

# A Case of Large Pericardial and Pleural Effusions Associated With Pulmonary Emboli in a User of Crack Cocaine

Hien Nguyen, MD  
 Connie Le, MD  
 Hanh Nguyen, MD

## Abstract

We submit here an unusual case in which a user of crack cocaine presented with progressive dyspnea of subacute duration and was subsequently found to have concurrent pericardial and pleural effusions and pulmonary emboli. To our knowledge, there is only one prior case report that describes a potential causal relationship between crack cocaine and the development of a pleural effusion, via an eosinophilic process. In contrast in our patient, the most probable mechanism is that crack cocaine induced a prothrombotic state that promoted formation of pulmonary emboli, which are known to be directly associated with exudative pleural or pericardial effusions. An alternative hypothesis is that sympathetic activation or neurostimulation, which is mediated through release of adrenergic neurotransmitters by cocaine, may cause inflammatory changes in the pleura or pericardium. Finally, the pericardial effusion, pleural effusion, and pulmonary emboli could be concurrent but independent processes.

## Case History

A man, age 56 years, who had undergone a partial colectomy for a benign polyp in the past presented to the Emergency Department (ED), reporting three months of progressive dyspnea on exertion with routine daily activities. He said that he had no chest pain, upper respiratory symptoms, hemoptysis, fever, weight loss, or other constitutional symptoms. The patient acknowledged using crack cocaine on the day before his presentation, and at least once weekly for the preceding four months. There was no history of chest trauma. His blood counts, metabolic panel findings, cardiac

enzymes, and B-type natriuretic peptide levels were normal, and his D-dimer level was elevated. An electrocardiogram revealed low voltage with sinus tachycardia, rate of 106 beats per minute, and no ischemic changes. Chest radiography revealed cardiomegaly and bilateral pleural effusions. Chest computed tomography confirmed large pericardial and bilateral pleural effusions, with compressive atelectasis and pulmonary emboli in the left lower lobe. Emergency echocardiography revealed free-flowing pericardial effusion without tamponade, and a normal ejection fraction. Serology for HIV, antinuclear antibody, rheu-

matoid factor, hepatitis, and thyroid were all normal, as were findings for hypercoagulability. Concurrent thoracotomy with drainage of the pleural effusion and a pericardial window for the pericardial effusion were performed. During the procedures, 1500 mL of serosanguineous fluid was evacuated from the pericardial space and another 1500 mL from the pleural space. The fluid analysis was consistent with an exudative process, with a lactate dehydrogenase of >4000 U/L. Eosinophilia was not observed in the effusions. Gram stains for bacteria and acid-fast bacilli produced normal findings. Pericardial and pleural biopsies demonstrated chronic inflammation but no malignant changes. An infra-renal vena cava filter was placed, and interval radiographs revealed complete resolution of the effusions. The patient was discharged to home.

## Discussion

To our knowledge, crack cocaine abuse in association with concurrent pericardial and pulmonary effusions has not been previously reported.<sup>1,2</sup> The most probable link between the crack cocaine use and the effusions are the pulmonary emboli. Cocaine is known to induce a prothrombotic state that may lead to pulmonary emboli, which are known to be as-

**Hien Nguyen, MD**, (left) is an Internist at the Camp Springs Medical Center in Temple Hills, MD, and an Attending Internist at the Washington Hospital Center in Washington, DC. E-mail: hientrinhnguyen@yahoo.com.

**Connie Le, MD**, (center) is an Attending Internist at the Fairfax Hospital in Fairfax, VA. E-mail: drconniele@aim.com.

**Hanh Nguyen, MD**, (right) is a Resident at the University of California Irvine Medical Center in Irvine, CA. E-mail: hanhnguyenmd@gmail.com.



sociated with pericardial or pleural effusions.<sup>3</sup> Alternatively, cocaine may cause direct cardiac and pulmonary toxicity. It is also speculated that sympathetic nervous system activation and release of adrenergic neurotransmitters by cocaine may lead to inflammatory changes in the pleural or pericardial surfaces

in a hypothetical process of neurostimulation.<sup>4</sup>

### Epidemiology

Cocaine is the second most commonly used illicit drug in the US, which is the world's foremost consumer of this drug. An estimated 1.5 million Americans use cocaine

regularly, defined as use at least once monthly. Approximately 25% of patients ages 18 to 45 presenting with chest pain to the ED admit to cocaine use.<sup>5-8</sup>

### Pharmacology

Cocaine is derived from the erythroxyline coca plant and historically has had medicinal uses, including as a local anaesthetic and as a treatment for depression.<sup>5,6</sup> Cocaine stimulates the sympathetic nervous system by blocking reuptake of catecholamines, including norepinephrine, epinephrine, and dopamine at the presynaptic receptors. Excess catecholamines at postsynaptic receptors activate the sympathetic system, and clinical manifestations include tachycardia, hypertension, vasoconstriction, and hyperthermia.<sup>5-8</sup>

### Cocaine and Cardiac and Pulmonary Toxicity

Cardiovascular complications associated with cocaine abuse include myocardial ischemia, myocarditis, cardiomyopathy, and aortic dissection.<sup>5-8</sup> These effects can be explained in terms of cocaine's pharmacologic effects. Elevations in heart rate, blood pressure, and afterload lead to increased myocardial oxygen demand in the face of concomitant reductions in coronary blood flow and cardiac contractility induced by cocaine.<sup>5-9</sup>

Pulmonary complications associated with crack cocaine inhalation include asthma, eosinophilic pneumonitis, bronchiolitis obliterans and organizing pneumonia, pneumothorax, and pneumomediastinum.<sup>10,11</sup>

### General Etiology and Mechanisms of Formation of Pericardial and Pleural Effusions

A brief schematic differential diagnosis of pericardial effusions



Figure 1. Chest computed tomography scan demonstrating large bilateral pleural effusions.

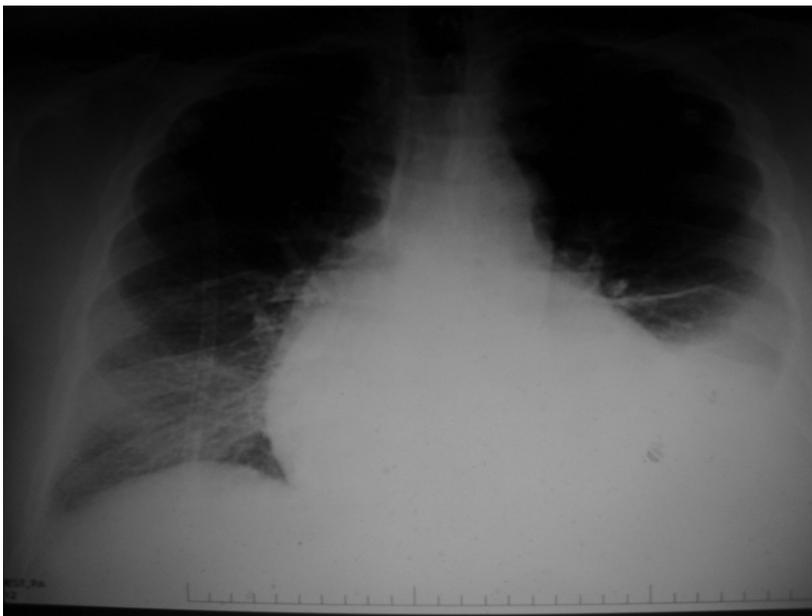


Figure 2. Chest radiograph demonstrating large bilateral pleural effusions and cardiomegaly.

includes infections (coxsackievirus A and B, hepatitis, HIV, pneumococci, streptococci, staphylococci, tuberculous, fungal, syphilitic, protozoal, parasitic); idiopathic disorders; uremia; neoplasms, including primary tumors such as mesothelioma and tumors metastatic to the pericardium; myocardial infarction and aortic dissection with leakage into the pericardial sac; collagen vascular diseases (systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, scleroderma), trauma, and drug-induced (procainamide, hydralazine, isoniazid, minoxidil, phenytoin, anticoagulants, methysergide) disorders. These different etiologies also account for most cases of pleural effusions.<sup>9</sup>

In general, the mechanism of accumulation of pericardial fluid accumulation is injury or inflammation of the pericardium. Transudative fluids arise from obstruction of lymphatic channels, and exudative fluids occur from inflammatory, infectious, or autoimmune processes within the pericardium.

In general, pleural effusions result from disturbances in normal pleural fluid transport. There are three main mechanisms behind the disturbances—abnormalities in Starling equilibrium, increased capillary and mesothelial permeability, and obstruction of lymphatic drainage.<sup>10,11</sup> For instance, an inflammatory process may increase capillary and mesothelial permeability and elevate intrapleural oncotic pressure.<sup>10,11</sup>

### Cocaine and Thrombosis

The clinical finding of pulmonary embolus in the patient under discussion here may be explained in terms of the prothrombotic effects of cocaine. The drug promotes platelet aggregation and activation and enhanced production of throm-

boxane and plasminogen activator inhibitor, leading to thrombosis at sites of intense vasospasm.<sup>3</sup>

### Pulmonary Embolus as the Link Between Cocaine and Pleural Effusion

The patient under discussion in the prior case by Strong and colleagues<sup>1</sup> uses crack cocaine and has pleural effusion. It was these authors' contention that there was a causal relationship between the two, through an eosinophilic process. An eosinophilic pleural effusion was observed in this patient that mimicked an empyema, and glucocorticoids led to prompt resolution of the effusion. Inflammatory cytokines, including interleukin-5 (IL-5), IL-6, and IL-8, and a leak-mediating vascular endothelial growth factor were implicated.<sup>1</sup>

Like the patient whose case was reported by Strong and colleagues,<sup>1</sup> our patient had an exudative effusion, determined on the basis of Light's criteria. However, hypereosinophilia was not present in either serum or the effusions. In the most recently reported case series, pulmonary embolisms were associated with exudative pleural effusions in 30% of patients and tended to be small, unilateral, and on the ipsilateral side of the emboli.<sup>12</sup> The case reported here is different in that the effusions were large and bilateral. Restriction of cardiac contractility by the large pericardial effusion might also have promoted development of the bilateral pleural effusions.<sup>12,13</sup>

### Cardiac Toxicity and Pericardial Effusions Induced by Drugs and Pulmonary Emboli

Large pericardial and pleural effusions have been reported in association with chemotherapeutic

agents such as carmustine (BCNU), an alkylating agent that causes cardiopulmonary toxicity. Early use of glucocorticoids significantly reduced the BCNU-related pleural-pericardial toxicity.<sup>13</sup> Large pericardial effusions have been described in conjunction with pulmonary emboli, and timely insertion of catheters for their drainage was recommended because of the high probability of cardiac tamponade.<sup>13,14</sup>

It is possible that cocaine is related more than temporally to the pericardial and pleural effusions in our patient. One potential mechanism is that cocaine may promote development of the pulmonary emboli, which subsequently cause a pleural-pericardial syndrome.<sup>13-15</sup> Another alternative is that cocaine may cause direct toxicity similar to that caused by the chemotherapeutic drug just described.

An alternate, albeit speculative, theory of neurostimulation contends that a variety of physiologic and systemic stressors lead to an activation of the sympathetic nervous system with release of stress hormones, catecholamines, and renin.<sup>4</sup> Acute or repeated physiological stress by cocaine, and mediated by catecholamines and neuro-hormonal factors, may produce acute or chronic inflammatory changes in the pericardium.<sup>4</sup> Interestingly, minoxidil is a drug that is associated with pericardial and pleural effusions, and it shares a common pharmacology with cocaine, which is reflex activation of the sympathetic system and renin-angiotensin system.<sup>16-18</sup> More studies should be performed to better elicit the pharmacology of drug-induced pericardial effusions, as multiple mechanisms are likely, owing to the diverse categories of drugs that are involved. However, it could be possible that the pulmonary emboli

and pericardial and pleural effusions arose through independent processes in this patient whose case is discussed here.

### Conclusion

Our patient had concurrent pericardial and pleural effusions and pulmonary emboli associated with crack cocaine abuse. This case illustrates the broad differential diagnosis that the clinician must have when evaluating a patient with cocaine-induced chest pain or dyspnea. ❖

### Disclosure Statement

*The author(s) have no conflicts of interest to disclose.*

### Acknowledgment

*Katharine O'Moore-Klopf, ELS, of KOK Edit provided editorial assistance.*

### References

- Strong DH, Westcott JY, Biller JA, Morrison JL, Effros RM, Maloney JP. Eosinophilic "empyema" associated with crack cocaine use. *Thorax* 2003 Sep;58(9):823-4.
- Singh B, Greenebaum E, Cole R. Carbon-laden macrophages in pleural fluid of crack smokers. *Diagn Cytopathol* 1995 Nov;13(4):316-9.
- Wright MJ, Martin M, Goff T, Morgan J, Elworthy R, Ghoneim S. Cocaine and thrombosis: a narrative systematic review and in vivo studies. *Subst Abuse Treat Prev Policy* 2007 Sep 19;19:27.
- Black PH. Stress and the inflammatory response: a review of neurogenic inflammation. *Brain Behav Immun* 2002 Dec;16(6):622-53.
- Jones JH, Weir WB. Cocaine-induced chest pain. *Clin Lab Med* 2006 Mar;26(1):127-46.
- Levis JT, Garmel GM. Cocaine-associated chest pain. *Emerg Med Clin North Am* 2005 Nov;23(4):1083-103.
- Rashid J, Eisenberg MJ, Topol EJ. Cocaine-induced aortic dissection. *Am Heart J* 1996 Dec;132(6):1301-4.
- Wang RY. pH-dependent cocaine-induced cardiotoxicity. *Am J Emerg Med* 1999 Jul;17(4):364-9.
- Hoit BD. Pericardial disease and pericardial tamponade. *Crit Care Med* 2007 Aug;35(8 Suppl):S355-64.
- Haim DY, Lippmann ML, Goldberg SK, Walkenstein MD. The pulmonary complications of crack cocaine. A comprehensive review. *Chest* 1995 Jan;107(1):233-40.
- Baldwin GC, Choi R, Roth M, et al. Evidence of chronic damage to the pulmonary microcirculation in habitual users of alkaloidal ("crack") cocaine. *Chest* 2002 Apr;121(4):1231-8.
- Krishnan GS, Chaudhary V, Al-Janadi A, Ramanarayanan J, D'Silva KJ. BCNU toxicity presenting with a large pericardial and pleural effusion. *Ann Transplant* 2008;13(1):44-7.
- Stelzner TJ, King TE Jr, Antony VB, Sahn SA. The pleuropulmonary manifestations of the postcardiac injury syndrome. *Chest* 1983 Oct;84(4):383-7.
- Castaner A, Kostreva DR, Kampine JP. Changes in autonomic nerve activity during acute pericardial tamponade. *Cardiology* 1980;66(3):163-73.
- Jerjes-Sanchez C, Ibarra-Perez C, Ramirez-Rivera A, Padua-Gabriel A, Gonzalez-Carmona VM. Dressler-like syndrome after pulmonary embolism and infarction. *Chest* 1987 Jul;92(1):115-7.
- Houston MC, McChesney JA, Chatterjee K. Pericardial effusion associated with minoxidil therapy. *Arch Intern Med* 1981 Jan;141(1):69-71.
- Palomar E, Morales P, Sanz de Castro S, et al. Pleural effusion secondary to minoxidil in a peritoneal dialysis patient. *Nephrol Dial Transplant* 2004 Oct;19(10):2688.
- Shirwany A, D'Cruz IA, Munir A. Very large pericardial effusion attributable to minoxidil: resolution without drainage of fluid. *Echocardiography* 2002 Aug;19(6):513-6.

### Less Barbaric

The local manufacture of catgut from ox peritoneum, the distillation of alcohol, our main antiseptic, from rice, and the spinal use of cocaine as an anaesthetic helped to make surgery less barbaric than it might have been.

—Alfred E Coates, *Medical Journal of Australia*. 1946