Case Report Open Access

Archives Of Breast Cancer

DOI: 10.32768/abc.2024114418-422

Tuberculous Pleurisy in a Patient with a History of Breast Cancer: Diagnostic Challenges and Management Options

Asel Imankulova[a], Melis Sholpanbai Uulu[b], Elmira Mamytova[c], Nurbek Monolov[c], Tugolbai Tagaev*[d]

[a]*Department of Surgical Disciplines, Salymbekov University, Bishkek, Kyrgyzstan*

[b]*Department of Infectious Diseases, I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan*

[c]*Department of Clinical and Morphological Disciplines, Salymbekov University, Bishkek, Kyrgyzstan*

[d]*Department of Hospital Internal Medicine with a Course of Hematology, I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan*

ARTICLE INFO

Received:
13 June 2024
Revised:
19 July 2024
Accepted:
6 August 2024

Keywords:
Breast cancer, tuberculous pleurisy, tuberculosis, pleural biopsy, granulomatous inflammation

ABSTRACT

Background: Tuberculosis (TB) and cancer are increasingly prevalent diseases that can be challenging to diagnose due to similarities in clinical and radiological findings. This case report describes a 46-year-old woman with a history of breast cancer who developed tuberculous pleurisy (TP).

Case presentation: A 46-year-old woman who underwent mastectomy and chemotherapy for BC in 2023 had hypertension, but no history of TB. The patient presented with dry cough, fever, and stomach discomfort, with an oxygen saturation level of 60%, but no respiratory distress before her appointment. Microscopy and culture tests were negative for *Mycobacterium TB*. A positive result was observed with an IFN-γ level of 0.35 IU/ml and 26% of the negative control after TB antigen stimulation. Histological analysis using hematoxylin and eosin staining showed Langhans giant cells, epithelioid cell granulomas, caseous necrosis, and necrotic foci. These findings indicated granulomatous inflammation with no signs of malignancy. Following the diagnosis, the patient received a daily dose of 300 mg isoniazid, 600 mg rifampin, 1500 mg pyrazinamide, and 10 mg pyridoxine for six months without any adverse effects.

Conclusion: Physicians must employ a combination of diagnostic techniques, including morphological and microbiological confirmation, to accurately diagnose pleural effusion in this patient population.

INTRODUCTION

The association between tuberculosis (TB) and oncological processes is complex and continues to be significant due to various factors, including the recent increase in the prevalence of both diseases. Diagnostic difficulties arise due to similarities in clinical and radiological findings between TB and tumor processes in the respiratory system, leading to frequent diagnostic errors.[1]

Tuberculous pleurisy (TP) or fluid accumulation on one side of the pleura caused by TB outside the lungs commonly affects young people with strong immune systems and presents with symptoms such as breathing difficulty, fever, cough, sharp chest pain, nocturnal sweating, weight loss, and general discomfort.[2,3]

***Address for correspondence:**
Tugolbai Tagaev,
Department of Hospital Internal Medicine with a Course of Hematology, I.K. Akhunbaev Kyrgyz State Medical Academy, Bishkek, Kyrgyzstan
Email: ttagaev22kg@gmail.com

Diagnosis can be challenging due to the low sensitivity of microbiological tests on pleural fluid, such as direct examination and cultures, which typically ranges from 10-30%.[4] Biomarkers such as pleural adenosine deaminase and polymerase chain reaction can help diagnose *Mycobacterium (M.) TB* infection,[5] as can the Mantoux test and interferon gamma release assays, such as QuantiFERON-TB Gold.[6-8] However, a pleural biopsy obtained through medical thoracoscopy or a transthoracic route is the most reliable method for diagnosing *M. TB* infection, as it directly isolates bacteria and demonstrates the presence of caseating granulomas. Despite being the preferred diagnostic method, this approach is highly invasive and has a significant number of documented cases in the literature where the results are falsely negative, ranging from 15-20%.[9]

In this case report, we describe the occurrence of TP in a patient with a history of malignancy, and the challenges in diagnosing this condition. A patient with a history of breast cancer (BC) and TP received a combination anticancer treatment at our hospital. The patient underwent routine clinical, radiological, laboratory, and instrumental examinations, including parietal pleural puncture biopsy, as well as microbiological and immunological tests.

CASE PRESENTATION

Clinical presentation

A 46-year-old woman who underwent mastectomy and chemotherapy for BC in 2023 had hypertension, but no history of TB. In her past history of BC, a 2x3cm solid, immobile mass with nipple retraction, skin thickening, and redness was found in the central left breast during clinical examination. A preliminary BC diagnosis was made, and excisional biopsy revealed a granulomatous lesion with caseation granulomas, multinucleated Langhans cells, giant cells, epithelioid histiocytes, and high-grade ductal carcinoma in situ with an invasive component. The patient presented with dry cough, fever, and stomach discomfort, with an oxygen saturation level of 60%, but no respiratory distress before her appointment. After a deep inhalation session, oxygen saturation increased to 85%; however, she later experienced breathing difficulties. The family doctor recorded oxygen saturation levels between 65% and 75%, suspected pneumonia, and pulmonary embolism and referred the patient to our hospital. Upon admission, the patient received azithromycin for 24 h, which reduced the fever (38.5°C). Although breath shortness decreased and appetite worsened, coughing persisted. A chest radiograph from March 22, 2023, showed fluid (pleural effusion) in the left pleural cavity (Figure 1). On August 13, 2023, the patient was hospitalized with normal body temperature, intact skin, and a mastectomy scar.

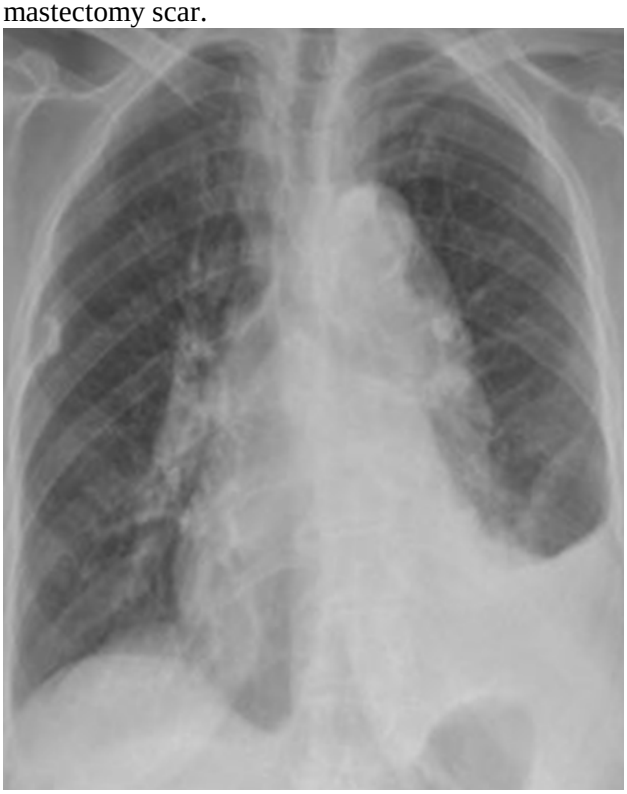

Figure 1. A chest radiograph showing fluid (pleural effusion) in the left pleural cavity

Diagnosis

The patient's height and weight were 156cm and 76kg, respectively. There were no enlarged lymph nodes, and the left lung showed decreased resonance and diminished respiratory sounds. The heart had a normal rhythm, with a pulse rate of 83 beats per minute, and the blood pressure was 140/80 mmHg. Blood tests revealed a hemoglobin level of 128g/l, erythrocyte count of 3.9×1012/l, color index of 0.80, leukocyte count of 4.8×109/l, eosinophil count of 1%, lymphocyte count of 15%, monocyte count of 3%, and ESR of 18mm/h. Mantoux and Diaskin tests produced papules of 11 and 10 mm, respectively. The T-SPOT test result was negative, indicating the absence of the target condition. However, soluble interleukin-2 receptor levels were slightly elevated. Thoracentesis was performed due to significant left-sided pleural effusion, resulting in the removal of 1,600mL of yellowish-brown fluid and placement of a chest drain. The pleural effusion was a serous exudate with a protein content of 42.3g/l and a lymphocyte count of 100%, and high ADA levels of 79.4U/L. The initial drainage was serosanguinous, with blood observed only on the first day, which got severe and then gradually decreased, totaling approximately 3200mL over six days. There was no reduction in the pleural effusion or improvement in the patient's condition; therefore, the drainage

catheter was removed. Microscopy and culture tests were negative for *Mycobacterium TB*, but for interferon-gamma release assays, 1 ml of the whole blood was collected in three heparinized tubes: one with TB antigens (Early Secreted Antigenic Target 6kDa and culture filtrate protein-10), one positive control with phytohemagglutinin, and one null control. The samples were incubated for 20-24 hours at 37°C. Plasma was extracted, and IFN-γ levels were measured using a single-step, sandwich-type enzyme-linked immunosorbent assay. A positive result was observed with an IFN-γ level of 0.35IU/ml and 26% of the negative control after TB antigen stimulation. Fiberoptic bronchoscopy revealed no abnormalities in the bronchi. Histological analysis using hematoxylin and eosin staining showed Langhans giant cells, epithelioid cell granulomas, caseous necrosis, and necrotic foci (Figure 2). These findings indicated granulomatous inflammation with no signs of malignancy.

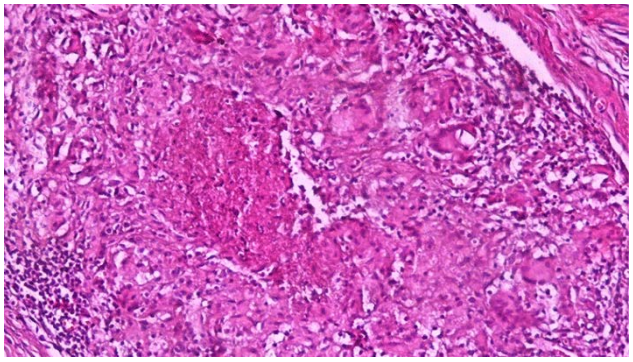

Figure 2. Hematoxylin and eosin staining demonstrating Langhans giant cells, epithelioid cell granulomas, caseous necrosis, and necrotic foci

Treatment

The patient's health improved after undergoing anti-TB treatment and pleural puncture, resulting in cessation of exudation within a week. The diagnosis was further confirmed based on the patient's response to medication and identification of TB lesions. On December 29, 2023, a fluorographic examination revealed moderate pleural overlays on the left side. Upon discharge, only minor changes were observed in the pleural region and the sinuses were completely obstructed. Following the diagnosis, the patient received a daily dose of 300mg isoniazid, 600mg rifampin, 1500mg pyrazinamide, and 10mg pyridoxine for six months without any adverse effects. The patient was closely monitored for an additional 12 months and no signs of recurrence were detected.

DISCUSSION

Previous studies have provided substantial evidence supporting the co-occurrence of cancer and pulmonary TB.[9-13] Patients with cancer who undergo radiation and chemotherapy may have compromised immune systems, making them more susceptible to contracting TB.[14] However, there is a lack of detailed information regarding this phenomenon, and the current research has not provided a comprehensive understanding of the association between BC and TP.

Diagnosing TP in patients with cancer is complicated by the non-specific symptoms exhibited by clinical, laboratory, and radiological tests, as well as the absence of *M. TB* in sputum. TP must be considered when a patient presents with fresh pleural effusion. Overlooking this can lead to pulmonary or extrapulmonary TB.[15] To accurately diagnose pleural effusion in patients with cancer, physicians must employ various diagnostic techniques, including morphological and microbiological confirmation, and seek specialist consultation.

Malignant tumors, dull chest pain, large pleural effusion, blood-contaminated pleural effusion, and abnormal chest radiograph shadowing strongly indicate malignant pleural effusion, whereas a temperature of 37°C or higher and recent illness within 30 days decrease the probability. Irregular silhouettes on chest CT scans have demonstrated high sensitivity and specificity.[16,17] Pleural fluid tumor markers, such as carcino-embryonic antigen (threshold of 5ng/mL) with 98.6% accuracy and cancer antigen 19-9 (cut-off of 100ng/mL) with 100% specificity, are diagnostically valuable. However, their positivity rate of approximately 70% makes them unreliable for excluding malignant tumors. Pleural effusion cytology has a diagnostic accuracy of 75%, suggesting limited sensitivity.[18]

TP may resolve without intervention; however, it can later lead to the development of active TB.[19] A diagnosis of TP cannot be solely based on the resolution of pleural effusion with anti-TB medication. A mycobacterial culture of sputum is recommended for diagnosing suspected TP.[20,21] In our case, the patient had characteristic Langhans giant cells on histological examination, consistent with previous research involving a larger number of cases.[22]

Diagnosing the cause of TB can be difficult, particularly when attempting to differentiate between TP and BC. The clinical, laboratory, and radiological signs of tuberculous pleurisy are not sufficiently specific, and microbiological methods are rarely used to verify diagnosis. In some cases, the absence of TB in sputum may be due to isolated pleural lesions without lung tissue involvement. TB is also rarely found in pleural exudates due to dilution and can only be detected in very rare cases by culture or microscopy. Given the uncertainty of examination

data in hospitals, it is essential to develop personalized diagnostic strategies for pleural effusions in oncological patients. An accurate diagnosis and treatment plan requires a comprehensive range of diagnostic methods, including morphological and microbiological verification and consultation with a physician.

Although no diagnostic test methods uses chest computed tomography in detecting carcinomatous pleurisy, repeated pleural effusion cytology is crucial to exclude this condition, even after initiating anti-TB treatment. Furthermore, pleural biopsy is a valuable diagnostic tool for identifying malignant pleural effusion and TB.

In this case, radiography also identified fluid in the left pleural cavity with lung parenchymal involvement, supporting the use of sputum culture for diagnosing TP. Therefore, using both effusion and sputum cultures is a rational approach for diagnosing TP that can provide accurate diagnostic results.

CONCLUSION

Physicians must employ a combination of diagnostic techniques, including morphological and microbiological confirmation, to accurately diagnose pleural effusion in this patient population. The co-occurrence of cancer and TB is supported by previous studies, and patients with compromised immune systems due to cancer treatment may be more susceptible to TB. Prompt diagnosis and treatment of TP are crucial to prevent the development of active TB.

ETHICAL CONSIDERATIONS

The patient signed an informed consent for the presentation of detail of her disease in this journal.

FUNDING

This research did not receive any funding grants from public, commercial, or nonprofit agencies.

CONFLICT OF INTEREST

No conflicts of interest exist regarding the publication of the present study.

ACKNOWLEDGEMENTS

None.

REFERENCES

1. Bhatt M, Kant S, Bhaskar R. Pulmonary tuberculosis as differential diagnosis of lung cancer. *South Asian J Cancer*. 2012;1(1):36–42. doi: 10.4103/2278-330X.96507.
2. Thomas R, Jenkins S, Eastwood PR, Lee YC, Singh B. Physiology of breathlessness associated with pleural effusions. *Curr Opin Pulm Med*. 2015;21(4):338–45. doi: 10.1097/MCP.0000000000000174.
3. Zhai K, Lu Y, Shi HZ. Tuberculous pleural effusion. J Thorac Dis. 2016;8(7):E486–94. doi: 10.21037/jtd.2016.05.87.
4. Shaw JA, Diacon AH, Koegelenberg CFN. Tuberculous pleural effusion. Respirology. 2019;24(10):962–71. doi: 10.1111/resp.13673.
5. Shaw JA, Irusen EM, Diacon AH, Koegelenberg CF. Pleural tuberculosis: A concise clinical review. *Clin Respir J*. 2018;12(5):1779–86. doi: 10.1111/crj.12900.
6. Nayak S, Acharjya B. Mantoux test and its interpretation. *Indian Dermatol Online J*. 2012;3(1):2–6. doi: 10.4103/2229-5178.93479.
7. Starke JR. Tuberculosis skin testing: new schools of thought. *Pediatrics*. 1996;98(1):123–5.
8. Chaturvedi N, Cockcroft A. Tuberculosis screening in health service employees: who needs chest X-rays? *Occup Med (Lond)*. 1992;42(4):179–82. doi: 10.1093/occmed/42.4.179.
9. Trajman A, Pai M, Dheda K, van Zyl Smit R, Zwerling AA, Joshi R, et al. Novel tests for diagnosing tuberculous pleural effusion: what works and what does not? *Eur Respir J*. 2008;31(5):1098–106. doi: 10.1183/09031936.00147507.
10. Hwang SY, Kim JY, Lee HS, Lee S, Kim D, Kim S, et al. Pulmonary Tuberculosis and Risk of Lung Cancer: A Systematic Review and Meta-Analysis. *J Clin Med*. 2022;11(3):765. doi: 10.3390/jcm11030765.
11. Silva DR, Valentini DF Jr, Müller AM, de Almeida CP, Dalcin Pde T. Pulmonary tuberculosis and lung cancer: simultaneous and sequential occurrence. J Bras Pneumol. 2013;39(4):484–9. doi: 10.1590/S1806-37132013000400013.
12. Farrokh D, Marashi M, Fallah Rastegar Y, Boloursaz Mashhadi S. The Coexistence of Carcinoma and Tuberculosis in One Breast: A Case Report and Literature Review. *Int J Cancer Manag*. 2017;10(8):e6185. doi: 10.5812/ijcm.6185.
13. Levi G, Rocchetti C, Mei F, Stella GM, Lettieri S, Lococo F, et al. Diagnostic role of internal mammary lymph node involvement in tuberculous pleurisy: a multicenter study. *Pulmonology*. 2022:S2531-0437(22)00022-8. doi: 10.1016/j.pulmoe.2022.01.010.
14. Nanthanangkul S, Promthet S, Suwanrungruang K, Santong C, Vatanasapt P. Incidence of and Risk Factors for Tuberculosis among Cancer Patients in Endemic Area: A Regional Cohort Study. *Asian Pac J Cancer Prev*. 2020;21(9):2715–21. doi: 10.31557/APJCP.2020.21.9.2715.
15. Cohen LA, Light RW. Tuberculous Pleural Effusion. *Turk Thorac J*. 2015;16(1):1–9. doi: 10.5152/ttd.2014.001.

16. Marel M, Stastny B, Melínová L, Svandová E, Light RW. Diagnosis of pleural effusions. Experience with clinical studies, 1986 to 1990. *Chest*. 1995;107(6):1598–603. doi: 10.1378/chest.107.6.1598.
17. Ferrer J, Roldán J, Teixidor J, Pallisa E, Gich I, Morell F. Predictors of pleural malignancy in patients with pleural effusion undergoing thoracoscopy. *Chest*. 2005;127(3):1017–22. doi: 10.1378/chest.127.3.1017.
18. Lo Cascio CM, Kaul V, Dhooria S, Agrawal A, Chaddha U. Diagnosis of tuberculous pleural effusions: A review. *Respir Med*. 2021;188:106607. doi: 10.1016/j.rmed.2021.106607.
19. ROPER WH, WARING JJ. Primary serofibrinous pleural effusion in military personnel. *Am Rev Tuberc*. 1955;71(5):616–34. doi: 10.1164/artpd.1955.71.5.616.
20. Conde MB, Loivos AC, Rezende VM, Soares SL, Mello FC, Reingold AL, et al. Yield of sputum induction in the diagnosis of pleural tuberculosis. *Am J Respir Crit Care Med*. 2003;167(5):723–5. doi: 10.1164/rccm.2111019.
21. Porcel JM. Tuberculous pleural effusion. *Lung*. 2009;187(5):263–70. doi: 10.1007/s00408-009-9165-3.
22. Arrington CW, Hawkins JA, Richert JH, Hopeman AR. Management of undiagnosed pleural effusions in positive tuberculin reactors. *Am Rev Respir Dis*. 1966 Apr;93(4):587-93. doi: 10.1164/arrd.1966.93.4.587.

How to Cite This Article

Imankulova A, Uulu MS, Mamytova E, Monolov N, Tagaev T. Tuberculous Pleurisy in a Patient with a History of Breast Cancer: Diagnostic Challenges and Management Options. Arch Breast Cancer. 2024; 11(4):418-22.
Available from: https://www.archbreastcancer.com/index.php/abc/article/view/970