

# Malignancy and tuberculosis coexistence: a case series study

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## ABSTRACT

**Background.** Tuberculosis (TB) remains the most common infectious disease that kills people worldwide. The occurrence of cancer and Tuberculosis is rare, yet they are the major causes of illness and mortality worldwide.

**Case presentation.** We present four cases of female patients with primary malignancy and Tuberculosis (TB). The first case was diagnosed histopathologically as TB and nodular sclerosis subtype Hodgkin lymphoma. The other two cases were invasive breast carcinoma with TB, and the final case was nasopharyngeal carcinoma with TB. All four patients received six months of antituberculosis medication, followed by anticancer treatment.

**Conclusion.** The probability of coexisting TB and cancer necessitates a thorough histological evaluation to minimize diagnostic failure and hence treatment errors.

**Keywords:** tuberculosis, malignancy, Hodgkin lymphoma, breast carcinoma, nasopharyngeal carcinoma

## Abbreviations:

BM – Bone marrow

FNAC – Fine needle aspiration cytology

H&E – Hematoxylin and eosin

HL – Hodgkin lymphoma

IHC – Immunohistochemistry

LAP – Lymphadenopathy

LN – Lymph node

MTB – Mycobacterium tuberculosis

NP – Nasopharyngeal

NPTB – Nasopharyngeal tuberculosis

TB – Tuberculosis

WHO – World Health Organization

## INTRODUCTION

Cancer and tuberculosis (TB) are the two leading causes of morbidity and mortality worldwide, which also pose a significant threat to public health [1]. Since the incidence of both cancer and tuberculosis (TB) is on the rise, they can coexist together [1]. The simultaneous occurrence of two illnesses in one organ is nearly causing diagnostic and treatment difficulties [2]. Tuberculosis (TB) is an important public health problem [2]. Among all infectious diseases, tuberculosis has one of the highest mortality rates, according to recent World Health Organization (WHO) research [3]. In most cases,

Mycobacterium tuberculosis (MTB) is difficult to detect and identify [4]. Furthermore; because the radiographic features and clinical signs of TB and cancer are so similar, TB can easily be mistaken for cancer [4]. A series of metaplasia and dysplasia that lead to neoplasia can be started by a chronic inflammatory illness like TB [5]. Disrupted defensive mechanisms in cancer patients also have the potential to activate the dormant bacilli [1]. Tuberculosis can be discovered in cancer patients during diagnostic procedures or treatment [6]. Numerous epidemiologic studies have verified that the risk of malignancy is highest during the first two years following a TB diagnosis, but it remains high for extended pe-

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riods of time [6,7]. The majority of TB cases were identified in patients with hematologic malignancies, followed by individuals with lung, larynx, skin, and unknown primary tumors [6,8].

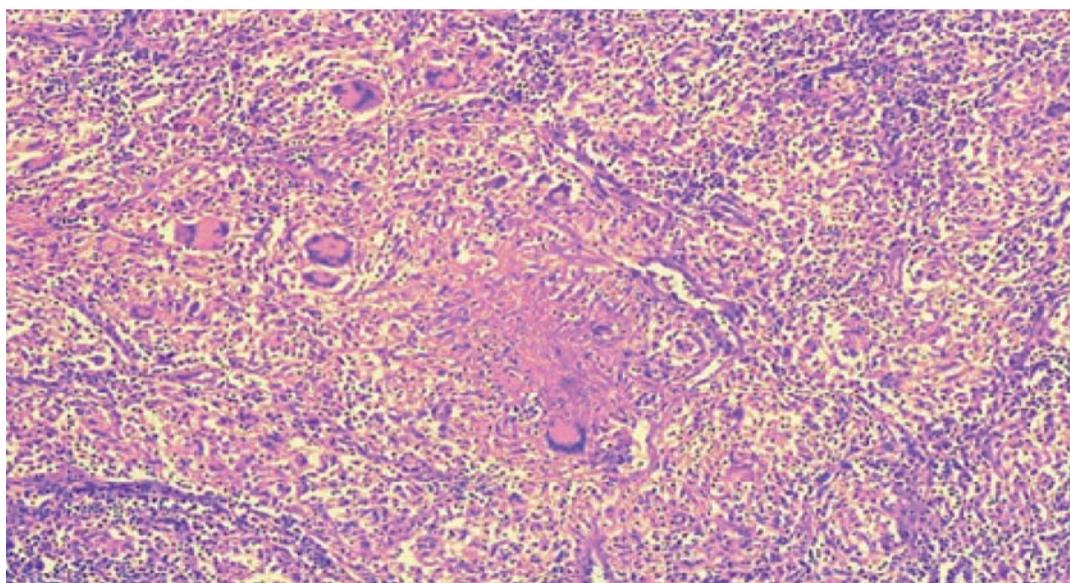
In this study, we report four cases of patients diagnosed as tuberculosis with malignancy. The study was approved and registered by the ethical committee of the college of medicine, university of Basrah. Informed consents were taken from the patients.

## CASE REPORT

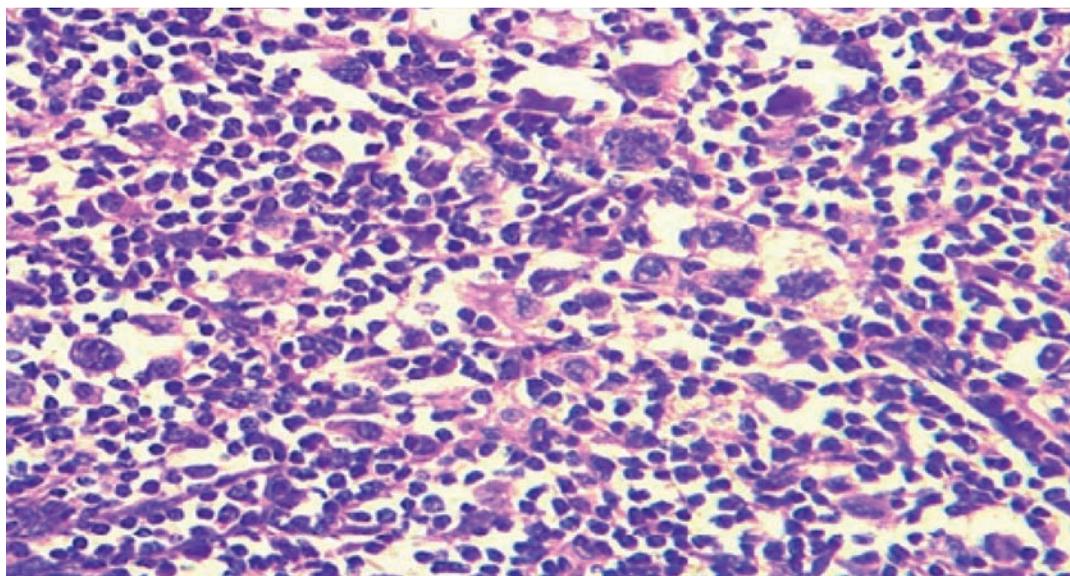
### Case 1

A 9-year-old female child with no medical history consulted for fever, decreased appetite, weight loss,

nocturnal sweats, and cervical lymphadenopathy (LAP). The lymph node was excised and sent for histopathology. Microscopical examination of the tissue section revealed epithelioid granuloma, giant cells with caseous necrosis typically associated with tuberculosis. Then the patient received a full course of antituberculosis treatment for 6 months but showed no improvement. Following that, a second biopsy was done and subjected to histopathological examination, which revealed that the diagnosis was Hodgkin lymphoma, a nodular sclerosis subtype concomitant with tuberculosis that was confirmed by the immunohistochemistry (IHC). The patient showed a significant response to chemoradiotherapy and anti-TB treatment. (Figure 1-2)



**FIGURE 1.** Tuberculosis with nodular sclerosis classical Hodgkin lymphoma in the cervical lymph node showing caseating epithelioid granuloma (in the center) with Langhans giant cells (H&E, 100X)



**FIGURE 2.** Classical Hodgkin lymphomatous tissue showing numerous lacunar cells, Hodgkin cells and Reed-Sternberg cells within reactive inflammatory background (H&E, 400X)

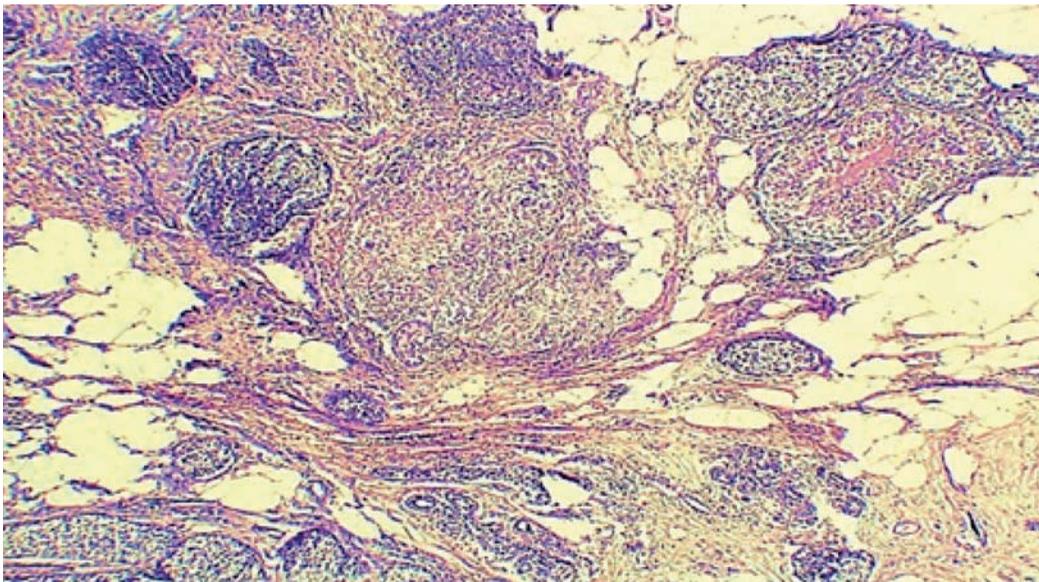
## Case 2

A 45-year-old female presented to the breast clinic with a rapidly expanding mass in her right breast. When examined, the mass was large and firm, with no skin changes or nipple discharge. There was no recent exposure to a TB patient or family history of breast carcinoma. Radiological investigations were suspicious for malignancy. The patient had routine fine needle aspiration cytology (FNAC) that revealed a cluster of malignant epithelial cells on a reactive background. A modified radical mastectomy of the right breast was carried out, as well as axillary dissection. The histopathological examination revealed the presence of invasive lobular carcinoma, which had spread to the axillary lymph nodes. The breast tissue also showed necrotizing granulomatous inflammation and Langhans multinucleated type giant cells, but there was no nodal involvement.

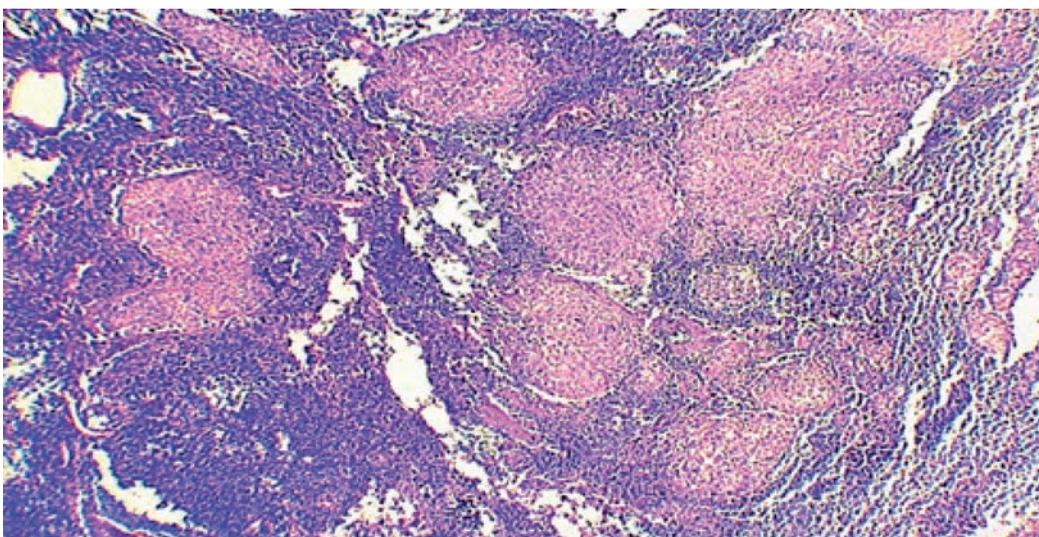
This leads to the diagnosis of invasive lobular carcinoma of the breast with lymph node metastasis and primary breast tuberculosis. (Figure 3)

## Case 3

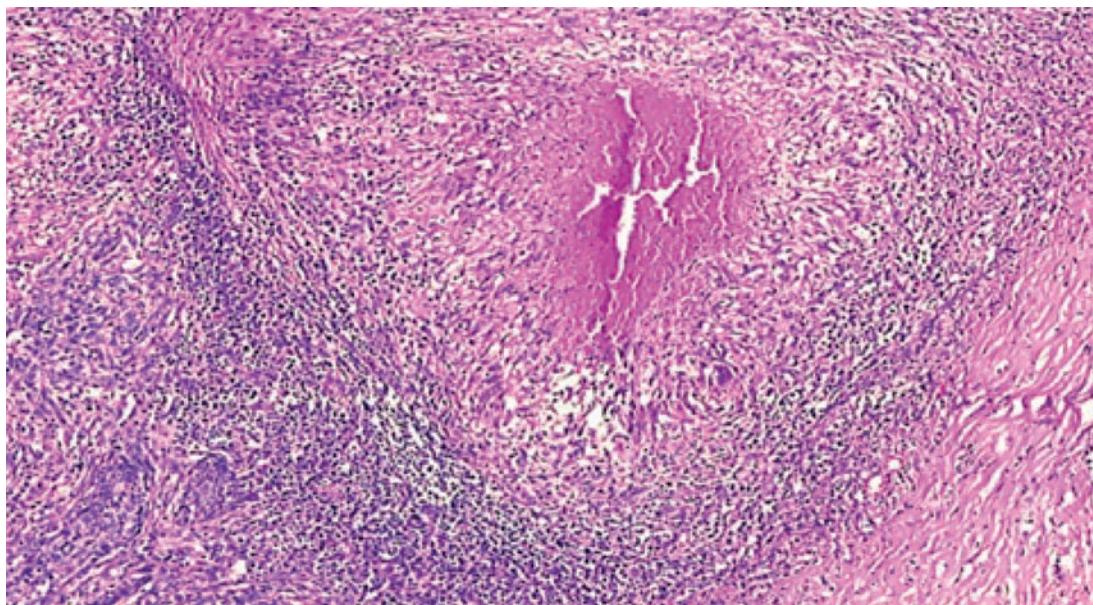
A 51-year-old woman accidentally discovered lump in her left breast over a few days. The mass was firm and well defined in the upper outer quadrant of the left breast. Ultrasonography was suspicious for malignancy. FNAC was performed and the malignant ductal epithelial cells were described in the cytology. Then the patient underwent a modified radical mastectomy of the left breast, along with axillary lymph node clearance and was sent for histopathology. Histopathological examination revealed invasive ductal carcinoma of the breast. The axillary lymph nodes exhibited TB but no malignancy. (Figure 4).



**FIGURE 3.** Tuberculosis with invasive breast lobular carcinoma (H&E, 40x)



**FIGURE 4.** Tuberculosis in the axillary lymph node without metastatic involvement in patient with invasive breast ductal carcinoma. Caseating epithelioid granulomas are present (H&E, 400X)



**FIGURE 5.** Caseating epithelioid granulomas with metastatic undifferentiated nasopharyngeal carcinoma in the cervical lymph node (H&E, 100X)

#### Case 4

Fifty-five-year-old woman underwent a full course of treatment for nasopharyngeal carcinoma. Two years later, she presented with a left cervical lymphadenopathy. The lymph node was removed and histologically showed metastatic tumor cells and tubercle granuloma with caseous necrosis; therefore, she was diagnosed with metastatic undifferentiated nasopharyngeal carcinoma and TB. (Figure 5)

## DISCUSSION

Tuberculosis continues to be the leading infectious illness that causes death globally. People who have malignancies are more likely to have active TB than those without cancer [9]. There are various ways in which tuberculosis and cancer might coexist simultaneously. Possible associations include: coincidence with no apparent correlation; cancer developing in an old TB focus; concurrent development of tuberculosis and cancer; or secondary infection of cancer as a result of immunosuppression, chemotherapy, or postponed treatment [8,10]. The occurrence of tuberculosis and Hodgkin lymphoma is a rare entity. Both TB and HL share similar criteria, laboratory tests and imaging features, which can lead to a misdiagnosis or delay in the detection of both diseases [11]. Suppression of immunity caused by Hodgkin lymphoma may increase the risk of concurrent tuberculosis infection [12], however, the inflammatory environment can encourage cancer cell mutagenesis, penetration and metastasis because it is full of chemicals that damage DNA and factors that facilitate cell proliferation and mutation [13]. A small

number of co-occurring cases of HL and TB were reported in the literatures. (Table 1)

Granulomatous inflammation of the breast is a multifactorial inflammatory condition. Breast cancer, TB, granulomatous mastitis, sarcoidosis and traumatic fat necrosis are some of the possible causes [18]. Primary TB of the breast is believed to originate from skin abrasions or openings in the lacrimal ducts in the nipple [19]. Usually, an underlying tuberculous focus elsewhere in the body causes secondary TB of the breast. An axillary, internal mammary, or paratracheal lymph node, or a pulmonary origin, could be the source of this pre-existing focus [18,19]. Rarely, tuberculosis and breast cancer may coexist, but there are typically no pathognomonic signs or symptoms that can differentiate the two conditions [20]. The literature documents a few cases of coexisting TB and breast cancer. (Table 2).

Along with these findings, concomitant breast cancer and tuberculosis are typically identified in ipsilateral axillary lymphadenopathy, with the majority of cases being invasive ductal carcinoma.

The occurrence of nasopharyngeal carcinoma with TB is relatively rare and the nasopharynx is the least prevalent location for TB [25]. (Table 3)

Cervical lymphadenopathy is the most usual presenting symptom of primary NPTB (Nasopharyngeal tuberculosis) [25].

Our data clearly imply that TB and various forms of cancer might resemble each other and have unusual clinical and radiological manifestations. To lower the risk of a diagnostic error and a treatment failure, one should always look for rapid diagnostic procedures, thorough histological confirmation, and microbiologic investigation.

**TABLE 1.** A literature review of Hodgkin lymphoma cases that coexisted with tuberculosis

Year	Age (years)	Sex	Diagnosis	Lymph node involvement
2004 [14]	41	Male	HL, mixed cellularity subtype with TB	Right cervical anterior LN
2004 [14]	40	Female	HL of nodular sclerosis subtype with TB	Right axillary LN
2004 [14]	49	Male	HL of nodular sclerosis subtype with TB	Bilateral cervical, supraclavicular, left axillary, right inguinal chains and intra-abdominal LN
2014[12]	29	Female	HL of nodular sclerosis subtype with TB	Cervical and mediastinal LN
2016 [15]	18	Male	HL, lymphocyte-rich subtype with TB	Cervical, inguinal, axillary, para-aortic and paratracheal LNs
2020 [13]	15	Female	HL, lymphocyte-rich subtype with TB	Right cervical LN
2020 [16]	15	Female	HL, lymphocyte-rich subtype with TB	Supraclavicular (more in the right), mediastinal, and retroperitoneum regions LNs
2021 [17]	48	Female	HL, mixed cellularity subtype with TB	Periportal, para-aortic, mesenteric, and inguinal LN with BM involvement
2022 [11]	63	Male	HL of nodular sclerosis subtype with TB	Bilateral cervical, paratracheal and hilar LN
Our case	9	Female	HL of nodular sclerosis subtype with TB	Bilateral cervical LN

HL: Hodgkin lymphoma, TB: tuberculosis, LN: lymph node, BM: Bone Marrow

**TABLE 2.** A literature review of cases of breast cancer that coexisted with tuberculosis

Year	Age (year)	Sex	Diagnosis	Site of TB
2006 [21]	36	Female	Invasive ductal carcinoma of the left breast with nipple involvement and the axillary nodes showed TB with no evidence of malignancy	Left axillary LN
2006 [21]	49	Female	Invasive ductal carcinoma, one of the five axillary nodes showed metastatic deposits and the level three nodes showed TB.	Axillary LN
2006 [21]	60	Female	Right breast carcinoma with TB in seven axillary LN with no evidence of malignancy	Right axillary LN
2006 [21]	60	Female	Left breast carcinoma with TB in five axillary LN with no evidence of malignancy	Left axillary LN
2006 [21]	81	Female	High-grade invasive ductal carcinoma with tuberculous. Four axillary nodes showed tuberculous (no malignancy)	Left breast and axillary LN
2008 [18]	47	Female	Invasive ductal carcinoma along with TB	Right breast and right axillary LN
2015 [22]	45	Female	Coexistent breast carcinoma and TB (granuloma present in both breast +axillary LN)	Left breast with axillary LN
2017 [20]	40	Female	High grade ductal carcinoma in situ with invasive component and TB	Left breast
2022 [23]	60	Female	Invasive lobular carcinoma of the right breast with TB in left axillary LN.	Left axillary LN
2023 [24]	39	Female	Invasive ductal carcinoma with metastasis to 7 axillary LN (TB was found in 5 of these LN)	Right axillary LN
Our case	45	Female	Invasive lobular carcinoma with TB	Right breast
Our case	51	Female	Invasive ductal carcinoma of the breast with TB in the axillary LN	Axillary LN

TB: tuberculosis, LN: lymph node

**TABLE 3.** A literature review of cases of nasopharyngeal cancer that coexisted with tuberculosis

Year	Age (year)	Sex	Diagnosis	Site of TB
1998 [25]	44	Female	TB of the nasopharynx following radiotherapy for undifferentiated NP carcinoma	posterior nasal space
2014 [26]	28	Male	Non-keratinizing squamous cell carcinoma of the NP with TB	Tonsil
2019 [27]	34	Male	Metastasis undifferentiated NP carcinoma with TB	Left cervical LN
Our case	55	Female	Metastatic undifferentiated nasopharyngeal carcinoma and TB	Left cervical LN

NP: nasopharyngeal

## CONCLUSION

Accurate diagnosis of coexisting tuberculosis with malignancy is crucial to prevent incorrect cancer staging and avoid aggressive treatment for these patients. As a result, before beginning definite treatment, a thorough histological examination is required to

minimize diagnostic failure and hence treatment errors.

*Patient consent:* Informed consents were taken from the patients.

*Conflict of interest:* none declared

*Financial support:* none declared

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