A 64-year-old diabetic and dyslipidemic woman was admitted to our hospital with a history of 3 episodes of acute pulmonary edema in the past 4 months, without evidence of organic heart disease. She was affected by a hypopituitarism and was treated with levothyroxine and desmopressin. She had atypical chest pain 1 year before, but 2 exercise stress tests were negative. In the past 4 months, she had been admitted 3 times for severe dyspnea at rest of sudden onset without chest pain, requiring endotracheal intubation because of severe acute pulmonary edema. Basal physical examination was normal. ECGs and serial troponin levels were normal. Clinical treatment was successful with early extubation. Echocardiography (echo) at rest was completely normal with normal left ventricular systolic and diastolic function and no valvular regurgitations. Coronary angiography revealed normal coronary arteries and normal global and regional left ventricular systolic motion. Thoracoabdominal computerized tomography was normal; and pulmonary thromboembolism, aortic disease, and suprarenal tumor were ruled out. Pulmonary biopsy also was normal. Laboratory tests including hemoglobin, electrolytes, autoantibodies, catecholamine, and thyroid hormones were also normal. Holter and telemetry did not reveal arrhythmias. Gated single-photon emission computed tomography and stress echo were negative for ischemia. Most of the causes for cardiogenic and noncardiogenic pulmonary edema were ruled out. Although coronary arteries were angiographically normal, we thought that in a diabetic and dyslipidemic woman, coronary spasm or endothelial dysfunction had to be ruled out as a possible cause of severe recurrent acute pulmonary edema. As a consequence, the patient was sent back to the catheterization laboratory where right heart catheterization, transthoracic echocardiography, and coronary angiography were performed under basal conditions and after left intracoronary infusion of increasing doses of acetylcholine (20, 50, and 100 μg in 2 minutes). The maximal dose of acetylcholine induced severe vasospasm in the medium and the distal segments of both anterior descending artery and circumflex artery (Figure 1), associated with chest pain, severe dyspnea, ST-T changes in the ECG (Figure 2), moderate mitral regurgitation, severe left ventricular systolic dysfunction (ejection fraction, 34%; previous, 62%; Figures 3 and 4), and a remarkable increase in pulmonary capillary wedge pressure from 10 mm Hg at rest to 40 mm Hg (Figures 5 and 6). After intracoronary nitroglycerin administration, symptoms, ECG changes, echo abnormalities, coronary spasm, and elevated pulmonary capillary wedge pressure levels disappeared in <2 min-

**Figure 1.** Angiography showing severe spasm in both medium and distal segments of left anterior descending artery and left circumflex coronary artery (arrows) which improve after nitroglycerin infusion. Basal condition (A), angiography after intra coronary acetylcholine infusion (B), and release of coronary spasm after intracoronary nitroglycerin (C). Post-ACT indicates after intra coronary acetylcholine; post-NTG, after intra coronary nitroglycerin.
utes. The patient recognized the clinical symptoms induced in the catheterization laboratory as those she had been suffering during the spontaneous episodes. She was discharged with calcium antagonists and nitrates. During the 6 months of follow-up, she has been asymptomatic.

Discussion

Coronary vasospasm is the main mechanism of dynamic coronary artery stenosis and has been associated with many ischemic heart disease manifestations1 (angina, myocardial infarction, syncope, or sudden death). Although less fre-
quently described, coronary spasm also has been related with acute pulmonary edema due to severe left ventricular dysfunction or papillary muscle ischemia causing mitral regurgitation.\textsuperscript{2,3} We reported a patient who initially denied chest pain preceding the episode of acute pulmonary edema without ECG changes at rest and with negative troponins. All initial studies seeking for cardiac etiologies of severe acute pulmonary edema, however, were negative and excluded exercise-induced myocardial ischemia. Nevertheless, intracoronary acetylcholine demonstrated severe left coronary spasm, which precisely reproduced symptoms and was associated with important ECG, hemodynamic, and echo changes. Severe left ventricular systolic dysfunction and mitral regurgitation, which improved after nitroglycerin infusion, were

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure4.png}
\caption{M-mode echocardiography at rest (A), after acetylcholine infusion (B), and after nitroglycerin infusion (C). Echocardiography shows severe acute left ventricular dysfunction after acetylcholine infusion (decreased ejection fraction and increased diastolic and systolic left ventricular diameters) that normalizes after nitroglycerin infusion. Post-ACT indicates after acetylcholine infusion; post-NTG, after nitroglycerin infusion.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure5.png}
\caption{Changes in systemic arterial blood pressure and pulmonary capillary wedge pressure after acetylcholine infusion at rest (A) and with symptoms after acetylcholine infusion (B). AoP indicates aortic pressure; PCWP, pulmonary capillary wedge pressure.}
\end{figure}
Pressure Results (mmhg)

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Figure 6. Changes in aortic and pulmonary capillary wedge pressure (medium, A wave and V wave) at rest and during acetylcholine test. A wave indicates A wave of the pulmonary capillary wedge pressure; ACT MAX, after the highest acetylcholine doses infusion; AO, aortic pressure; Dias, diastolic aortic pressure; HR, heart rate; Mean, mean pulmonary capillary wedge pressure; PA, pulmonary artery pressure; PCW, pulmonary capillary wedge pressure; Post-NTG, after nitroglycerin infusion; Sys, systolic aortic pressure; V wave, V wave of the pulmonary capillary wedge pressure.

documented. Echo performed during acetylcholine test infusion in a supine position revealed mitral regurgitation, which was absent before the test. The patient did not suffer another episode of acute pulmonary edema in the catheterization laboratory because of the short duration of the coronary spasm induced by acetylcholine, which was reversed with nitrates. However, the severity of left ventricular dysfunction, the development of mitral regurgitation, and the striking increase in pulmonary capillary wedge pressure induced by coronary spasm may be the physiopathologic mechanism that leads to acute pulmonary edema. On the other hand, although desmopressin has not been linked to coronary spasm, its role in favoring its presence in our patient cannot be ruled out. The case herein reported is of particular relevance because it documents that in patients with idiopathic acute pulmonary edema, coronary spasm might be a possible cause and should be considered in the differential diagnosis.

Disclosures

None.

References

Recurrent Severe Acute Pulmonary Edema Caused by Transient Left Ventricular Insufficiency With Mitral Regurgitation Related to Severe Coronary Artery Spasm
Oscar Alcalde, Enric Domingo and Jaume Figueras

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