Delirium and Pulmonary Embolism in the Elderly

To the Editor: Delirium, an acute confusional state, is a common, complex medical disorder associated with substantial morbidity and mortality among persons 65 years or older.[1] This potentially reversible cognitive disturbance is increasingly recognized as a sign of serious underlying illness.[1] Despite the fact that hypoxia is a well-known precipitating factor for delirium and that pulmonary embolism (PE) is a common cause of hypoxia, neither customary medical practice nor recent reviews[1-4] specifically consider delirium as a possible presentation of PE. We describe 5 elderly patients with delirium in whom PE was subsequently diagnosed. We suggest a causal relationship between both entities.

From January 2003 to December 2007, 215 consecutive adult patients at our hospital were diagnosed as having PE. Of these 215 patients, 5 presented with clinical features of delirium (Table). These 5 patients were all older than 72 years and had 1 or more predisposing factors for delirium, including older age, cognitive impairment, severe illness, fracture, and surgery. No metabolic or electrolyte disturbances were evident, and intravascular volume appeared normal. Moreover, none of the admission medications were discontinued during hospitalization. After ruling out common causes of delirium, we suspected PE as a precipitating factor because of chest pain and left calf swelling (patient 1), acute dyspnea (patient 2), sudden worsening dyspnea (patient 3), and otherwise unexplained D-dimer level increase (patients 4 and 5). In addition, PE was suspected in one patient (patient 4) because of the clinicians' recent experience with the first 3 patients. High-probability ventilation-perfusion lung scans were obtained in patients 1 through 4 (bilateral findings in patients 1, 3, and 4 and right-sided alterations in patient 2). Specifically, the lung scan performed in patient 3 was regarded as high probability even in light of the patient's prior lung disease. Chest computed tomography revealed signs of bilateral pulmonary embolic disease in patient 5. All 5 patients received sequential therapy with subcutaneous dalteparin (100 UI/kg every 12 hours) and warfarin. Delirium resolved within 2 to 5 days after anticoagulation was initiated. No new episodes of delirium or PE developed after these patients were discharged.

Elderly patients can experience delirium secondary to almost any acute condition, including simple conditions like untreated urinary tract infection, urinary retention, constipation, colds, and undermanaged pain, and more serious causes including a variety of vascular conditions such as myocardial infarction, cerebral ischemia, and PE. Delirium may complicate PE in patients with other evidence of the disease but occasionally may be the sole evidence (other than increased D-dimer level) of PE, as occurred in 2 of our patients. Moreover, the diagnosis of PE "is missed more often than it is made,"[2] in part because of its frequent atypical presentations.[2,5] We believe that delirium in the elderly should be regarded as an atypical presentation of PE. Consequently, when clinicians search for the underlying cause of delirium, they should remember that PE is one of the many acute conditions that can cause delirium in the elderly. Although PE-related hypoxemia, acute ventricular impairment, hypotension, and/or paradoxical embolism could

TABLE. **Characteristics of the Patients**[a]

Patient No./ age (y)/sex	Relevant prior conditions	Psychomotor variant of delerium	Setting in which delirium occurred	Duration of delirium before PE diagnosis	Pa_{O_2} when PE was suspected (mm Hg)	D-dimer[b] (ng/mL)	Imaging test for PE diagnosis[c]	Treatment/ clinical outcome
1/72/M	Mild cognitive impairment Prostatic adenocarcinoma	Hyperactive	Outpatient	35 d	51	NP	Lung scanning	Anticoagulation/ delirium resolved 5 d
2/72/F	None	Hyperactive	Inpatient (RFF, preoperative period)	18 h	59	7750	Lung scanning	Retrievable IVCF, anticoagulation/ delirium resolved 2 d
3/85/M	Severe COPD	Hyperactive	Inpatient (acute exacerbation of COPD)	1 d	47	4370	Lung scanning	Anticoagulation/ delirium resolved 3 d
4/73/F	Hypertension	Hypoactive	Outpatient	2 d	83	650	Lung scanning	Anticoagulation/ delirium resolved 3 d
5/79/M	Mild cognitive impairment	Hyperactive	Inpatient (CS and IHS, post-operative state	20 d	52	18,370	Chest CT	Anticoagulation/ delirium resolved 5 d

[a] COPD = chronic obstructive pulmonary disease; CS = cataract surgery; CT = computed tomography; IHS = inguinal hernia surgery; IVCF = inferior vena caval filter; NP = not performed; PE = pulmonary embolism; RFF = right femoral fracture.
[b] Normal level <500 ng/mL.
[c] Echocardiography was not performed.

work to explain this "lung-brain connection," the mechanisms remain unknown.

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1. Inouye SK. Delirium in older persons [published correction appears in *N Engl J Med*. 2006;354(15):1655]. *N Engl J Med*. 2006;354(11):1157-1165.
2. Laack TA, Goyal DG. Pulmonary embolism: an unsuspected killer. *Emerg Med Clin North Am*. 2004;22(4):961-983.
3. Goldhaber SZ. Pulmonary embolism. *Lancet*. 2004;363(9417):1295-1305.
4. Tapson VF. Acute pulmonary embolism. *N Engl J Med*. 2008;358(10): 1037-1052.
5. Shaw JE, Belfield PW. Pulmonary embolism: a cause of acute confusion in the elderly. *Postgrad Med J*. 1991;67(788):560-561.

Midventricular Variant of Transient Apical Ballooning: A Likely Demonstration of Its Pathophysiologic Mechanism

To the Editor: Transient apical ballooning (TAB) probably comprises a spectrum of transient ventricular dysfunctional patterns that lead to typical apical ballooning or midventricular, basal, or biventricular dyskinesia.[1-4] Herein, I introduce a theory regarding the pathophysiologic mechanism of the midcavity variant on the basis of a recent case.

A 71-year-old African American woman was admitted to a hospital elsewhere because of severe chest pain. Coronary angiography revealed mild atherosclerotic plaques. Ventriculography showed akinesia of the mid left ventricle, with well-preserved apical contractility (Video 1). Carvedilol and losartan were prescribed for hypertension. While continuing to have episodes of resting chest pain relieved by nitroglycerin, the patient came to our hospital for endoscopic evaluation of severe abdominal pain and chest pain with ST-T changes. Echocardiography (Video 2) revealed recurrent mid left ventricular (LV) akinesia, with preserved apical wall motion (ejection fraction, 30%). Troponin levels peaked at 1.5 ng/mL (to convert to μg/L [SI unit], multiply by 1.0). Chest pain quickly diminished after sublingual nitroglycerin. Two days later, repeated heart catheterization showed near-normal LV function (ejection fraction, 60%) and no coronary obstruction. Infusion of intracoronary acetylcholine (50 μg for 2 minutes) to detect endothelial dysfunction produced severe chest pain, T-wave changes, and diffuse narrowing of the diagonal, ramus medianus, and 2 marginal branches (Figure, left), with a Thrombolysis in Myocardial Infarction (TIMI) 0 flow pattern. The left anterior descending artery had TIMI-2 flow (Figure, left). Intracoronary nitroglycerin, 100 μg, promptly resolved these changes (Figure, right). Five minutes later, intracoronary acetylcholine (50 μg) was administered, with continuous echocardiographic monitoring. This infusion reproduced chest pain, electrocardiographic changes, and ventricular dysfunction of midcavity TAB (Video 3, clips 1 and 2). After repeated intracoronary nitroglycerin administration, these changes resolved in less than 30 seconds (Video 3, clip 3). Three days after her condition stabilized, the patient was discharged home with a treatment regimen of extended-release diltiazem (240 mg), nitrates, and L-arginine (1000 mg every 8 hours). At 6-month follow-up examination, she was symptom free; electrocardiography and LV contractility were normal.

Previously, in a small pilot study involving typical TAB,[5] I found that acetylcholine stimulation produced severe spasm of all coronay branches. I suggest that the midcavity variant results from similar intense, spontaneous spasticity that affects the diagonal, ramus, and circumflex branches and to a much lesser extent the left anterior descending artery. The patient's dominant circumflex pattern may have been important in causing the inferior/mid LV contractile changes.

Indeed, TAB involving any distribution seems to feature severe coronary reactivity to acetylcholine testing, characterized by sustained, diffuse spasticity that can induce myocardial stunning, unlike short-lived spontaneous spasm in Prinzmetal angina.[5] Intracoronary nitroglycerin can quickly

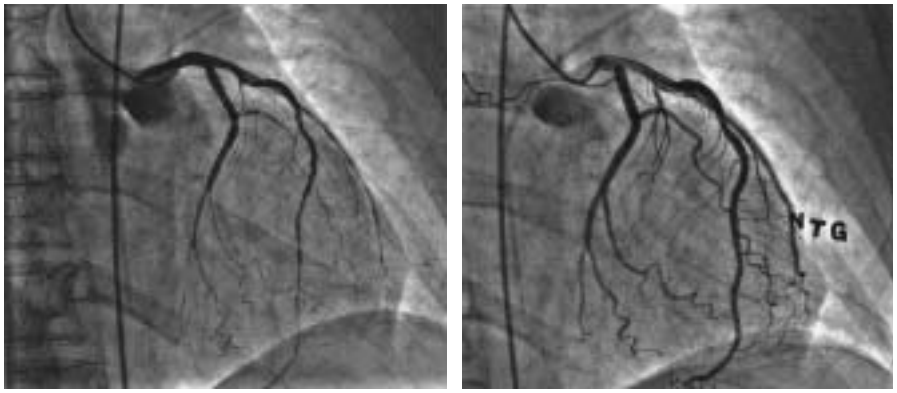

FIGURE. Coronary angiograms of the left side obtained during coronary infusion of acetylcholine (50 μg) (left) and after intracoronary nitroglycerin (NTG) administration (right) (see text).

resolve such episodes.[5] This degree of spasticity is unlike that seen in common coronary endothelial dysfunction. TAB variants seem to involve selective, not generalized, endothelial dysfunction.

The current case provides important evidence (although not final proof) that in any form of TAB, early echocardiographic LV monitoring can document acetylcholine-related reproduction of contractile dysfunction and its normalization after intracoronary nitroglycerin infusion.[5] This case supports my general theory regarding TAB[5] while explaining the midcavity variant. Generally, TAB seems to involve a spectrum of varying clinical patterns that depend on precipitating factors (which could be overwhelming in the presence of relatively "normal" endothelial function) and baseline endothelial dysfunction (which, when generalized, would be associated with recurrent apical TAB, but, when selective, would lead to atypical TAB variants).

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1. Abe Y, Kondo M, Matsuoka R, Araki M, Dohyama K, Tanio H. Assessment of clinical features in transient left ventricular apical ballooning. *J Am Coll Cardiol.* 2003;41(5):737-742.
2. Bybee KA, Kara T, Prasad A, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST-segment elevation myocardial infarction. *Ann Intern Med.* 2004;141(11):858-865.
3. Wittstein IS, Thiemann DR, Lima JA, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med.* 2005; 352(6):539-548.
4. Kurowski V, Kaiser A, von Hof K, et al. Apical and midventricular transient left ventricular dysfunction syndrome (tako-tsubo cardiomyopathy): frequency, mechanisms, and prognosis. *Chest.* 2007 Sep;132(3):809-816. Epub 2007 Jun 15.
5. Angelini P. Transient left ventricular apical ballooning: a unifying pathophysiologic theory at the edge of Prinzmetal angina. *Catheter Cardiovasc Interv.* 2008;71(3):342-352.

Supplemental videos are linked to the full-text version of this article at www.mayoclinicproceedings.com.

VIDEO 1. Left ventricular cineangiograms.
VIDEO 2. Left ventricular video-echocardiograms of a recurrent episode.
VIDEO 3. Motion echocardiogram of the left ventricle at baseline (clip 1), after acetylcholine administration (clip 2), and after nitroglycerin infusion (clip 3), showing the onset of transient midventricular akinesia without apical ballooning.

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