Pulmonary Complications of Illicit Drug Use

Differential Diagnosis Based on CT Findings

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Objective: The aim of this manuscript is to summarize an approach to the differential diagnosis of the pulmonary complications of illicit drug use based on the computed tomography findings.

Conclusions: The various pulmonary complications of illicit drug use result in 5 main patterns of parenchymal abnormality: nodules, ground-glass opacities, consolidation, air trapping, and emphysema. Other thoracic manifestations of illicit drug use include pulmonary arterial hypertension, pneumomediastinum, bacterial endocarditis, discitis, and septic arthritis.

Key Words: drug abuse, computed tomography, cardiopulmonary, interstitial lung disease, talcosis

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Abuse of inhaled or intravenously injected illicit drugs is an increasingly common health problem worldwide. It is associated with a spectrum of pulmonary complications including talcosis, emphysema, pneumonia, septic embolism, aspiration, pulmonary edema, pulmonary hemorrhage, mycotic aneurysms, and pulmonary hypertension.[1–4] History of illicit drug use is often unavailable or delayed which may preclude clinical diagnosis and prompt treatment of pulmonary complications. We propose a computed tomography (CT) imaging-based algorithm for the differential diagnosis of pulmonary complications in patients with suspected or known drug abuse.

ALGORITHM FOR DIFFERENTIAL DIAGNOSIS OF COMPLICATIONS OF ILLICIT DRUG USE

The differential diagnosis of the pulmonary complications of illicit drug use on CT is based on the pattern and distribution of parenchymal abnormalities (Fig. 1). The 5 main patterns of abnormality are nodules, ground-glass opacities, consolidation, air trapping, and emphysema.

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Nodules

Small Nodules (< 1 cm Diameter)

The most common causes of small nodules in illicit drug users are talcosis and septic embolism. Talcosis is a known complication of intravenous injection of medications intended for oral use such as Ritalin (methylphenidate), cocaine, and pentazocine but has also been reported after inhalation of talc found in cocaine and other illicit drugs.[2,5–7] Talcosis may result in diffuse, well-defined, and randomly distributed micronodules (Fig. 2) which represent talc particles which have embolized to the pulmonary arterioles and capillaries causing vascular obstruction and occasionally thrombosis and transient pulmonary arterial hypertension.[8] The talc particles may migrate over time into the adjacent peri-vascular interstitium where they incite a foreign body granulomatous reaction and fibrosis. With disease progression, the micronodules may coalesce and form large perihilar opacities that contain areas of high attenuation (Fig. 3) due to talc deposition,[7] resembling progressive massive fibrosis seen in pneumoconiosis.[7,9] Similar pulmonary foreign body granulomatous reactions may be seen after intravenous injection of oral medications containing other insoluble fillers such as cornstarch or cellulose.[10]

Septic embolism may result in multiple small or, more commonly, large pulmonary nodules. Occasionally, small centrilobular nodules may be due to eosinophilic vasculitis (Fig. 4), a rare complication of cocaine use.[11] The pathophysiology is unknown. Other unusual causes of small nodules include amyloidosis[12] and hypersensitivity drug reaction.[13]

Large Nodules (1 to 3 cm diameter)

The most common causes of large nodules in illicit drug users are septic embolism, fungal infections (such as Aspergillus, Cryptococcus, Blastomyces, Mucor, and Candida species)[14] and organizing pneumonia (bronchiolitis obliterans organizing pneumonia, BOOP-like reaction).[15] Septic emboli typically present as multiple

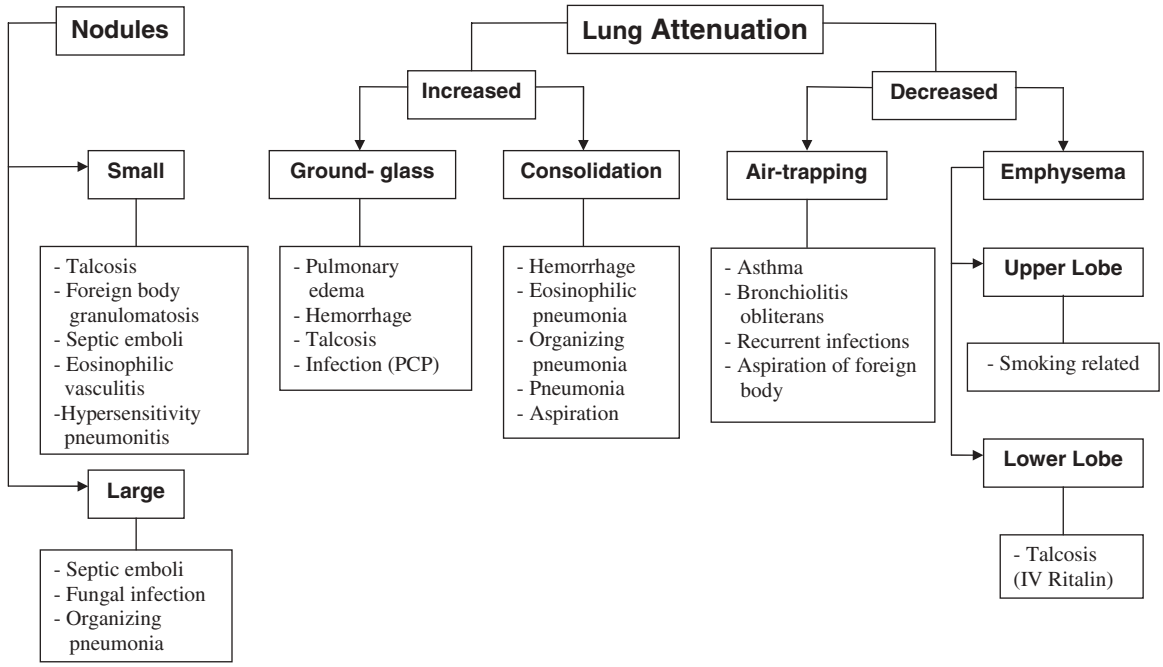

FIGURE 1. Algorithm for differential diagnosis of pulmonary complications of illicit drug users based on CT findings.

peripheral large nodules that frequently cavitate (Fig. 5). Focal areas of organizing pneumonia and fungal infection can also present as large nodules or mass-like areas of consolidation.

Increased Lung Attenuation

Ground-glass Opacity

Ground-glass opacity is defined as increased lung attenuation on CT where underlying vessels remain visible and are normal in number and caliber. The most common causes of ground-glass opacities in drug users are pulmonary edema, pulmonary hemorrhage, and opportunistic infections.

Pulmonary edema is a relatively common complication of smoking crack cocaine or intravenous injection of cocaine (Fig. 6) or heroin. The edema is at least in part secondary to increased vascular permeability.[3] Crystal methamphetamines may result in cardiomyopathy or acute myocardial infarction and associated pulmonary edema.[4] Pulmonary hemorrhage is also a well-known complication of smoking crack cocaine but the pathophysiology is unclear.[1,2] Talcosis, after intravenous injection of drugs intended for oral use, may present as diffuse or patchy bilateral ground-glass opacities (Fig. 7).[5–7]

Infections are common among intravenous drug abusers due to sharing of nonsterile needles, malnutrition, and immunosuppression due to comorbidities or HIV infection. Infections resulting in ground-glass opacities are seen mainly in intravenous drug users with HIV infection and are usually due to opportunistic organisms such as *Pneumocystis* (Fig. 8) and cytomegalovirus.

FIGURE 2. A 35-year-old man with talcosis due to intravenous drug abuse. High-resolution CT image at the level of aortic arch demonstrates diffuse micronodules in a random distribution (courtesy of Dr Sarah Howling, Whittington Hospital, London, England).

Consolidation

Consolidation is defined as increased lung attenuation that obscures the underlying vessels. Complications related to illicit drug use that may result in consolidation include pulmonary hemorrhage, eosinophilic pneumonia, and organizing pneumonia. These patients also have a

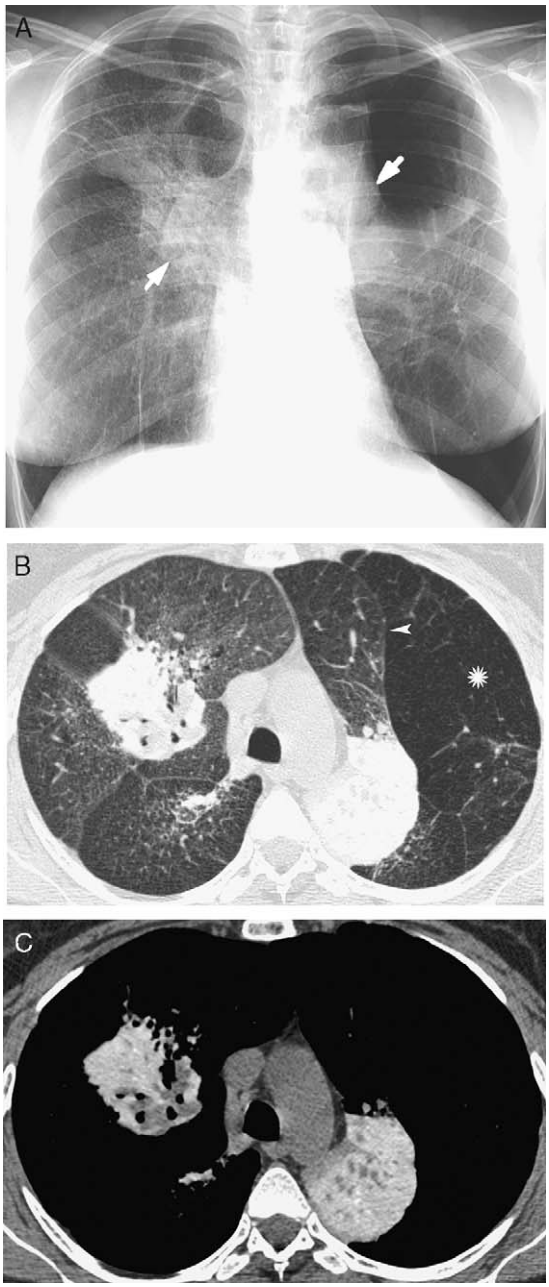

FIGURE 3. A 30-year-old woman with talcosis due to intravenous drug abuse. A, Posteroanterior chest radiograph shows large peri-hilar opacities (arrows), extensive upper lobe scarring and decreased attenuation and vascularity in the left lung. Tiny nodules are visualized in the right lung involving mainly the upper and middle lung zones. B, High-resolution CT scan shows conglomerate masses within the upper lobes and bilateral architectural distortion. Note displacement of the left major fissure (arrowhead) due to compensatory hyperinflation of the left lower lobe. Also note markedly decreased attenuation and vascularity of the left lower lobe (asterix) consistent with panacinar emphysema. Multiple small nodules and ground-glass opacities are seen bilaterally. C, CT image at the same level as B photographed at soft tissue settings demonstrates high attenuation of the bilateral masses consistent with talc deposition.

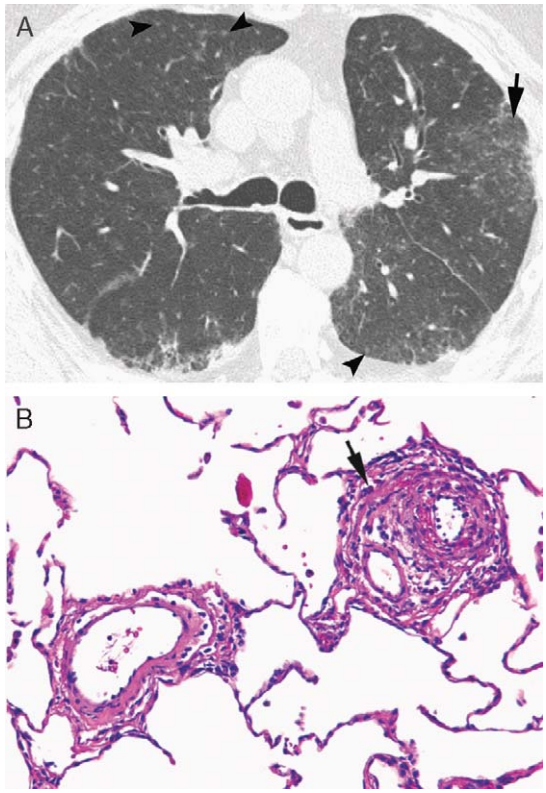

FIGURE 4. A 55-year-old man with eosinophilic vasculitis due to cocaine. A, High-resolution CT image shows multiple small centrilobular nodules throughout both lungs (arrowheads). A cluster of nodules and ground-glass opacity are noted in the left upper lobe (straight arrow). B, Specimen obtained from a right lower lobe wedge biopsy shows infiltration of small pulmonary vessels by inflammatory cells consisting of a mixture of mononuclear cells and eosinophils (straight arrow) (hematoxylin and eosin, $\times 100$).

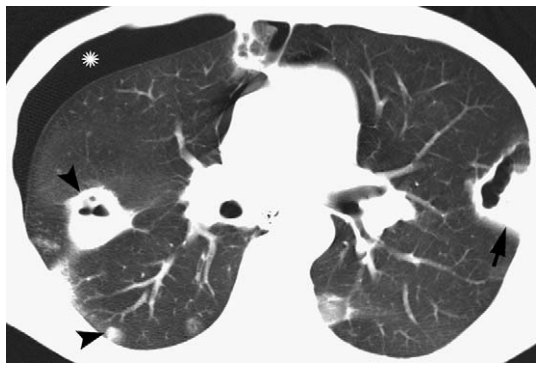

FIGURE 5. A 41-year-old man with septic embolism due to intravenous drug use. CT image (5-mm collimation) shows multiple peripheral nodules (arrowheads) of varying sizes, some of which are cavitary. A cavitating subpleural wedge-shaped opacity is noted within the left upper lobe (straight arrow). Small right pneumothorax (asterix) is presumably related to rupture of a cavitary lesion (not shown) into the pleural space.

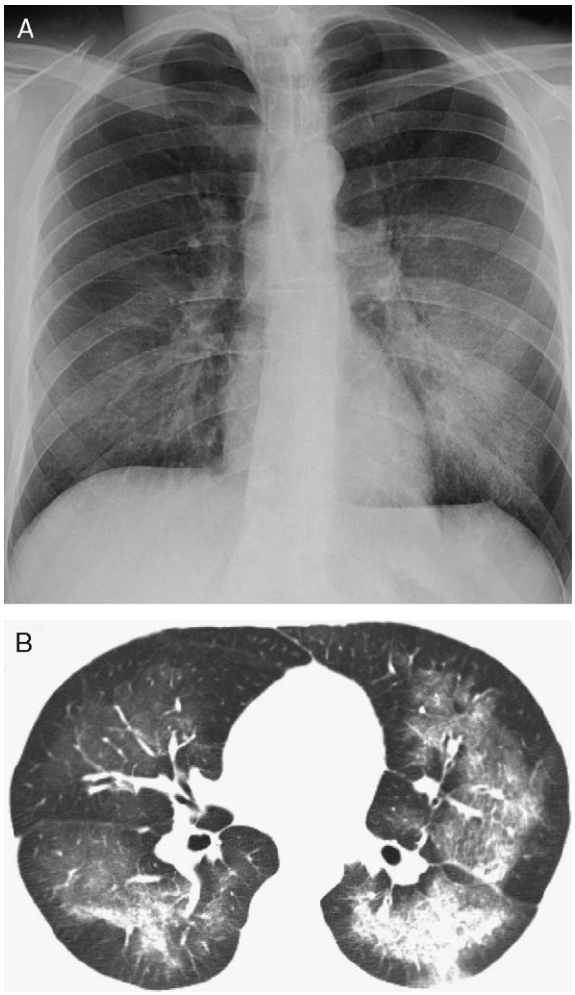

FIGURE 6. A 34-year-old man with pulmonary edema due to crack cocaine. A, Posteroanterior chest radiograph shows faint, bilateral peri-hilar opacities. B, High-resolution CT image shows symmetric bilateral ground-glass opacities with relative sparing of the subpleural regions. Areas of consolidation are present in the dependent lung regions.

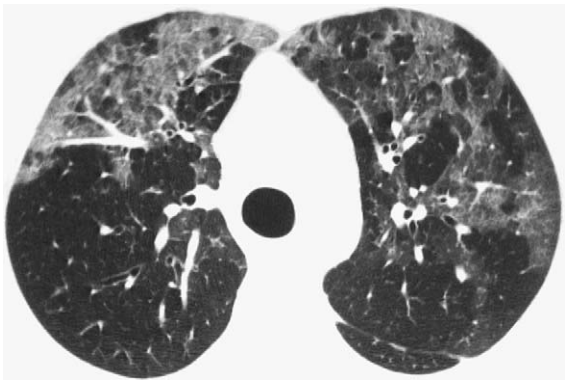

FIGURE 7. A 46-year-old man with talcosis due to intravenous drug abuse. High-resolution CT image demonstrates patchy bilateral ground-glass opacities.

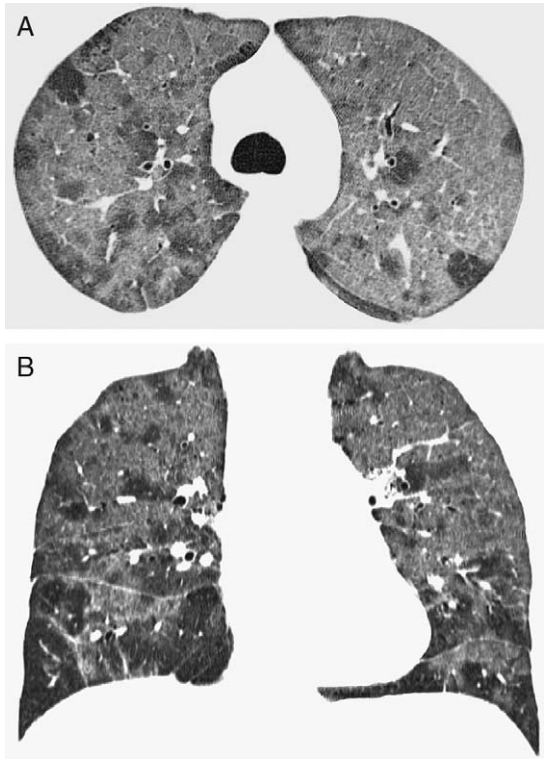

FIGURE 8. A 36-year-old male HIV-positive intravenous drug user with *Pneumocystis* pneumonia. A, High-resolution CT image obtained on a multidetector CT scanner demonstrates extensive bilateral ground-glass opacities. Several pulmonary lobules seem normal or have mild abnormalities resulting in an inhomogeneous appearance of the lungs. B, Coronal image better demonstrates the overall distribution of the ground-glass opacities.

greater likelihood to develop infectious pneumonia and to aspirate.

Pulmonary hemorrhage is seen most commonly as a complication of crack cocaine (Fig. 9). Cocaine in any form may result in eosinophilic pneumonia.[16] Illicit drugs, similar to medications, may also result in organizing pneumonia. More commonly, the consolidation in illicit drug users is due to bacterial pneumonia or due to aspiration. Because the patients may have prolonged periods of time of decreased consciousness the pneumonias have a greater likelihood to be extensive and associated with complications such as empyema (Fig. 10).

Decreased Lung Attenuation

Air Trapping

Cocaine may cause asthma and obliterative bronchiolitis, both of which manifest as areas of decreased

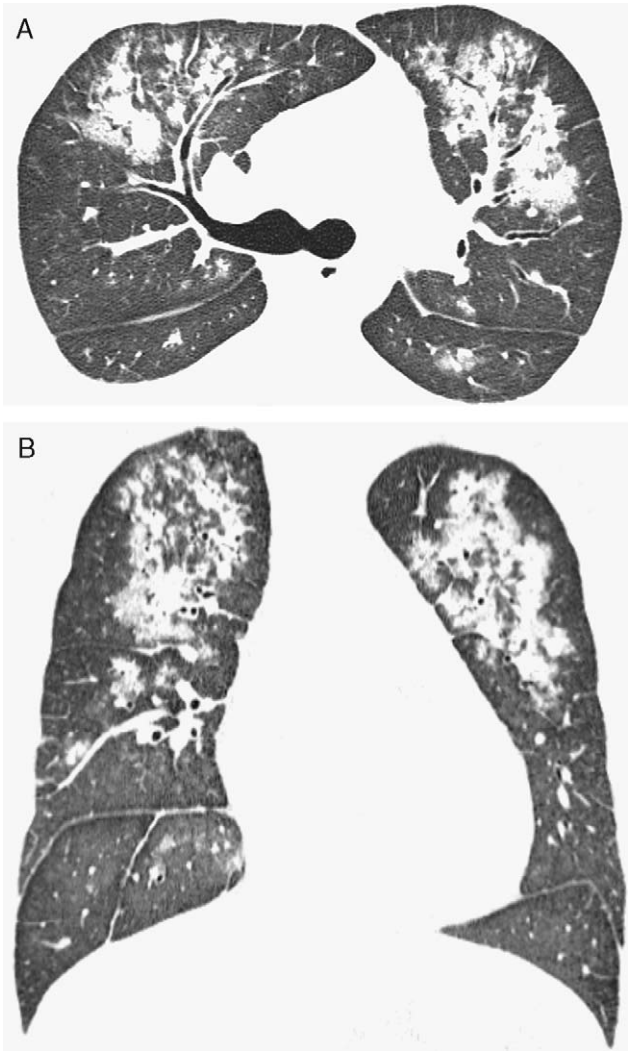

FIGURE 9. A 23-year-old man with pulmonary hemorrhage due to intravenous cocaine use. A, High-resolution CT image obtained on a multidetector CT scanner shows consolidation and ground-glass opacities involving mainly the anterior segments of the upper lobes. B, Coronal image better demonstrates the predominant upper lobe distribution of the consolidation. Also note relative sparing of the subpleural regions and lung apices.

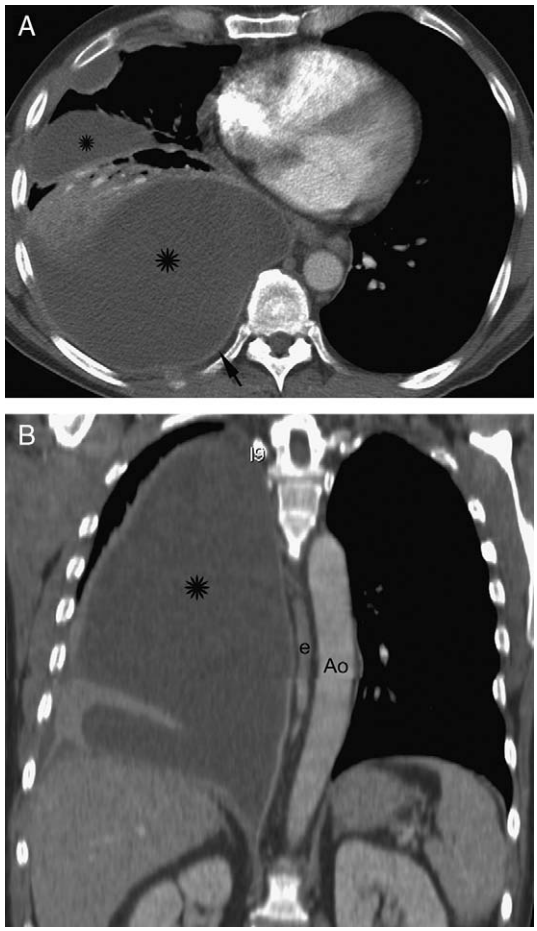

FIGURE 10. A 44-year-old male intravenous drug user with empyema. A, Contrast-enhanced CT image obtained on a multidetector CT scanner at the level of the lower lung zones shows large multiloculated right pleural effusion (asterixes). Also noted is mild thickening and enhancement (arrow) of the pleura consistent with empyema. B, Coronal image demonstrates the mass effect of the right pleural collection (asterix), causing displacement of the descending thoracic aorta (Ao) and esophagus (e) to the left. Cultures of the pleural aspirate grew *Staphylococcus aureus*.

lung attenuation and vascularity on inspiratory CT and air trapping on expiratory CT.[1,2] Air trapping in these patients may be also secondary to acute infectious bronchiolitis, recurrent infections, or, occasionally, aspiration of a foreign body during inhalation of an illicit drug (Fig. 11).

Emphysema

Emphysema is commonly seen in illicit drug users because many of them are also cigarette smokers. Emphysema has also been described in smokers of marijuana. Talcosis due to IV drug use may result in panacinar emphysema involving mainly the lower lung zones (Fig. 12). This complication is particularly common after intravenous injection of talc-containing oral Ritalin (methylphenidate).[2,5–7]

Other Thoracic Manifestations

Pulmonary arterial hypertension can result from intravenous injection of talc containing medications

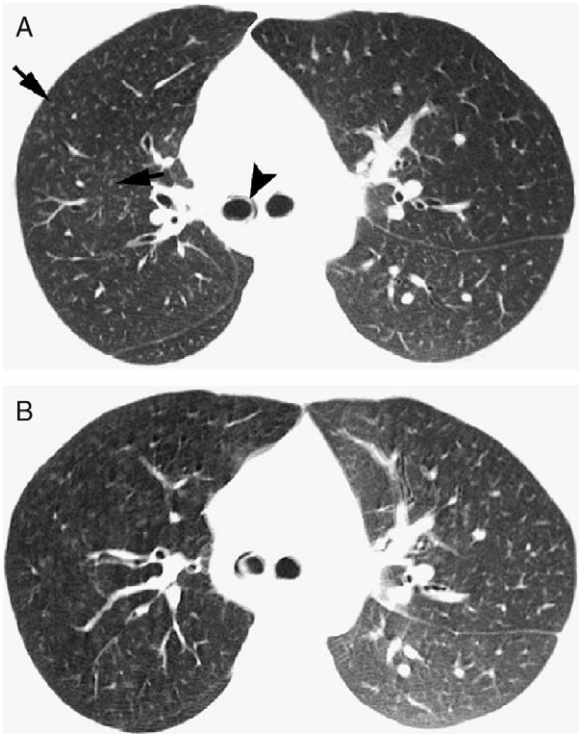

FIGURE 11. A 23-year-old female cocaine user with partial right bronchial obstruction and air trapping due to inhalation of a straw. A, High-resolution CT image shows a circular opacity in the right mainstem bronchus (arrowhead) and decreased volume of the right lung. Also noted are few small centrilobular nodules in the right upper lobe (arrows). B, Expiratory CT image at the same level as A demonstrates air trapping in the right lung and contralateral mediastinal shift. The foreign body in the right mainstem bronchus was removed bronchoscopically and was proven to be a straw aspirated during rigorous cocaine sniffing. The small centrilobular nodules in the right upper lobe were presumably secondary to postobstructive bronchiolitis.

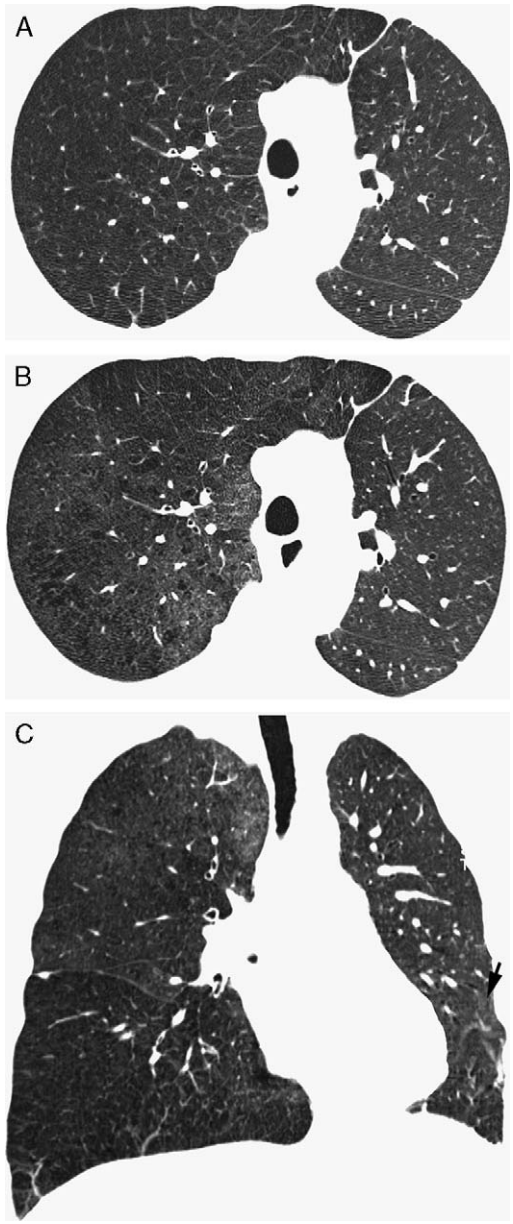

FIGURE 12. A 46-year-old man with panacinar emphysema and recurrent talcosis due to intravenous injection of oral Ritalin (methylphenidate). A, High-resolution CT image obtained on a multidetector CT scanner demonstrates panacinar emphysema in the native right lung. No abnormalities are noted in the transplanted left lung. B, High-resolution CT image obtained at the same level as A 3 years later shows development of diffuse nodularity and ground-glass opacities within the native right lung. C, Coronal image better demonstrates the marked hyperinflation of the emphysematous right lung. Also note diffuse micronodules in the right lung and ground-glass opacities in the right upper lobe. The left lung is relatively normal apart from a small focus of ground-glass opacity in the lingula. The patient had panacinar emphysema due to talcosis proven at the time of left lung transplant. Clinical history confirmed that the patient was continuing his habit of intravenous injection of oral Ritalin (methylphenidate) after lung transplantation.

intended for oral use and has been reported with cocaine use (Fig. 13). Bacteremia from contaminated needles can lead to bacterial endocarditis, septic embolism, mycotic pulmonary artery aneurysms, septic arthritis (Fig. 14), discitis, and osteomyelitis (Fig. 15).[2] Sniffing cocaine and smoking marijuana can result in pneumothorax and pneumomediastinum (Fig. 16). Attempts to inject intravenous drugs directly into the internal jugular vein can also lead to pneumothorax from lung puncture as well as hemothorax and pseudoaneurysms due to vessel injury.[1] Widened mediastinum from acute aortic dissection has also been reported with cocaine use.[17] Pulmonary venoocclusive disease is a rare complication of cocaine use characterized by diffuse fibrous occlusion

FIGURE 13. A 42-year-old woman with history of cocaine use and pulmonary arterial hypertension. CT image (5-mm collimation) photographed at soft tissue settings shows enlargement of the main, right, and left pulmonary arteries.

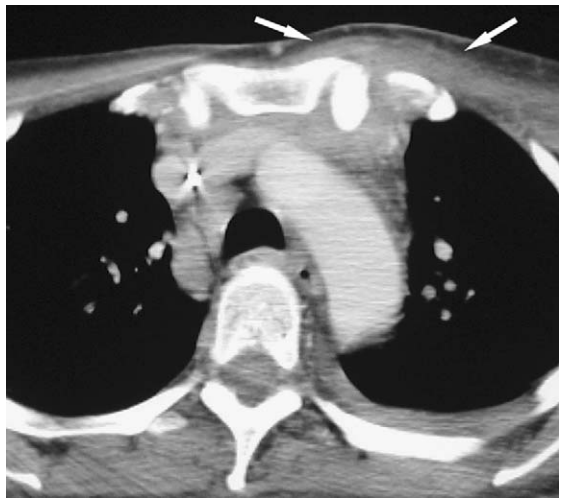

FIGURE 14. A 45-year-old female intravenous drug user with septic arthritis. Contrast-enhanced CT image (7-mm collimation) shows swelling of the soft tissues adjacent to the left sternoclavicular joint (arrows). Culture of joint aspirate grew *Staphylococcus aureus* confirming septic arthritis. Bone scintigraphy was negative for osteomyelitis or other sites of involvement.

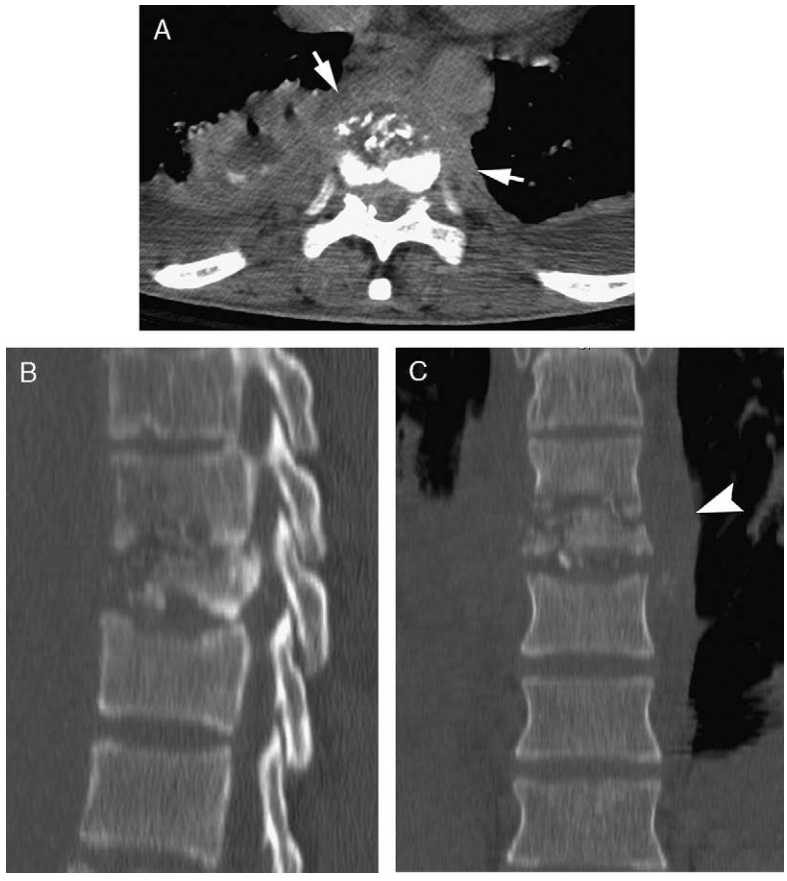

FIGURE 15. A 33-year-old female intravenous drug user with discitis and osteomyelitis. A, Cross-sectional CT image obtained on a multidetector CT scanner shows destruction of the T9 vertebral body and widening of the paravertebral soft tissues (arrows). B and C, Sagittal and coronal CT images photographed on bone window settings show destruction of the T9 vertebral body and narrowing of the adjacent intervertebral disc space. Widening of the paravertebral soft tissues is well demonstrated on the coronal (C) image (arrowhead). Blood culture grew *Staphylococcus aureus*.

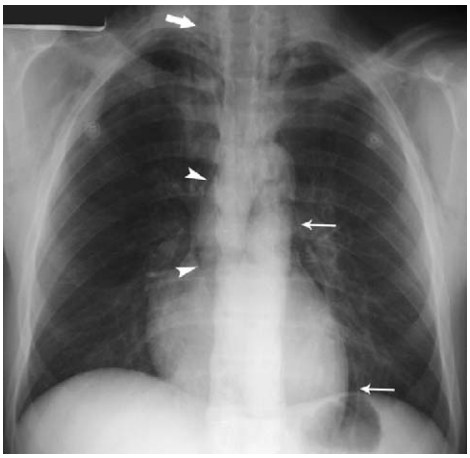

FIGURE 16. A 17-year-old man with pneumomediastinum after sniffing cocaine. Posteroanterior chest radiograph shows a linear density (thin arrows) outlining the left heart border representing the mediastinal pleura displaced by pneumomediastinum. Air is seen outlining the ascending aorta (arrowheads) and extending superiorly to the soft tissues of the neck and chest wall (thick arrows).

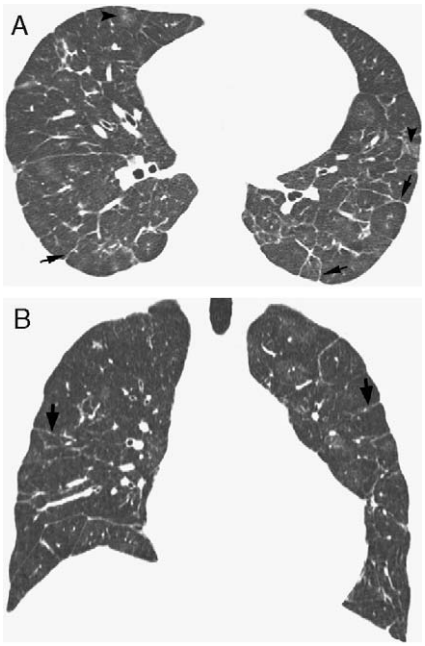

FIGURE 17. A 20-year-old male cocaine user with venoocclusive disease. A, High-resolution CT image obtained on a multidetector scanner at the level of the inferior pulmonary veins shows patchy bilateral ground-glass opacities (arrowhead) and septal lines (straight arrows). B, Coronal image demonstrates septal lines (straight arrows) mainly in the peripheral lung regions. Also noted is enlargement of the main pulmonary artery consistent with pulmonary arterial hypertension and cardiomegaly. The diagnosis of venoocclusive disease was made at surgical lung biopsy.

of pulmonary veins and venules giving rise to pulmonary edema and pulmonary arterial hypertension (Fig. 17). The underlying pathophysiology is not well understood.

CONCLUSIONS

Awareness of the imaging findings of thoracic complications related to illicit drug use facilitates prompt diagnosis and treatment. The CT imaging-based algorithm described in this manuscript outlines an approach to the differential diagnosis of pulmonary complications related to illicit drug use in patients presenting with cardiorespiratory symptoms.

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