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Pulmonary talcosis caused by intravenous methadone injection

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TO THE EDITOR:

A 38-year-old woman presented to our pulmonology clinic with complaints of progressive dyspnea and dry cough for more than three months. She denied fever or weight loss. On physical examination, she presented as hypoxemic, with a room air oxygen saturation of 92% and an RR of 24 breaths/min. Pulmonary function tests showed that spirometric values were within normal limits, but there was a slight increase in residual volume (127% of predicted), as well as a reduction in DLCO (70% of predicted). Other laboratory test results were normal. A CT of the chest showed bilateral centrilobular nodules, most of them showing tree-in-bud appearance, scattered diffusely in the lung parenchyma (Figures 1A and 1B). After the CT examination, flexible bronchoscopy was then performed. Cultures of BALF were negative. Transbronchial biopsy performed in the left lower lobe showed multinucleated giant cell granulomas with birefringent foreign material, compatible with talc (Figures 1C and 1D). The centrilobular nodules were determined histopathologically to be tiny foreign body particles lodged in the centrilobular arterioles and perivascular space.

Upon further discussion, the patient remembered that approximately one month before the onset of symptoms, she had self-administered an i.v. injection of a crushed methadone pill diluted in water, due to strong pain caused by trigeminal neuralgia. Based on the clinical history, CT findings, and pulmonary biopsy results, the diagnosis of pulmonary talcosis secondary to i.v. drug injection was made. Echocardiogram results were normal. No signs of pulmonary hypertension were seen. During 3 years of follow-up, the patient showed clinical stability with the persistence of dyspnea on exertion and dry cough. Findings of control CT examinations were unchanged.

Pulmonary talcosis is most commonly observed after inhalation of talc due to occupational exposure

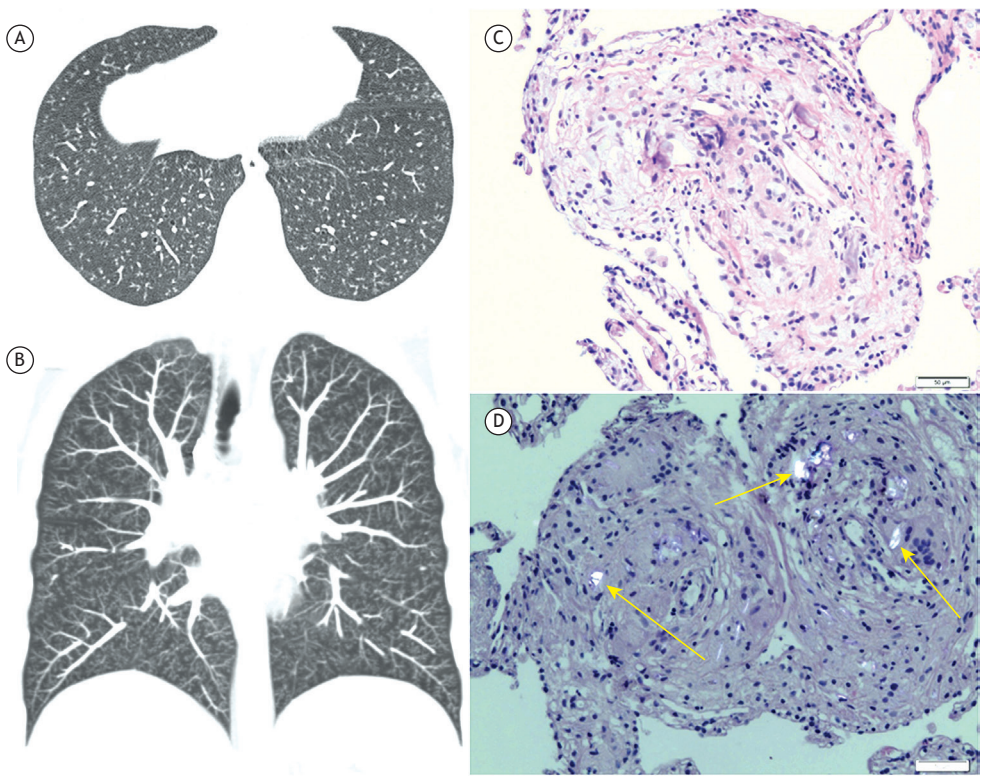

Figure 1. Axial (in A) and coronal (in B) reformatted CT images showing numerous small bilateral centrilobular nodules, associated with the tree-in-bud pattern. In C, lung tissue biopsy demonstrating an interstitial granulomatous reaction to the talc particles with a giant-cell reaction (H&E; magnification, ×100), whereas, in D, under polarized light, birefringent crystals (arrows) are visible (H&E; magnification, ×100).

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(talc-induced pneumoconiosis), i.v. drug abuse (intravascular talcosis), and, occasionally, excessive use of cosmetic talc. Clinical symptoms, imaging findings, and histological presentations of pulmonary talcosis are essentially identical in these different etiologies.[1-4]

The most common form of pulmonary talcosis is caused by i.v. talc administration. Illegal street drugs commonly contain adulterants to increase their mass, and these adulterants commonly contain microscopic insoluble material. Another common source of such material is the injection of medications intended for oral use. The medications are typically crushed, mixed with water, heated, and then injected i.v. The filler materials (excipients) used in oral tablets include not only talc, but also other insoluble particles, such as cellulose, crospovidone, and starch, which can induce a foreign-body reaction in pulmonary arterioles. Heroin, cocaine, and methadone are the most commonly injected drugs.[1-5] However, other medications, particularly analgesics and stimulants, are also used. Some authors[2] have suggested that the term "intravascular talcosis" is a misnomer, since talc is only one of various possible materials used as excipients, and have proposed the term "excipient lung disease" to identify this condition.

Patients with talcosis can be asymptomatic or present with respiratory failure. The symptoms are usually nonspecific and can include dyspnea, cough, fever, weight loss, chronic respiratory failure due to emphysema, and conditions related to pulmonary hypertension or fibrosis. Other complications of i.v. drug abuse resulting from the lack of a sterile technique include infections, such as endocarditis, septic embolism, HIV, and HCV. Physical examination and laboratory test findings are usually unremarkable in patients with talcosis. A characteristic finding of fundoscopy is the presence of crystals in retinal vessels. A history of i.v. drug abuse is an important clue to making the diagnosis; however, most i.v. drug abusers are reluctant to provide histories of exposure, and most diagnoses are made after lung biopsy.[1-4] The i.v. administration of talc or other excipients results in acute embolization of small vessels. Numerous tiny particles become lodged in the pulmonary vessels and migrate to the pulmonary interstitium, where they cause a granulomatous foreign-body reaction, with or without fibrosis. The granulomas can be visualized under polarized light as birefringent needle-shaped talc crystals in multinucleated giant cells.[1-3]

The earlier CT findings of talcosis consist of a diffuse fine nodular pattern, which corresponds basically to small centrilobular nodules and areas of ground-glass attenuation in all lung zones. The centrilobular nodules were determined histopathologically by tiny foreign body particles lodged in the centrilobular arterioles, and also in the perivascular space. The ground glass opacities may represent the confluence of these micronodules and/or microscopic granulomas below the resolution of HRCT.[1-3]

Periarteriolar, centrilobular micronodules can create a tree-in-bud pattern, mimicking bronchiolar disease. Centrilobular and panacinar emphysema patterns have been reported in i.v. drug users, with the lower-lobe panacinar pattern being predominant. Over time, talc micronodules may coalesce into perihilar conglomerate masses, resembling progressive massive fibrosis from silicosis or coal workers' pneumoconiosis. The conglomerate masses in talcosis may contain high-attenuation material.[1,2,4,5] The differential diagnosis for our patient (considering the presence of small bilateral centrilobular nodules, most with a tree-in-bud appearance) included arteriolar and bronchiolar diseases. The main conditions considered were infectious diseases (fungal, viral, and bacterial, particularly tuberculosis), noninfectious bronchiolitis, cystic fibrosis, aspiration/inhalation diseases, and peripheral pulmonary vascular diseases, such as pulmonary intravascular tumor embolism. There is no established treatment for talc granulomatosis. Patients must stop exposure and all tobacco use. Most authors believe that the use of steroids and immunosuppressants has no benefit. Associated pulmonary hypertension should be treated with vasodilators. Lung transplantation is considered to be a viable option for the treatment of talcosis. It is reserved as a last resort for patients with end-stage disease.[1] In our case, it was agreed that no treatment was required due to the stable nature of the disease. In conclusion, the CT manifestations of intravascular talcosis consist of diffuse centrilobular nodules associated with a tree-in-bud pattern and ground-glass opacities, heterogeneous conglomerate masses containing areas of high attenuation, and panlobular emphysema in the lower lobes. The diagnosis should be considered in the setting of a history of i.v. drug abuse, but the final diagnosis is made after lung biopsy in most cases.

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