


Tuberculosis and Malignancy: A Menacing Coexistence

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Received on: 12 May 2023; Accepted on: 06 June 2023; Published on: 30 June 2023

ABSTRACT

Introduction: Tuberculosis (TB) and malignancy are major public health problems in India. We often encounter circumstances where both these entities may coexist and pose a host of challenges in management.

Case description: We report a case series of patients who were diagnosed with coexistent tuberculosis and malignancy and discuss the etiopathogenesis, its implications in concurrent chemotherapy, antitubercular therapy, and caveats for surgery in this subset of patients.

Discussion: Tuberculosis in patients with malignancy may be more prevalent secondary to immunosuppression due to the malignancy or chemotherapy, local structural changes to the lung, local damage due to radiotherapy and common risk factors such as smoking, alcohol and poor nutrition. It may be prudent to screen for latent infection prior to initiation of systemic chemotherapy or targeted therapy.

Conclusion: Disease burden of tuberculosis and malignancy, drug toxicity, compliance, surgery in TB patients, and infection prevention have to be considered to formulate a guideline for management of these patients.

Clinical significance: This case series discusses a practical approach to the common scenario where the two important public health problems of tuberculosis and malignancy coexist.

Keywords: Antitubercular therapy, Chemotherapy, Malignancy, Tuberculosis.

Indian Journal of Endocrine Surgery and Research (2023): 10.5005/jp-journals-10088-11209

INTRODUCTION

Tuberculosis (TB) is a rampant disease in India accounting for 26% of the burden worldwide.¹ With improvement in the overall socioeconomic status, better healthcare infrastructure, and governmental programs to detect and treat TB, the incidence has gradually plateaued. On the other hand, increasing urbanization and changes in diet and lifestyle have seen the rise of noncommunicable diseases, of which cancer is responsible for maximal morbidity and mortality. Clinicians often come across scenarios where both these entities coexist, and this poses challenges in management of either condition.

CASE DESCRIPTION

Patient 1

A 62-year-old female presented with a lump in the left breast for 5 months. There was no history of pain, nipple discharge, skin changes, or symptoms suggestive of metastases. On examination, there was a 2.5 × 2 cm lump in the upper outer quadrant of the left breast, not involving skin or muscle with a single mobile ipsilateral axillary lymph node.

Core-needle biopsy from the left breast lump was reported as invasive ductal carcinoma (hormone receptor positive, Her2neu negative, and Ki-67 proliferative index – 60%). During evaluation with positron emission tomography–computed tomography scan (PET–CT) at another medical center, she was diagnosed to have conglomerate para-aortic and iliac lymphadenopathy. Image-guided biopsy from the same was positive for *Mycobacterium tuberculosis* on cartridge-based nucleic acid amplification test (CBNAAT). She was hence started on antitubercular therapy (ATT). She experienced severe gastrointestinal side effects after initiation of ATT, which resulted in symptomatic hyponatremia with altered sensorium. She was started on intravenous 3% sodium chloride and fluid restriction, with which she improved symptomatically. After

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How to cite this article: Raam M, Singh KR, Ramakant P, *et al.* Tuberculosis and Malignancy: A Menacing Coexistence. *Indian J Endoc Surg Res* 2023;18(1):27–30.

Source of support: Nil

Conflict of interest: Dr Pooja Ramakant is associated as Editor-in-Chief of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of the Editor-in-Chief and his research group.

discussion in the multidisciplinary tumor board, she was started on neoadjuvant hormonal therapy with aromatase inhibitors. After completion of the intensive phase of ATT, she underwent left-modified radical mastectomy.

Patient 2

A 55-year-old female presented with gradually progressive swelling in front of the neck for 1.5 years with a rapid increase in size in the past 3 months. She had complaints of dysphagia, voice change, and breathing difficulty. On examination, there was a hard ill-defined, lobulated swelling in the anterior triangle of the neck with restricted mobility measuring 10 × 8 cm with bilateral cervical lymphadenopathy.

On evaluation, she was noted to have a mass arising from the left lobe of the thyroid measuring 8.5 × 7 × 10.9 cm with the cervical lymph nodal mass. She was also noted to have encasement of the left common carotid artery with infiltration of the left internal jugular vein with thrombosis extension into the superior mediastinum and left brachiocephalic vein thrombosis. The presence of multiple tiny

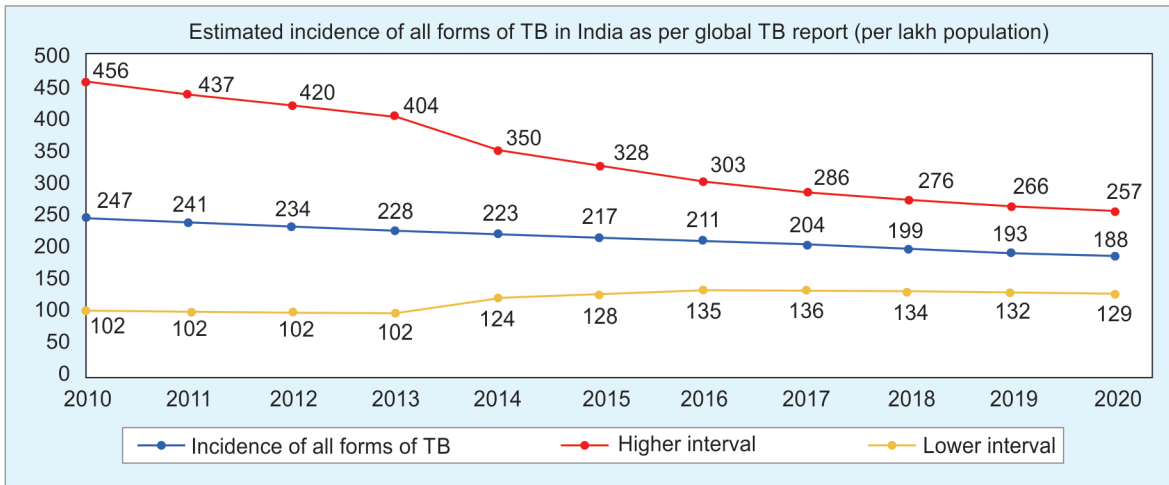


Fig. 1: Incidence of TB in India

soft-tissue nodules in the lung measuring 11.3 × 9.6 mm was also noted. Core-needle biopsy from the thyroid gland was reported as well-differentiated papillary carcinoma thyroid.

In view of the inoperable locally advanced nature of the disease, she was started on tyrosine kinase inhibitor (TKI) therapy. After completing 9 cycles of TKI therapy, reassessment CT showed patchy areas of consolidation in the left apical–posterior segment of the left lower lobe with emphysematous changes in bilateral upper lobes and enlarged mediastinal lymphadenopathy. She underwent bronchoscopy, which showed an infiltrative mass lesion in the right main bronchus. Cartridge-based nucleic acid amplification test of the bronchoalveolar lavage fluid was positive for *M. tuberculosis*. She was hence started on ATT and continued on TKIs that she tolerated well.

Patient 3

A 57-year-old female presented with gradually progressive swelling in front of the neck for 7 years with rapid increase in size since 5 months. She had complaints of dysphagia and voice change. She also had a history of productive cough, fever, and weight loss. On examination, there was a 10 × 8 cm swelling with variable consistency in the anterior triangle of the neck, involving the right lobe of thyroid. Fine-needle aspiration cytology from the lesion was reported as anaplastic carcinoma thyroid. Sputum analysis showed the presence of acid-fast bacilli suggestive of *M. tuberculosis*. She was hence started on ATT and TKIs. She developed hepatotoxicity within 2 weeks of therapy, following which both ATT and TKI were stopped. After the resolution of liver function, injectable ATT was initiated, followed by reinitiating of ATT with gradually increasing doses, and subsequently TKIs with dose reduction were restarted.

DISCUSSION

Tuberculosis is a major public health problem across the world. Global TB report, 2021, states that in 2020, a total of 1.3 million HIV-negative and a further 214,000 HIV-positive people died from TB and an estimated 10 million people fell ill worldwide. Eight countries accounted for two-thirds of the total, with India leading the count (26%), followed by China, Indonesia, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. India accounted for 2,950,000 new cases in 2020 with TB occurring in 210 per 100,000 people.¹ The incidence of all forms of TB in India for the year 2020 was 188 per 100,000 (129–257 per 100,000 population), whereas

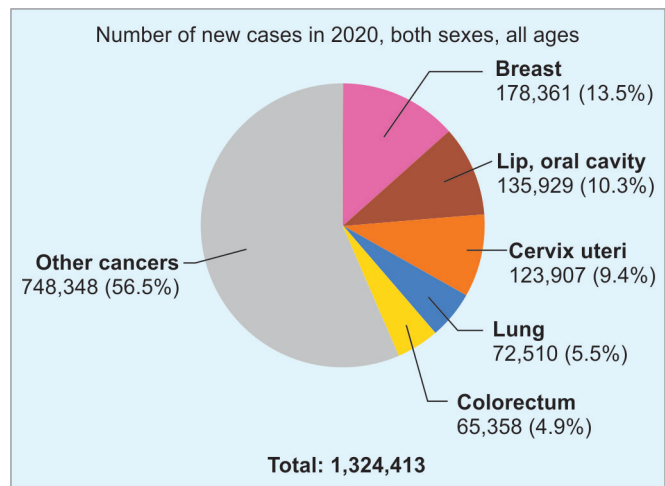


Fig. 2: Incidence of cancer – (site-wise) in India

the total number of incident TB patients (new and relapse) notified during 2021 was 19,33,381, which was 19% higher than that of 2020² (Fig. 1).

Noncommunicable diseases, on the other hand, also significantly affect global health, killing nearly 41 million every year, with cancer responsible for 9.3 million deaths yearly.³ Cancer is diagnosed in 1,324,413 new patients in India yearly, with breast cancer leading the pack (13.5%). It is responsible for 851,678 deaths⁴ (Fig. 2).

Global burden of latent TB infection is estimated to be 33% (2 billion people).^{5,6} In the majority of patients in high-TB-burden countries, TB is mostly clinically asymptomatic and latent, with disease reactivation occurring in about 5–10% during their lifetime. Increased risk of reactivation exists in the following populations: HIV co-infection, CKD on hemodialysis, diabetics, and immunosuppressive therapy, such as TNF-alpha inhibitors and malignancy.

The burden of TB in patients with malignancy is a relevant issue. Immunosuppression from the malignancy itself or secondary to cytotoxic chemotherapy, local structural changes due to primary lesion or lung metastases, or local damage due to radiotherapy predispose the patient to TB. In addition, common risk factors such as smoking, alcohol, poor nutrition, cancer cachexia, and

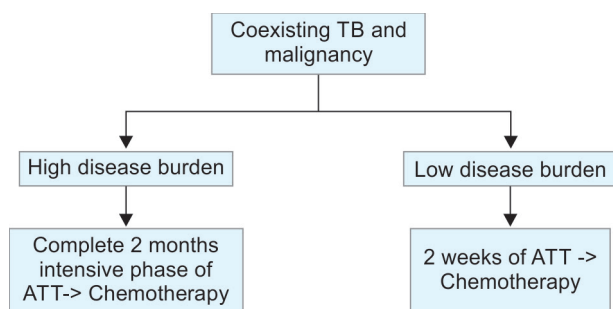


Fig. 3: Practical approach to ATT and concurrent cytotoxic chemotherapy

increased lifespan due to advanced treatment are other reasons for coexistence of TB in malignancy patients.

In a retrospective study done by Shu et al. from Taiwan, 1,105,009 patients with malignancy were studied. About 19,906 patients were newly diagnosed with TB infection after diagnosis with malignancy. Despite the decreasing overall TB numbers, the authors found no such change in the malignancy subgroup and noted an increase in the proportion of patients with TB and malignancy from 3 to 13% over 15 years. Head and neck cancers were found to be the most common (382 per 100,000).⁷

Bhaskar et al., in a retrospective analysis of 134 patients with TB and cancer, showed that pulmonary TB was more common (62%), with the majority of extrapulmonary TB being TB lymphadenitis (78%). Tuberculosis was concurrently diagnosed with a malignancy in 34%, with hematological malignancies being the most common. About 19 patients developed TB while undergoing chemotherapy. The authors thus advocated for active screening for TB at diagnosis of cancer, especially in high-prevalence countries.

Chen et al., in a systematic review and meta-analysis of 23 studies with 593 tuberculosis cases occurring in 324,041 cancer patients over 7 decades, reported the highest risk for patients with hematologic and head and neck malignancy. Breast cancer and other solid tumors had a risk of developing TB in 41/100,000. Even though the risk was not as high as hemotologic or head and neck cancer, the number of patients with breast cancer at risk were very large. Hence, in high-prevalence countries such as India, it may be a worthwhile strategy to screen for latent TB infection prior to initiation of chemotherapy.

ATT and Chemotherapy

None of the international (CDC, WHO) or national (NTEP/RNTCP) guidelines have set down well-defined guidelines for ATT in cancer patients or concomitant chemotherapy with ATT. A practical solution to this problem would be to stratify patients into low or high disease burden, based on clinicoradiological features. In patients with low disease burden, it would be prudent to initiate 2 weeks of intensive-phase ATT followed by chemotherapy, whereas, in patients with high disease burden, chemotherapy may be initiated after completion of intensive phase of chemotherapy (Fig. 3).

Another important point to ponder is the toxicity of ATT that may be compounded by toxicity of chemotherapy/targeted therapy. This may influence the compliance to ATT, chemotherapy/targeted therapy, or both and hence influences the overall quality of life for the patient. In our case series, the patient with breast carcinoma (patient 1) experienced severe hyponatremia after initiation of ATT, which required 3% sodium chloride correction

Table 1: Tuberculosis and anesthetic drugs

Drug class	Effect of TB treatment	Recommendation
Induction agents	Unchanged	Beware of risk of awareness with TIVA
Volatile agents	Increased risk of halothane hepatitis	Use newer agents
Local anesthetics	Unchanged	Avoid GA and opioids
Muscle relaxants	Increased metabolism of rocuronium and vecuronium	Titrate and monitor response using nerve stimulator
Opiates	Increased metabolism	Titrate and use regional techniques and patient-controlled analgesia

and fluid restriction. The patient with anaplastic carcinoma thyroid, on the other hand (patient 3), developed hepatotoxicity, which required discontinuation of both ATT and targeted therapy followed by gradual reinitiation and dose reduction.

While initiating ATT, we must consider poor performance score, extensively drug-resistant MTB (XDR), and severe organ dysfunction. Drug interactions with rifampicin and hence reduced efficacy of chemotherapy should also be taken into consideration.

Surgery in TB

Factors that need to be kept in mind while taking up a patient with TB for surgery include the general state of the patient's health and the impact of the disease on organ function, the treatment that the patient is receiving, and the considerable potential for drug interactions and last but not the least, the risk of transmission of tuberculosis to staff and other patients.⁸

The effect of TB treatment on various anesthetic agents is given above (Table 1):

Infection Prevention

Strategies to mitigate the risk of infection during surgery in TB patients include delaying elective surgery till at least 2–3 weeks of initiation of ATT with evidence of clinical improvement. These patients will have to be taken as the last case for the day. All healthcare workers and the patient must be provided with N95 respirators. Adequate plane of anesthesia must be ensured with muscle relaxation to avoid cough stimulus. Bacterial filters must be used on the airway and the expiratory limb of the certificate. Postoperatively, the patient must be allowed to recover in isolation. It is also prudent to consider preventive therapy for latent TB infection in healthcare workers.

CONCLUSION

The high burden of TB and the ever-increasing numbers of cancer patients in our scenario create a unique situation where coexistence of both these entities brings about a number of issues that need to be addressed. It is important to formulate a guideline for management of these patients with appropriate weightage for treatment of TB as well as management of malignancy. Issues in relation to drug toxicity, compliance, surgery in TB patients, and infection prevention have to be taken into consideration.

Clinical Significance

This case series discusses a practical approach to the common scenario where the two important public health problems of tuberculosis and malignancy coexist.

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