

Extrapulmonary tuberculosis presenting as a gynaecologic malignancy: A case series

M. Ramnath (MBBS), N. McEachnie (MBBS), N. Rambocas (MBBS, MRCOG), M. Johncilla (BA, M.D)
Department of Obstetrics and Gynaecology, Department of Pathology, Port of Spain General Hospital, Trinidad and Tobago

INTRODUCTION

Tuberculosis (TB) remains a global health problem today despite increased access to and advancements in medicine, with a quarter of the world’s population being affected. Extrapulmonary tuberculosis (EPTB) refers to tuberculosis that occurs outside of the lungs and accounts for 15-20% of all TB manifestations^{1,2}. Accurate diagnosis of this condition poses quite a challenge as it may have a myriad of presentations of which an oncologic process namely an ovarian or peritoneal malignancy is a differential. We would like to present two such cases of EPTB presenting as metastatic gynaecologic malignancies.

CASE PRESENTATION

Case 1
A 24year old female presented with a three-month history of abdominal distension, pain, weight loss and cough. She had no significant travel, medical, surgical or family history. Her blood investigations were normal except a haemoglobin of 72g/dL and a Ca125 level of 504.6 U/ml (0-35U/ml). Radiologic imaging showed bilateral pleural effusions, peritoneal thickening and lymphadenopathy. A pelvic ultrasound performed was normal.

She underwent paracentesis and a pleural tap which were both negative for malignant cells but instead showed abundant lymphocytes and inflammatory cells. Sputum cultures were negative for TB. Her Mantoux test, however, was positive.

Due to the high suspicion that her symptoms were TB related, she was counselled on either an image guided or laparoscopic peritoneal biopsy. Despite counselling on the need for a definitive diagnosis, she refused to undergo any form of biopsy. She then divulged that she had a recent high-risk contact with someone who had TB. Following a multidisciplinary meeting, it was decided to start her on the anti-TB medications in the TMU. This resulted in resolution of her symptoms.

Case 2
A 42year old female presented with a one-month history of cough and shortness of breath. She had no significant travel, medical or surgical history. Clinical examination revealed a pleural effusion and ascites. Her blood investigations were normal except for a haemoglobin of 87g/dL and a Ca-125 level of 363 U/ml (0 – 35U/ml). Radiologic imaging showed gross ascites, adnexal masses, widespread lymphadenopathy and a left sided pleural effusion. To further evaluate the adnexal masses, a transvaginal pelvic ultrasound was performed which was essentially normal.

Ascitic and pleural taps were performed. Both fluids had no malignant cells but instead, showed abundance of lymphocytes and inflammatory cells. An acid-fast bacilli (AFB) stain on the fluids was negative as were the sputum cultures. A Mantoux test, however, was positive.

Due to the high index of suspicion that her symptoms were TB related, a definitive diagnosis was obtained when a nodal biopsy was performed. This revealed necrotizing granulomata, and the staining confirmed mycobacterial infection (Figure 1). She was referred to the Thoracic Medical Unit (TMU) where anti-TB medications were commenced with resolution of her symptoms.

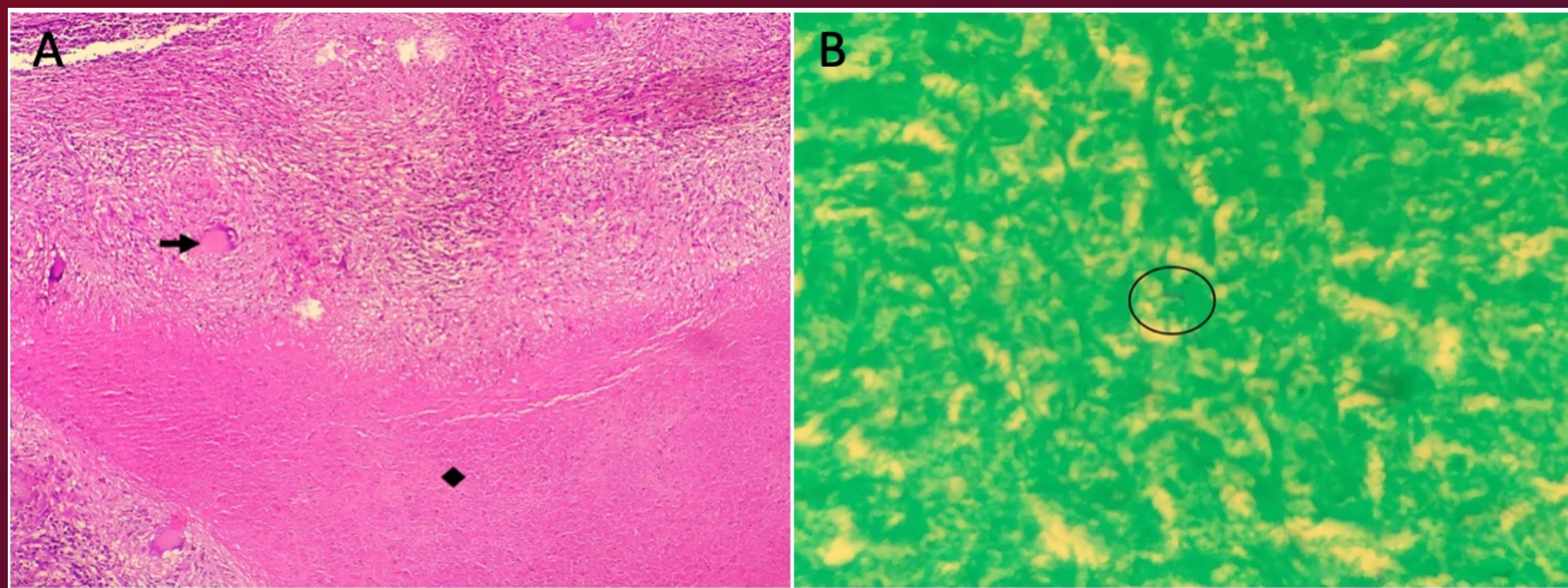


Figure 1. Hematoxylin and eosin staining of the lymph node biopsy (A) shows abundant necrotizing granulomata with palisading histiocytes, occasional giant cells (arrow) and central necrosis (diamond). A Ziehl Neelsen (Acid Fast Bacilli) stain (B) shows rare acid-fast bacilli within the area of necrosis (circle).

DISCUSSION

Tuberculosis continues to pose a major challenge especially for the developing world, so much so, that the World Health Organization (WHO) deemed it to be a worldwide pandemic. In 2020, 1.5 million persons died from TB, making it the 13th leading cause of death worldwide³. TB usually affects the lungs but when other organs of the body are affected apart from the lungs, it is known as extrapulmonary tuberculosis (EPTB). In 2019, EPTB accounted for 16% of the 7.8 million cases of TB⁴. Common sites of infection are the lymph nodes, gastrointestinal tract, urogenital tract, bone, meninges, pleura and spine. Due to the multiple target sites involved, symptoms are usually non-specific and varied thereby creating a diagnostic challenge.

Abdominal tuberculosis (ATB) accounts for 3% of EPTB cases and encompasses peritoneal and pelvic tuberculosis⁵. As such, it should be considered as one of the differential diagnoses in patients presenting with peritoneal thickening, ascites and an elevated Ca125 level, since an underlying ovarian or peritoneal metastatic malignancy is usually entertained first. Liu et al 2014 in trying to differentiate abdominopelvic tuberculosis from an advanced ovarian malignancy concluded that it is difficult to do so using clinical manifestations alone⁶.

Also, relying on the Ca-125 marker to assist with the diagnosis, creates further confusion due to its sensitivity and specificity. It is raised in approximately 50% of stage 1 epithelial ovarian cancers and in 80-85% of patients with advanced ovarian cancer⁷. However, it can also be elevated in many other medical conditions both malignant and benign. Many studies have shown elevated Ca-125 levels in ATB, even using it as a marker for follow up, as its value decreases 2-3 months after anti-TB therapy has been initiated⁸. Our patients presented in very much the same way as patients with advanced ovarian malignancies in that, they both had weight loss, ascites, pleural effusions and raised Ca125 levels.

Cytological investigations of bodily fluids are usually not sensitive to detect TB due to the paucibacillary nature of the disease. Hence, a negative test result cannot definitively rule it out. Both patients underwent paracentesis, pleural taps and sputum cultures which were all negative for TB. Sputum culture sensitivity varies based on site of EPTB, with ATB having a sensitivity of 28-50%⁹. According to Wu et al 2019, the sensitivity for ascitic fluid for Ziehl-Neelsen (ZN) and acid-fast bacilli (AFB) staining was 3% and 21-35% respectively¹⁰. Adenosine deaminase (ADA), a newer diagnostic tool, can be used as a molecular marker for the detection of ATB with reported sensitivities and specificities >90% with ascitic ADA levels >30 U/L⁹. It is an enzyme with increased activity in TB infections, rheumatological diseases, and malignant lymphomas. Several studies have shown promising results for its use in diagnosing EPTB¹¹.

Both patients had imaging which showed ascites, peritoneal thickening, lymphadenopathy and even the suggestion of ovarian masses. Sah et al 2017 retrospectively studied 32 cases of pelvic tuberculosis, recognising that more than half of the cases were misdiagnosed, as CT findings and clinical features for pelvic tuberculosis were non-specific. They concluded that together with clinical history and investigations, pelvic tuberculosis should be considered in young female patients with elevated CA125 levels and CT findings of adnexal mixed solid and cystic mass, ascites and thickened peritoneum¹².

Histopathological evidence from biopsy obtained either laparoscopically, image guided or an open procedure, is essential in the diagnosis of EPTB. Biopsies from these procedures have a diagnostic yield of 85-95%⁹. The presence of granulomas, caseation, and AFB usually confirms the diagnosis. ZN staining for AFB is used to diagnose over one third of TB cases based on its affordability and accessibility, however, it has a low sensitivity of 0 – 44 % but high specificity¹³.

The mortality rate from EPTB varies from about 15% to 28.7%¹⁴. Initial misdiagnosis coupled with treatment delays may have a contributory effect on the mortality rate. Despite initial diagnostic challenges, both our patients were started on anti-TB medications under the supervision of a specialist.

Both reported resolution of their symptoms as well as weight gain. There was also radiological evidence of regression of the peritoneal effusions. Currently, they are both asymptomatic under the care of the thoracic medicine specialist.

CONCLUSION

EPTB, although uncommon, can mimic an advanced gynaecological malignancy. As such, it must be considered as one of the differential diagnoses to ensure that the appropriate investigations are undertaken so that timely treatment can be initiated if detected.

REFERENCES

- Rodriguez-Takeuchi, S.Y., Renjifo, M.E. and Medina, F.J. (2019). Extrapulmonary Tuberculosis: Pathophysiology and Imaging Findings. *RadioGraphics*, 39(7), pp.2023–2037. doi:10.1148/rg.2019190109.
- Abreu, N., Serrado, M.A., Matos, R., Carneiro, R. and Nunes, A. (2018). Pelvic tuberculosis: a forgotten diagnosis – case report. *Radiology Case Reports*, [online] 13(5), pp.993–998. doi:10.1016/j.rader.2018.07.006.
- World Health Organization (2021). Tuberculosis. [online] World Health Organization. Available at: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>.
- Gopalaswamy, R., Dusthacker, V.N.A., Kannayan, S. and Subbian, S. (2021). Extrapulmonary Tuberculosis – An Update on the Diagnosis, Treatment and Drug Resistance. *Journal of Respiration*, 1(2), pp.141–164. doi:10.3390/jor1020015.
- Ozgu, E. (2014). Tuberculosis in Gynecologic Oncology: Still a Diagnostic Dilemma. *Obstetrics & Gynecology International Journal*, 1(2). doi:10.15406/ogij.2014.01.00012.
- Liu, Q., Zhang, Q., Guan, Q., Xu, J. and Shi, Q. (2014). Abdominopelvic tuberculosis mimicking advanced ovarian cancer and pelvic inflammatory disease: a series of 28 female cases. *Archives of Gynecology and Obstetrics*, [online] 289(3), pp.623–629. doi:10.1007/s00404-013-3034-2.
- Wani, A.M. and Akhtar, M. (2008). CA-125: a marker for diagnosis and follow-up of pleuroperitoneal and lymph node tuberculosis. *Annals of Saudi Medicine*, 28(2), pp.142–143. doi:10.5144/0256-4947.2008.142.
- O’Riordan, D.K., Deery, A., Dorman, A. and Epstein, O.E. (1995). Increased CA 125 in a patient with tuberculous peritonitis: case report and review of published works. *Gut*, [online] 36(2), pp.303–305. doi:10.1136/gut.36.2.303.
- Lee, J.Y. (2015). Diagnosis and Treatment of Extrapulmonary Tuberculosis. *Tuberculosis and Respiratory Diseases*, 78(2), p.47. doi:10.4046/trd.2015.78.2.47.
- Wu, D.C., Averbukh, L.D. and Wu, G.Y. (2019). Diagnostic and Therapeutic Strategies for Peritoneal Tuberculosis: A Review. *Journal of Clinical and Translational Hepatology*, [online] 7(X), pp.1–9. doi:10.14218/jeth.2018.00062.
- Kaur, P.C., Surabhi Jaggi, Bela Goyal, Kranti Garg, Seema Gupta, Shivani Jaswal, Kamaljeet (n.d.). Utility of serum ADA estimation in the diagnosis of extrapulmonary tuberculosis. [online] [jmscrigmpublication.org](https://jmscrigmpublication.org/home/index.php/archive/138-volume-05-issue-05-may-2017/2339-utility-of-serum-ada-estimation-in-the-diagnosis-of-extrapulmonary-tuberculosis). Available at: <https://jmscrigmpublication.org/home/index.php/archive/138-volume-05-issue-05-may-2017/2339-utility-of-serum-ada-estimation-in-the-diagnosis-of-extrapulmonary-tuberculosis>.
- Sah, S.K., Shi, X., Du, S., Li, X., Li, C.H., Shah, S., Shrestha, T.K. and Li, Y. (2017). CT findings and analysis for misdiagnosis of female pelvic tuberculosis. *Radiology of Infectious Diseases*, [online] 4(1), pp.19–25. doi:10.1016/j.rjid.2016.04.001.
- Kourbatova, E.V., Leonard, M.K., Romero, J., Kraft, C., del Rio, C. and Blumberg, H.M. (2006). Risk factors for mortality among patients with extrapulmonary tuberculosis at an academic inner-city hospital in the US. *European Journal of Epidemiology*, 21(9), pp.715–721. doi:10.1007/s10654-006-9060-7.
- Ohene, S.-A., Bakker, M.I., Ojo, J., Toonstra, A., Awudi, D. and Klatser, P. (2019). Extra-pulmonary tuberculosis: A retrospective study of patients in Accra, Ghana. *PLOS ONE*, 14(1), p.e0209650. doi:10.1371/journal.pone.0209650.