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Case Report

Secondary syphilis with pulmonary involvement mimicking lymphoma: a case report

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Abstract

We present a case of atypical presentation of secondary syphilis with extensive lymph node involvement and pulmonary lesions, initially suspected as lymphoma. The patient presented with weight loss, dry cough, chest pain, palpable lymph nodes in several peripheral chains, and multiple pulmonary nodules and masses on chest imaging. The key features for secondary syphilis diagnosis were a lymph node biopsy suggestive of reactive lymphadenopathy, positive serologic tests for syphilis, and complete recovery after antisyphilitic treatment.

Keywords: Syphilis. Pulmonary lesions. Lymphoma.

INTRODUCTION

Syphilis is an infection caused by the spirochete *Treponema pallidum*. It is endemic in developing and underdeveloped countries. Most new cases are sexually acquired. Syphilis carriers may present with a wide range of symptoms depending on the disease stage, while some may only present with serological evidence of *Treponema*[1]. Secondary syphilis may present as a cutaneous lesion or, less commonly, mucosal lesions, diffuse lymphadenopathy, hepatosplenomegaly, liver disease, or nephrotic syndrome. Pulmonary involvement is rare in patients with secondary syphilis[2]. Diagnosing syphilis may prove challenging because of the diverse clinical presentations and cases mimicking other pathologies because of which it has been labelled "the great mimicker"[3]. Herein, we present a case of syphilis with diffuse and pulmonary nodal involvement, which was initially evaluated as probable lymphoma.

CASE REPORT

A 26-year-old man, with no comorbidities, sought medical care for fever, dry cough, and pleuritic chest pain for several weeks. He also reported unintentional weight loss of about 10 kg (approximately 15% of his total weight) over the past year, hyporexia, and sporadic night fever and sweats. Physical examination revealed palpable lymph nodes of elastic, painless, mobile consistency in the supraclavicular, epitrochlear, and bilateral inguinal regions, and a larger node in the left axilla, measuring around 3 cm. He reported no odynophagia or flu-like symptoms. There were no abnormalities in the complete blood count, liver enzymes, electrolytes, renal function, canalicular enzymes, or lactic dehydrogenase.

Computed tomography (CT) performed to evaluate the lymphadenopathy demonstrated a left pulmonary hilar mass, involving the pulmonary artery-vein segments, without reducing the calibers, and the bronchopulmonary segments. These findings were suggestive of a lymphoproliferative process. A similar mass was observed adjacent to the large right fissure in the lateral segment of the middle lobe (**Figures 1A, 1B, 1C**). Multiple pulmonary nodules and solid micronodules were present with a predominantly peripheral perivascular distribution, affecting all lobes, and associated with multifocal inter- and intralobular septal thickening. The findings suggested lymphatic and hematogenic dissemination of the primary process. Multiple left axillary, bilateral supraclavicular, prevascular, paratracheal, subcarinal, and hilar lymph nodes were swollen.

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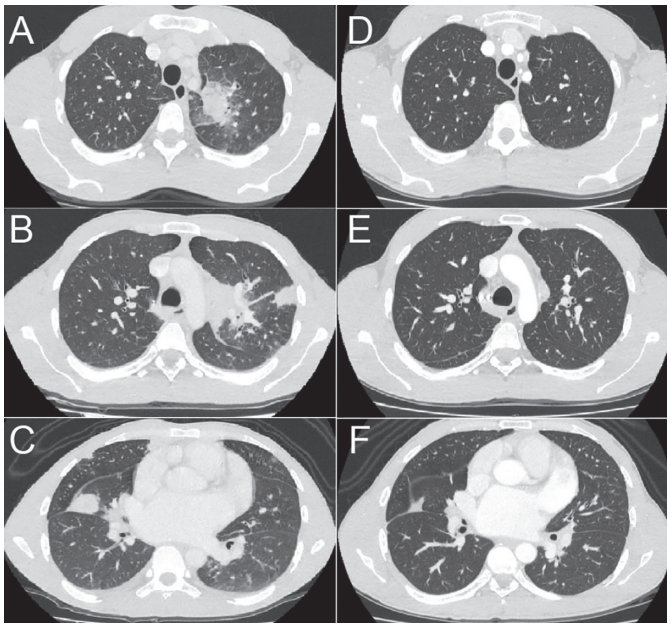

FIGURE 1: A, B, C: Pre-treatment chest computed tomography (CT) images showing pulmonary masses in the left hilum and adjacent to the right fissure and multiple pulmonary nodules secondary to pulmonary involvement in secondary syphilis. **D, E, F:** Chest CT images after treatment for syphilis with near total regression of previous lesions.

Suspecting a probable lymphoma, an excisional biopsy of the left axillary lymph node was performed. Histopathological and immunohistochemical studies were consistent with reactive lymphadenopathy, with centrofollicular hyperplasia and foci of progressively transformed germinal centers, and without evidence of neoplasia (**Figure 2**).

After excluding lymphoid malignancy, detailed tests were performed for the possibility of infectious disease-causing lymphadenopathy. Serologic tests were negative for human immunodeficiency virus (HIV), viral hepatitis, cytomegalovirus, and toxoplasmosis. The venereal disease research laboratory (VDRL) test was positive with a 1:64 titer. Syphilis was confirmed by a positive treponemal test. The patient presented with no chancre on the penis or typical skin changes and reported no previous lesions or treatment for syphilis. A treatment regimen was initiated for late latent syphilis with three weekly doses of intramuscular benzathine penicillin.

At the 2-month outpatient follow-up after discharge, total regression of palpable lymphadenopathy was observed at all foci of prior nodal involvement. The patient reported improvement in cough, night sweats, and weight loss and showed a negative VDRL test, with a 1:1 titer. Chest CT with controlled contrast demonstrated significant regression of lesions, with no hilar mass or mediastinal lymph node enlargement (**Figures 1D, 1E, 1F**). A regular-contour nodule was located in the lateral segment of the middle lobe, measuring 0.9 cm, where a 3-cm mass had been observed in the initial image.

DISCUSSION

According to the World Health Organization, approximately 17.7 million individuals aged 15-49 years worldwide presented

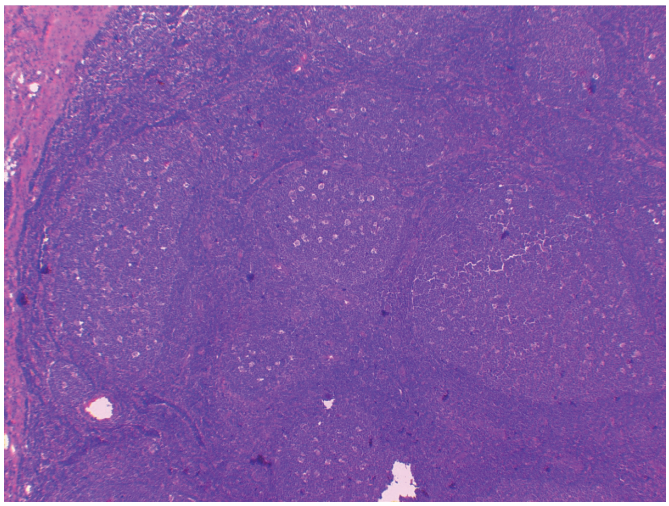

FIGURE 2: Histopathological findings of excisional lymph node biopsy, with expanded and "activated" lymphoid follicles and prominent germinative centers, consistent with reactive lymphadenopathy (hematoxylin and eosin; original magnification ×100).

with syphilis in 2012, followed by 5.6 million new cases every year. The prevalence and incidence of syphilis vary substantially with region and country. The highest prevalence is in Africa, and over 60% of new cases occur in low- and middle-income countries[1]. The prevalence of syphilis in HIV-infected patients has shown an increasing trend. HIV coinfection may alter the presentation of secondary syphilis by suppressing the immune system and commonly present atypically[1,4]. Despite atypical presentation, our patient did not show coinfection.

Although pulmonary involvement in cases of tertiary and congenital syphilis have been described, they have been rare in secondary syphilis[2,5]. Pulmonary lesions in secondary syphilis were first described in 1968 and may present as interstitial infiltrates, lung consolidation with or without pleural effusion and a solitary pulmonary nodule or multiple pulmonary nodules (most common finding) with or without cavitation[2,5]. Patients may be asymptomatic or present with respiratory symptoms, such as dry or productive cough and chest pain (most frequent symptom)[2]. As it is clinically non-specific, detection of pulmonary involvement with syphilis may be missed if chest imaging is not performed. Our patient presented with dry cough and chest pain and demonstrated multiple pulmonary nodules and masses on CT.

The differential diagnosis for pulmonary involvement in patients with syphilis is extensive and includes primary and metastatic lung cancer, lymphoma, fungal infection, tuberculosis, septic embolism, pulmonary infarction, sarcoidosis, rheumatoid nodules, and vasculitis[2,6]. While microbiological diagnosis of syphilis in these cases is difficult, transbronchial biopsy, open lung biopsy, bronchial lavage, immunohistochemistry, and polymerase chain reaction may reveal the presence of *Treponema pallidum*[7].

Proposed by Coleman et al. in 1983, clinical criteria for diagnosing pulmonary involvement in secondary syphilis are:

TABLE 1: Summary of clinical reports of syphilis mimicking a lymphoma.

Author	Age/Sex	Typical symptoms	Lymph nodes involved	Lung involvement	Systemic Symptoms
Park (2013)	45/Male	No	Gastrohepatic ligament, perigastric, aortocaval, splenic hilar, mesenteric, and bilateral inguinal, cervical, and supraclavicular	No	Weakness, hair loss, anorexia, weight loss, and night sweats
Cerchione (2017)	56/Male	No	Latero-cervical, supraclavicular, submandibular, and bilateral axillary	No	Fever, night sweats, and weight loss
Komeno (2018)	27/Male	No	Bilateral cervical and periportal	Yes	Fever, night sweats, and loss of appetite
Ohta (2018)	39/Male	Rashes on hands and feet	Bilateral cervical, left mediastinal, and bilateral axillary	Yes	None
Present study	26/Male	No	Supraclavicular, epitrochlear, bilateral inguinal, left axillary, bilateral supraclavicular, paratracheal, subcarinal, and pulmonary hilar	Yes	Fever, dry cough, respiratory chest pain, weight loss, hyporexia, and night sweats

(1) presence of history and clinical findings consistent with secondary syphilis; (2) pulmonary abnormalities on X-ray with or without pulmonary symptoms or signs; (3) positive serological tests for syphilis; (4) exclusion of other pulmonary diseases, when possible, using bacilloscopy, serological tests, cultures, and cytological examination of sputum; and (5) therapeutic response to treatment[8]. Clinical and radiological responses to penicillin confirm pulmonary syphilis and may help exclude differential diagnoses[7,9]. Reportedly, lung lesions respond well to treatment, and imaging findings are resolved in weeks or around six months[2]. In the present case, although the patient had no history or typical findings of secondary syphilis, the positive response to therapy within two months and partial resolution of a reactive lymph node led to the diagnosis.

Lymphadenopathy is a frequent clinical finding, with a wide differential diagnosis, including infectious diseases, malignant lymphoproliferative disorders, metastases, and autoimmune diseases[10,11]. Lymph node involvement is classic in secondary syphilis, including the cervical, inguinal, and epitrochlear lymph nodes, although even they may show atypical features[10-12]. Our patient presented with lymphadenopathy with some suggestive signs of malignancy, such as presence of systemic symptoms, lymph nodes larger than 2 cm, and supraclavicular and mediastinal lymph node involvement. Lymphoma was suspected because of lymph node involvement and lung lesions, and an excisional axillary lymph node biopsy was performed. Cases of secondary syphilis presenting with extensive lymph node disease mimicking a lymphoma have been reported[2,5,10,12] (**Table 1**). The five reported patients were men, and only one exhibited typical symptoms of syphilis, such as rashes on the hands and feet[2]. Almost all cases presented with systemic symptoms, and two cases presented with pulmonary involvement[2,5].

Histopathological analysis of lymph nodes affected by syphilis demonstrates a non-specific response pattern of reactive lymphadenopathy, as in our case, or non-caseous granulomatous lymphadenitis, hypertrophy, or capsular fibrosis[11,12]. In our cases, the histopathological and serological findings and resolution of lesions after treatment for syphilis were considered as diagnostic evidence of secondary syphilis.

Physicians should consider the possibility of syphilis in various clinical situations. This report reinforces the importance of high suspicion and a low threshold for diagnosing syphilis in patients with lymphadenopathy and unexplained pulmonary lesions, even in the absence of typical cutaneous and genital lesions. Despite reports of syphilis mimicking neoplastic diseases, especially lymphoma, this diagnosis is often neglected. Herein, we reported an unusual case of generalized lymphadenopathy and pulmonary lesions as an atypical presentation of secondary syphilis, which is rarely described in literature.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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