening; and caseous lymph nodes favour tuberculosis while well-defined, heterogeneous adnexal masses, nodular peritoneal thickening, and a nodular or caked omentum favour malignancy” [5,14]. In the current study, abdominal TB was not suspected, hence all patients had a staging laparotomy. However, in some patients with severe ascites and huge abdominal mass with highly elevated CA-125 levels, laparotomy may be the best option. To avoid unnecessary radical surgery in young women, intraoperative frozen section analysis that reveals caseous necrosis with granulomatous lesions should be recommended.

“Although the gold standard for diagnosis is culture growth of Mycobacterium species in ascitic fluid or a peritoneal biopsy, waiting up to 6 weeks for the culture result may increase the mortality rate of this disease by delaying treatment. As a result, the value of ascitic fluid cultures for Mycobacterium tuberculosis is debatable, because early detection is critical. The polymerase chain reaction (PCR) for mycobacterium may be useful in obtaining results, but it is expensive and not widely available” [11]. Adenosine deaminase (ADA) activity in ascitic fluid has been proposed as a useful diagnostic test for abdominal tuberculosis (TB). These tests, however, may not provide a conclusive diagnosis. Measurement of ADA in ascitic fluid may be a useful screening test in countries with a high incidence of tuberculosis and in high-risk patients.

Due to lack of specific features on preoperative assessment, the diagnosis of abdominal TB is often made after surgery for suspected ovarian malignancy. Surgical interventions in suspected ovarian malignancies should ideally be performed by surgeons who are familiar with the surgical treatment and staging of ovarian carcinoma.

Thus, clinical suspicion is critical in detecting abdominal tuberculosis in at-risk patients, particularly young immigrants from high-prevalence areas or immune-compromised individuals. When a female patient has symptoms and sonographic findings that are otherwise consistent with an ovarian neoplasm, tuberculosis should be considered in the differential diagnosis. Furthermore, the study highlights the importance of obtaining a histological confirmation of malignancy before commencing neoadjuvant chemotherapy in a patient with suspected advanced ovarian malignancy.

The strengths of the current study are its uniformity in diagnosis and management, and it is the first to be conducted at the study centre. The limitations are its retrospective nature and small sample size, hence may not have included the entire spectrum of patients with abdominal tuberculosis.

5. CONCLUSION

Our study showed that a high index of suspicion for abdominal TB is important in women of reproductive age with nonspecific symptoms of abdominal distension, weight loss, and ascites. Serum CA-125 levels are not helpful in the differential diagnosis of such cases but assist in the follow-up after anti-tubercular treatment is started. Polymerase chain reaction (PCR) of ascitic fluid for mycobacterium is considered a reliable method for diagnosis and should at least be attempted before surgical intervention. Laparoscopic tissue biopsy for frozen-section analysis is now a fundamental tool in diagnosis of abdominal TB to avoid unnecessary extended surgery.

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Ethical Approval

Ethical approval for the study was obtained from the research and ethics committee of the University of Port Harcourt Teaching Hospital.

UNDER PEER REVIEW

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