Secondary Syphilis With Pulmonary Involvement
A Case Without HIV Infection and Literature Review

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Abstract: Syphilis is a multisystem infection caused by the spirochete *Treponema pallidum*. A 63-year-old man admitted to the hospital with chest pain and rashes on the chest wall and hands for 14 days. Thorax computed tomography revealed multiple nodular shadows in the bilateral lower lobes of the lung. Skin lesions were considered compatible with secondary syphilis.

The antibody test for syphilis was positive. Screening for other associated sexually transmitted diseases (serology for HIV, hepatitis C, and hepatitis B) was negative. A specific therapy with crystallized penicillin G 2.4 MIU was applied. The key features for secondary syphilis diagnosis were positive serologic tests for syphilis and complete recovery on thorax computed tomography after antisyphilitic treatment. Pulmonary involvement in secondary syphilis is considered a rare occurrence.

Key Words: pulmonary nodule, secondary syphilis

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Syphilis is a complex infectious disease caused by the gram-negative bacterium *Treponema pallidum* of spirochete families. This spirochete can be transmitted sexually and congenitally, and it can spread to organs such as neurological system, liver, kidney, ocular system, lungs.[1] It is estimated that annually there are 357 million new cases of curable sexually transmitted infections among people aged 15 to 49 years. Syphilis accounts for 6 million of these cases. The World Health Organization aims 90% reduction of *T. pallidum* incidence globally by 2030.[2] Few cases of primary and secondary syphilis have been reported in Turkey. No cases of secondary syphilis with pulmonary involvement have been reported. This is the first report with pulmonary involvement in secondary syphilis from Turkey.

The disease is classified as early syphilis (primary, secondary, and early latent syphilis) and as late syphilis (late latent and tertiary syphilis). In untreated patients, syphilis gradually progresses to several stages. In secondary syphilis, *T. pallidum* spreads to multiple organs and appears systemic symptoms. Syphilis should be considered in the differential diagnosis of patients presenting with pulmonary infiltrates. Pulmonary involvement in secondary syphilis is considered a rare occurrence. Herein, we present a case of secondary syphilis with pulmonary nodules, which was seen rarely.

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CASE REPORT

A 63-year-old man admitted to our hospital with the complaint of left chest pain, night sweats, loss of appetite, and multiple rashes on his anterior and posterior chest wall and his hands. These symptoms had begun 3 weeks ago. His medical history revealed no relevant comorbidities. He had no history of smoking and no history of alcohol or drug use. One year ago, he had a thorax computed tomography (CT) for suspected COVID-19 pneumonia, and it is observed with normal radiological findings. He had no fever, cough, sputum, or weight loss. On physical examination, body temperature was 38.1°C, pulse was 75/min regular, blood pressure was 110/68 mm Hg, and Sp_{O_2} was 98%. Oral mucosa was normal, and there were no aphthous ulcers. Bilateral basal crackles were heard on auscultation. Numerous pale red, nodular erythematous patches 3 to 5 mm in size were scattered on the palms of the hands, and anterior and posterior chest wall; however, there was no blister formation (Figs. 1A–C).

The white blood cell count was 9600/mL, and the platelet count was normal. Serum biochemistry tests showed normal results. The serum C-reactive protein, erythrocyte sedimentation rate, and procalcitonin levels were elevated (73.6 mg/L, 58 mm/h, 0.94 ng/mL, respectively).

Chest x-ray did not reveal any nodular shadows in the lung field, although the costophrenic angle was blunt on the left side (Fig. 2). Thorax CT revealed multiple bilateral mostly periferal nodular opacities, the largest of which is 2.5 cm in the left lower lobe, in the bilateral lower lobes and a nodule with necrosis in the subpleural region of the lingula (Figs. 3A–C). Because of suspicion of lung cancer, positron emission tomography–CT (PET-CT) revealed a moderate uptake in the bilateral lower lobes maximum standard uptake value (SUV) 6.5, as well as mediastinal adenopathy (SUV, 4.4) but no uptake in any other organs, initially suggesting an infectious or inflammatory origin (Figs. 4A–C).

Empirical treatment with levofloxacin (750 mg intravenous once a day) was started because of high fever. Bronchoscopy demonstrated normal bronchial mucosa and anatomy with no endobronchial lesions and watery secretions. There was no growth in bronchoalveolar lavage (BAL) culture. Screening for acid-alcohol–resistant bacilli in BAL was negative. The cytological examination revealed benign findings. Bronchoalveolar lavage showed predominance of macrophages (92%), with no abnormal cells, and a CD4/CD8 ratio of 1.0.

On dermatological examination, skin lesions were considered compatible with secondary syphilis. The venereal disease research laboratory test and FTA-ABS (Fluorescence Treponemal Antibody Absorption Test) were positive (1:8 titer) on blood sample. Thus, a secondary syphilis infection was diagnosed. Secondary syphilis was diagnosed based on skin lesions and treponemal tests results. Screening for other associated sexually transmitted diseases (serology for HIV, hepatitis C, and hepatitis B) was negative. He had no history of suspected sexual intercourse. After the syphilis diagnosis, the syphilis antibody was detected as negative in BAL sample.

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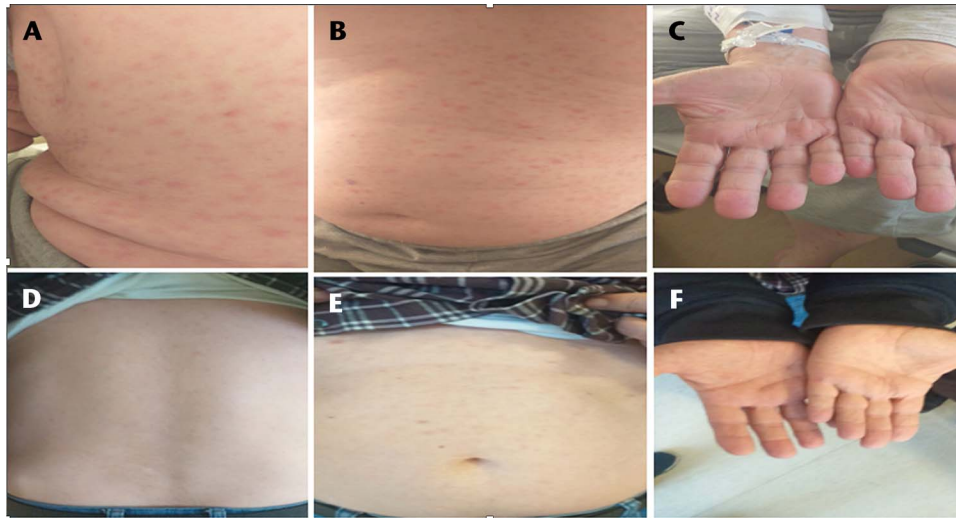


FIGURE 1. A to C, Numerous pale red, scaly nodular erythematous patches 3 to 5 mm in size were scattered on anterior and posterior chest wall, and the palms of the hands. C to E, All lesions regressed after treatment.

A diagnosis of secondary syphilis was made, and specific therapy with crystallized penicillin G was applied (2,400,000 UI intramuscular once a week for 3 weeks). He responded well to treatment, and his symptoms resolved within a few days. Thirty-five days after initiating treatment, most of the lesions on thorax CT were mostly resolved.

DISCUSSION

Syphilis is a sexually transmitted nonvaccine preventable infection caused by *T. pallidum*. Pulmonary involvement in cases of tertiary and congenital syphilis has been described.[3]

Pulmonary involvement in secondary syphilis is little known and rarely seen. There is limited number of case reports on secondary syphilis pulmonary involvement.

Kassem Youssef and colleagues[4] performed a literature review of case reports of secondary syphilis with pulmonary involvement from 1968 to 2015 using PubMed. Only 27 cases have been reported because the condition was first described in 1968.[4] Coinfection with HIV was reported in 5 cases of 27 reported cases. HIV infection is an important risk factor to be seen with other sexually transmitted diseases together.

Using PubMed, we searched for cases from 1968 to 2022 of secondary syphilis with pulmonary involvement in patients who are HIV-negative and found 15 reported cases (Table 1). Two of the patients had no pulmonary symptoms (chest pain, cough, dyspnea), 86% were male, and 80% had skin manifestations (rash). The most common pulmonary symptom was chest pain, which was thought to be the location of the nodular lesions mostly in the subpleural areas. Pulmonary syphilis can also be seen in HIV-negative cases, but its incidence is higher in HIV-positive cases.[18] The incidence of other immunosuppressive infections increases in HIV-positive cases, especially cryptococcal infections.[19] It is difficult to determine which infection is associated with lung involvement in HIV-positive patients. In HIV-negative cases, it was considered a more appropriate approach to say that



FIGURE 2. Chest x-ray on admission. The costophrenic angle was blunted on the left side.

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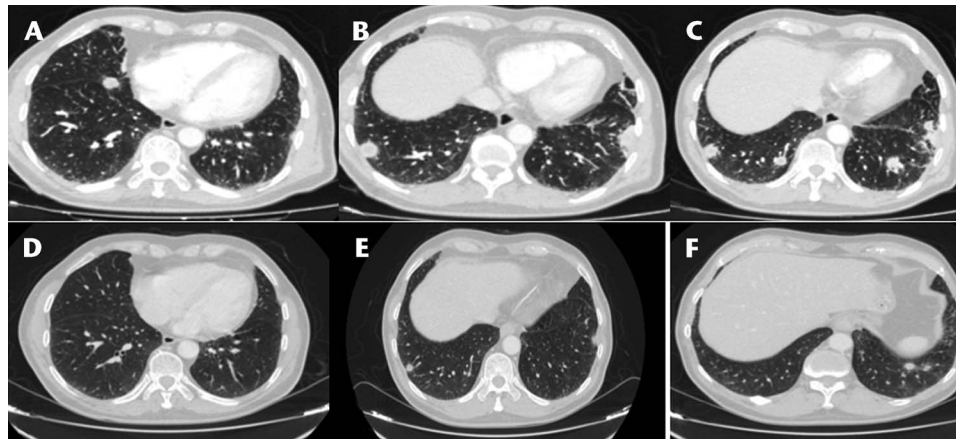


FIGURE 3. A to C, Pretreatment thorax CT images showing multiple noduler shadows, the largest of which is 2.5 cm in the left lower lobe, in the bilateral lower lobes and nodule with necrosis in subpleural region of lingula. D to F, Reduction in the number and size of nodules 35 days after treatment.

pulmonary nodules are compatible with secondary syphilis. All patients responded well to penicillin treatment, and pulmonary lesions regressed within a period of a few weeks.[4] The total duration of treatment with penicillin for our patient was 3 weeks. The Centers for Disease Control and Prevention suggests a single intramuscular injection of benzathine penicillin G as the first-choice treatment for syphilis regardless of HIV status.[20] HIV positivity does not change the treatment of secondary syphilis.

Bronchoscopy can be performed to obtain the bronchial sample. A bronchoalveolar lavage sample should be evaluated to determine syphilis. So microbiological culture, syphilis antibody, and cytological examination should be done to diagnose syphilis. Usually, BAL culture and/or BAL polymerase chain reaction do not provide definite information for diagnosis. Bronchoscopy was performed to diagnose 3 of 15 HIV-negative and nonimmunosuppressed patients, and *T. pallidum* PCR positivity was detected in 2 patients in BAL samples.[12,16,17] Bronchoalveolar lavage is not required for diagnosis, but PCR positivity supports the diagnosis of syphilis. In our case, the syphilis antibody was found to be negative in BAL samples.

In 1983, Coleman et al[21] defined several clinical criteria for the diagnosis of pulmonary involvement in secondary syphilis (Table 2). Our case was a nonimmunocompromised patient who had no suspicious sexual intercourse in his history. Using Coleman's criteria helped us diagnose syphilis. Because of the pulmonary involvement demonstrated on PET-CT, evaluation with fiberoptic bronchoscopy was necessary to exclude malignancy. Noduler opacities with and without necrosis in the bilateral lower lobes on thorax CT. The presence of multiple nodular lesions and enlarged lymph nodes in the lungs require the exclusion of primary or metastatic lung cancer and other diagnoses such as malignant lymphoma, mycosis, tuberculosis, septic embolization, rheumatoid nodules, and Wegener's granulomatosis.[3] When our patient was evaluated in terms of these differential diagnoses, no positive findings were detected. Although a transthoracic biopsy was planned, it could not be performed because lesions began to resolve because of empirical antibiotic therapy. In our case, the histopathological and serological findings and resolution of lesions after treatment for syphilis were considered diagnostic evidence of secondary syphilis.

CONCLUSIONS

Syphilis should be considered among the differential diagnosis in patients with diffuse mucocutaneous lesions in the body and central necrotic parenchymal nodules located in the lower lobes and subpleural areas in thorax CT. Syphilis pulmonary involvement responds well to penicillin treatment. The decrease in the number and size of the nodules on the control radiograph supports the diagnosis in terms of syphilis pulmonary involvement.

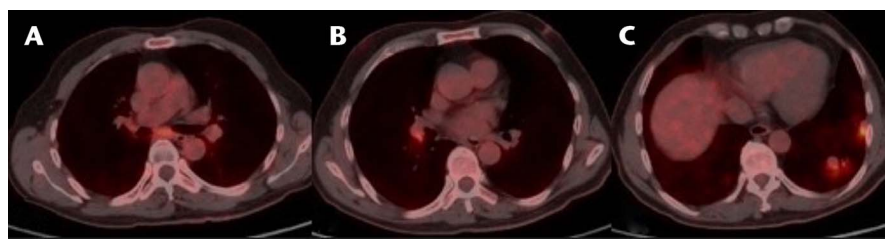


FIGURE 4. A to C, Positron emission tomography–CT. A and B, Mediastinal adenopathy (SUV, 4.4). C, Subpleural lesions in the left lower lobe (SUV, 6.5).

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TABLE 1. Case Reports of Secondary Pulmonary Syphilis Without HIV Infection From 1968 to 2022

Case No	Age	Sex	Symptoms	Radiological Images	Drug Treatment	Reference
1	50	Male	Rash, fever, cough	Multiple nodules in lower lung zones	Penicillin G	5
2	37	Male	Rash, chest pain, and painful adenopathy	Multiple pulmonary nodules in the lower lobes with a subpleural nodule with necrotic center	Penicillin G 2.4 MIU twice a week for 2 wk	6
3	56	Male	Rash, weight loss, left chest pain, uveit	Four subpleural nodules in right middle lob	Benzathine penicillin 2.4 MIU once a week for 3 wk	7
4	76	Male	Rash, cough, dyspnea	Bilateral pulmonary nodules and mass in right lung	Doxycycline for 2 wk because of allergic to penicillin	8
5	38	Male	Rash, pain in lateral chest wall, dyspnea	Right pleural effusion	Piperacilline/tazobactam	9
6	40	Male	Rash, chest pain	Subpleural nodules in right middle lobe	Benzathine penicillin 2.4 MIU once a week for 3 wk	10
7	51	Male	Rash, chest pain, fever, myalgia, cervical adenopathy	Multiple bilateral pulmonary nodules	Benzathine penicillin 2.4 MIU	11
8	49	Female	Fever, cough, cervical adenopathy	Infiltrates in right upper lobe	Penicillin G 2.4 MIU once a day for 14 d	12
9	41	Male	Rash, painless in left testis	Multiple pulmonary nodules	Doxycycline twice a day for 4 wk because of allergic to penicillin	13
10	34	Male	Rash, cough and swelling of the right inguinal nodes	A single mass lesion in the right lower lobe	Penicillin G 2.4 MIU once a day for 14 d	14
11	51	Male	Weight loss, oral ulcers	bilateral interstitial infiltrates and a 6-mm cavitated nodule in the upper left pulmonary lobe	Penicillin G 4 MIU every 4 h for 14 d	1
12	26	Male	Weight loss, dry cough, chest pain	Left pulmonary hilar mass, multiple pulmonary nodules	Benzathine penicillin	3
13	62	Female	Rash	Subpleural pulmonary nodule	Benzathine penicillin 2.4 MIU for 4 wk	15
14	52	Male	Fatigue, weight loss, fever, productive cough, and skin rash	Bibasilar consolidations and nodules	Benzathine penicillin G 2.4 MIU for 3 wk	16
15	44	Male	Fever, myalgia, headache and dry cough, rash	Subpleural consolidation	2.4 million units IM of benzathine penicillin G, single dose	17

TABLE 2. Coleman Clinical Criteria for the Diagnosis of Pulmonary Involvement in Secondary Syphilis[21]

1. Historical and physical findings typical of secondary syphilis
2. Serologic test results positive for syphilis
3. Pulmonary abnormalities seen radiographs with/without associated pulmonary symptoms or signs
4. Exclusion of other forms of pulmonary disease when possible, using serologic tests, sputum smears and cultures, and cytological examination of sputum
5. Therapeutic response to antisyphilitic therapy visible on radiograph

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