



CHALLENGES IN THE MANAGEMENT OF EXTRAPULMONARY TUBERCULOSIS – A CASE SERIES

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ABSTRACT **Introduction:** With 28% of cases, India leads among the eight countries accounting for more than two-third of total Tuberculosis patients, according to the world tuberculosis report 2022 of the World Health Organization. Extra-pulmonary Tuberculosis (EPTB) accounts for 15-20 % of all TB cases. Similarly, many therapeutic challenges are also faced especially in regard to the decision of starting ATT, the regimen to start, the duration of therapy, and identification of treatment failure. **MATERIALS AND METHODS:** A prospective case series of eight cases were taken highlighting the challenges faced during the work up of these cases. **RESULTS:** The present study describes eight cases of EPTB involving various organs including one lymph node case, four cases of abdominal TB, three cases of urogenital TB. Cases were diagnosed initial based on clinical suspicion followed by which the samples were sent to histopathological examination, PCR, Nucleic acid amplification test (NAAT). Anti tubercular therapy was started and were followed-up. **CONCLUSION:** In a country like India where TB is endemic, there is always a very high chance of different presentations of tuberculosis. A detailed history, examination and newer method of identification of mycobacterium tuberculosis is necessary.

KEYWORDS : EPTB, CASEATING GRANULOMA, POLYMERASE CHAIN REACTION, CBNAAT

INTRODUCTION:

With 28% of cases, India leads among the eight countries accounting for more than two-third of total Tuberculosis patients, according to the world tuberculosis report 2022 of the World Health Organisation. Tuberculosis affects various organs and thus presents a wide range of symptoms¹. Extra-pulmonary Tuberculosis (EPTB) accounts for 15-20 % of all TB cases in HIV-negative, while 40-50% in HIV-positive individuals. Diagnosis and management of extra-pulmonary TB cases are always challenging for clinicians. Clinical suspicion based on organ-specific symptoms, accessibility of specimens, uncertain diagnostic modalities, detection of drug resistance, etc. are among the various challenges in reaching a diagnosis of EPTB. Similarly, many therapeutic challenges are also faced especially in regard to the decision of starting ATT, the regimen to start, the duration of therapy, and identification of treatment failure, etc². The present case series describes eight cases of EPTB, highlighting the diagnostic dilemmas faced during the workup of these cases.

Case descriptions:

Site of lesion	Number of cases	Sex	
		Male	Female
Lymph node	1	0	1
Peritoneal	2	1	1
Intestinal	1	0	1
Spleen	1	0	1
Urogenital	3	0	3

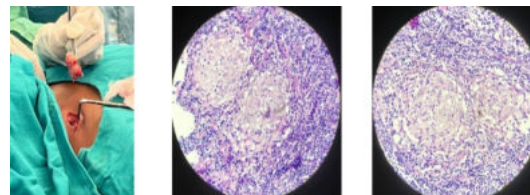
CASE 1

A 17-year-old female came with chief complaints of swelling in the neck and low-grade fever on and off episodes for 15 days. It was associated with loss of weight, and loss of appetite also. There was no history of any respiratory complaints and no other significant medical history in the past. On examination cervical lymphadenopathy was present – four cervical lymph nodes, soft, mobile, non-tender, skin over the swelling was pinchable. Chest x-ray was normal. Lymph node FNAC showed tubercular lymphadenitis, LN biopsy was done and sent for CNBAAT and histopathology. Histopathology examination showed a caseous granulomatous lesion suggestive of Tuberculosis. Lymphnode sample sent for CBNAAT showed MTB detected with Rifampicin resistance.

HPE REPORT-CASEOUS GRANULOMATOUS INFLAMMATION



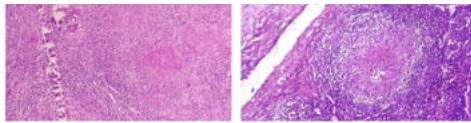
CHEST X-RAY-NORMAL



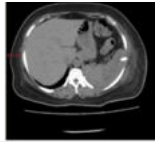
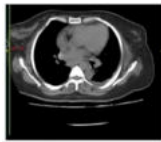
CASE 2

A 48 year old female patient came with chief complaints of pain abdomen-diffuse dull aching type, Fever since 3 days-intermittent type associated with chills and rigors, and shortness of breath since 1 day grade II mMRC. History of similar complaints was present 2 months back. She was diagnosed to have acute pancreatitis. Diabetic ketoacidosis was treated accordingly. He is a known diabetic since 8 years and was on regular medications. No history of any respiratory complaints in the past. Routine blood investigations were done which showed leukocytosis, and slightly elevated serum lipase, Chest x-ray showed mild obliteration of the left costophrenic angle, Ultrasound of the abdomen showed an irregular collection with low-level internal echoes in the spleen extending from the upper pole to lower pole s/o splenic abscess, mild left-sided pleural effusion. CT abdomen also showed a splenic abscess with left pleural effusion. Pigtail was placed and pus was drained. Sputum for Trunat was negative, pleural fluid CBNAAT was negative. Splenectomy was done and the specimen was sent for histopathological examination which showed caseating granulomatous inflammation. ATT was started for this patient and complete recovery was reported on follow-up.

CHEST X-RAY-NORMAL



H/P Study Report: Caseating granulomatous inflammation



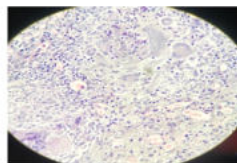
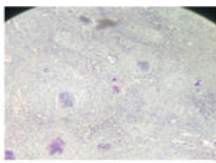
CT Abdomen- Splenic abscess with drain and minimal Lt PLEF

CASE 3

A 17 year old male came with chief complaints of pain abdomen-acute onset, diffuse dull aching type of pain over the abdomen, projectile type of vomiting since 1 day. No significant respiratory complaints and there was no significant past medical history. Investigations were normal. Chest x-ray was normal. Patient was posted for exploratory laparotomy. Intra-operatively multiple nodules over the entire wall of the abdomen were found. Omentum was sent for HPE it showed an epithelioid granulomatous lesion. Patient was started with ATT and there was a symptomatic improvement.



Multiple nodules over the entire wall of Abdomen



Granulomatous inflammatory lesion were found

CASE 4

A case of 34years old female came with chief complaints of pain abdomen since 15 days, and abdominal distension since 10 days. No history of significant respiratory complaints or any other medical history in the past. Blood investigations were normal. USG abdomen showed moderate to massive ascites with omental thickening and hepatosplenomegaly. CECT abdomen was done. Patient was posted for diagnostic laparoscopy Intra operative findings multiple deposits were present all over the parietal peritoneum, small bowel, and transverse colon. Omentum was studded with deposits. 2.5 Litres of straw-colored fluid was drained during the procedure and was sent for investigations. Ascitic fluid showed lymphocyte predominance, and ascitic fluid CBNAAT was negative. Omentum biopsy showed an epithelioid granulomatous lesion. Patient was started with ATT and showed improvement in the follow-ups.

CASE 5

A case of 23 year old female came with chief complaints of pain abdomen in the right iliac region and right lumbar region since 2 days, vomitings 5 episodes since 1 day, non-projectile type, loss of appetite, and loss of weight was also present. USG abdomen showed thickened and inflamed bowel loops in the right iliac fossa with free fluid and

mesenteric lymph nodes. CECT abdomen showed heterogeneously enhancing irregular wall thickening of the caecum and proximal ascending colon with luminal narrowing. Colonoscopy was done and it showed an ulcerated lesion or friable lesion in the caecum and proximal ascending colon, and a biopsy was taken from that area and sent for HPE. HPE showed the presence of granuloma with caseous necrosis and Langhans giant cells suggestive of TB. Patient was started with ATT drugs and showed improvement.

CASE 6

A case of 55years old female came with chief complaints of low back ache aggravated since 2 months, fever on and off episodes since 1 month, low-grade intermittent fever not associated with chills and rigor. History of urinary incontinence since 2 years. No history of shortness of breath, cough, cold, loss of appetite, or loss of weight. History of urinary incontinence was present since 3years, Total abdominal hysterectomy and bilateral salpingo-oophorectomy with pelvic lymph node dissection were done 2years back and the histopathological examination showed carcinoma in-situ of cervix, and epithelioid granulomatous lesion in lymph nodes. But no specific treatment was started for the patient by the gynecologists on the basis of these reports. Respiratory system examination was normal. Urine culture was sterile, urine for MTB-PCR was sent by collecting urine samples for two days and the result was positive. Chest X-ray was normal. Patient started anti-tubercular treatment. There was symptomatic improvement after the initiation of ATT on follow up.

CASE 7

A case of 23 years old female came with a complaint of secondary infertility. No other significant respiratory complaints or any past medical history. Ultrasound abdomen showed right hydrosalpinx .with adhesion. Diagnostic or therapeutic laparoscopy was planned. Intraoperative findings were diffuse omental adhesion with anterior abdominal wall and pelvis. Serial adhesiolysis was done. Both tubes were fibrosed distended with inverted fimbriated end features that were suggestive of chronic pelvic inflammatory disease with bilateral pyosalpinx. B/L salpingectomy was done and specimen was sent for HPE and TB-PCR. TB-PCR report was positive and the patient was started with ATT.

CASE 8

A case of 23 years old female came with chief complaint of primary infertility. No history of any other complaints. No previous medical history. Blood investigations and other routine investigations were normal. Endometrial biopsy was taken and was sent TB-PCR. Endometrial TB-PCR was positive. Patient was started on ATT for 6 months. She was regular follow-ups and she conceived after the completion of treatment.

DISCUSSION:

Extrapulmonary disease accounts for almost 10-15% of all tuberculosis. TB lymph node accounts for 20-40% of extrapulmonary tuberculosis. They usually present as painless swelling and some may also have systemic symptoms like fever, weight loss, and loss of appetite. Usually nowadays many are preferring FNAC for the diagnosis of TB lymph nodes as it is less invasive, painless, cheap, and safe. The ideal procedure is biopsy³. In our case patient had the classic symptoms of TB lymphadenitis. Biopsy was taken and the material was crushed and sent to CBNAAT. The report was MTB detected with rifampicin resistance. Many times physicians start ATT based on the FNAC report only it is better to do a biopsy and send the sample for detection of mycobacterium tuberculosis and drug sensitivity, so that we won't miss drug-resistant cases.

Primary involvement of spleen is rare. The most common symptoms that patients present with are fever, fatigue and weight loss, and splenomegaly. Patient infected with HIV or who are immunocompromised reported to have a higher risk for splenic tuberculosis. Some cases have been reported in immunocompetent patients also⁴. In most of the reported cases, the diagnosis was initially made by radiological findings followed by pathological examination of a fine-needle aspirate, splenic biopsy, or splenectomy. In our case patient presented with fever, and abdominal pain. Radiological findings on ultrasound and CT abdomen confirmed splenic abscess, laparoscopic guided splenectomy was done and the specimen was sent for HPE which showed caseating granulomatous inflammation.

Histopathological examination is an ideal method to confirm the diagnosis. There are five types of pathomorphological classification

including miliary TB, nodular TB, TB spleen abscess, calcific tuberculosis, and mixed-type TB.

Antitubercular treatment is the primary treatment for splenic tuberculosis. Our patient was also started with ATT drugs and the patient showed symptomatic improvement in the follow-up.

Urogenital TB refers to TB of the genital tract and the urinary tract. It makes up approximately 4% of all EPTB cases annually. Diagnosing urogenital TB is difficult due to lack of clear case definitions.

The most common symptoms in urinary TB were irritative bladder such as dysuria and diurnal or nocturnal frequency (51.5%), flank pain (27.3%), microscopic hematuria (18.2%), gross hematuria (9.1%) according to study conducted by Mohammad Yazdani et al.⁵

Diagnosis of urinary tuberculosis is usually made very late. Early morning urine sampling for three to five days was collected for staining and microscopy for AFBs and culture for Mtb. Sensitivity to these tests is low, culture remains the most reliable way to conform urinary TB. The sensitivity of PCR on urine samples was reported to be around 60%. The results of PCR may be affected by metabolites, drugs, and other biological materials in the fluids of body, and non-homogenous distribution of the bacteria may be reason for false negative.

Treatment is similar to pulmonary tuberculosis i.e, 6 months of ATT drugs.

In our case patient was having irritative bladder symptoms, urine TB-PCR was done and it was positive. so the patient was started with ATT. Patient showed improvement in the symptoms in the follow-up.

Female genital TB is most commonly present in premenopausal women. Around 11% of patients present with no other complaints other than primary or secondary infertility. Other symptoms include pelvic pain, menstrual disturbances, vaginal discharge, and poor general condition. Usually, the diagnosis is based on laparoscopic appearance typical of female genital TB, any gynecological specimen positive for AFBs on microscopy or positive for Mtb on culture, and on histopathological examination.⁶

The polymerase chain reaction is a useful supporting test for the diagnosis. U.N. Jindal et al. conducted a study regarding the sole basis of a positive polymerase chain reaction test in the initiation of anti-tubercular treatment for endometrial tuberculosis in infertility cases and observed that early ATT treatment had an excellent chance of early spontaneous conception.⁷ Our patient presented with primary infertility, based on endometrial TB-PCR patient was started ATT and after completion of treatment, patient was conceived.

Laparoscopy is an important diagnostic tool in infertility cases as it helps in direct visualization of the pelvic organs, patency of the tubes, and abdominal organs in a single procedure. Our patient presented with secondary infertility with pyosalpinx and the specimen was sent for HPE and TB-PCR. Laparoscopy showed adhesions to the anterior abdominal wall. B/L salpingopherctomy was done and ATT was started. Abdominal TB contributes to 3% of extrapulmonary TB cases in India. Abdomen TB is divided based on the site of involvement. The most common presentation of abdominal TB if the peritoneum is involved is abdominal distension, pain, and fever which was similar to the two cases in our study. Visual appearance on laparoscopy can be highly suggestive of TB which includes thickened peritoneum with or without tubercles or adhesions may be observed. Confirmation is based on microscopy, culture, or validated PCR, or in case of clinical suspicion histopathological findings can also be taken to start ATT. Our cases showed abdomen studded with tubercles on laparoscopy and HPE showed features suggestive of TB. Patients were started on ATT and showed improvement.^{6,8}

The ileocaecal area is the most common site of involvement in intestinal TB, and ulcerative or ulcero-constructive type of ulcers are most common. The colonoscopic examination provides visualization of the area and access for biopsy. The most common symptom is usually a colicky type of abdominal pain, nausea, vomiting, constipation, and bleeding manifestation. Our patient presented with the colicky type of abdominal type, vomiting, colonoscopic was done and a biopsy was taken from the ulcerative lesion which showed features suggestive of TB in HPE. Patient was started on ATT and showed improvement in symptoms.

CONCLUSION:

Tuberculosis can present with a huge spectrum of different symptoms. In a country like India where the prevalence of TB is more. A detailed history, examination, and vital investigations are necessary for identifying extrapulmonary TB. Culture is also an essential step in the diagnosis. Sophisticated techniques like PCR may also be helpful along with histopathological examination. Anti-tubercular therapy is effective in all cases.

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