obstruction.

This unusual presentation of aortic dissection serves to highlight the myriad clinical manifestations of this disease process.

ACKNOWLEDGMENT: The authors thank Louise Funke for preparation of the manuscript and Dr. M. Bourke for supplying the photograph of the patient.

REFERENCES

1 Eagle KA, DeSanctis RW. Aortic dissection. Current Prob Card 1989; May:229-78
5 Kahn SE, Kolter MN, Goldman AP, Abalaza S. Superior vena cava obstruction secondary to acute dissecting aneurysm of the aorta. Am Heart J 1986; 111:606-08
7 Calenda DG, Urichioe JP. Superior vena cava syndrome, differentiation between simple obstruction and aortocaval communication. Arch Intern Med 1983; 91:800

Noncardiogenic Pulmonary Edema Complicating Massive Diltiazem Overdose*

Vernon H. Humbert, Jr., M.D., F.C.C.P.;† Nancy J. Munn, M.D.;‡ and Randall F. Hawkins, M.D.

Non-cardiogenic pulmonary edema has not been previously described in calcium channel blocker overdose. We describe a case of non-cardiogenic pulmonary edema occurring during the course of therapy for massive diltiazem overdose in a young patient with anorexia nervosa. Review of the current literature suggests that major and minor pulmonary complications occur with some frequency in the setting of calcium channel blocker overdose although their exact incidence remains unclear. (Chest 1991; 99:258-60)

Although mild arterial desaturation is common after calcium channel blocker overdose, no well-documented case of non-cardiogenic pulmonary edema in this setting has previously been reported. Prior reports of pulmonary edema occurring after calcium channel blocker use have generally ascribed the condition to negative inotropy related to the drug or to fluid resuscitation during overdose-induced hypotension.

CASE REPORT

A 30-year-old nurse was hospitalized after having been found apathetic and unable to ambulate. She was known to be taking diltiazem for migraine headaches and had a long history of stress disorder and depression and had previously been evaluated for anorexia nervosa.

On examination, she was lethargic but responsive to noxious stimuli. The blood pressure varied from 58/32 mm Hg to 90/60 mm Hg and the pulse from 35 to 45 per minute. The respiratory rate was 18. She had warm skin and full pulses distally.

The initial chest radiograph showed a very small heart, no infiltration, and a paucity of vascular markings. The electrocardiogram showed atrial inactivity with a slow ventricular escape rhythm. Arterial blood gases on a 100 percent rebreathing mask revealed a blood pH of 7.23, Pco2 of 27 mm Hg, and a PaO2 of 306 mm Hg. The initial serum albumin level was normal.

Initial therapy with atropine, isoproterenol and calcium gluconate raised the heart rate to 45 to 50 per minute; sinus bradycardia alternated with ventricular escape rhythm. Infusions of saline solution (totaling 4 L during the first 24 hours) and dopamine gradually raised the blood pressure to a consistent 90/60 mm Hg over several hours. Urine flow remained copious.

After 24 hours of steady improvement, the patient developed shortness of breath and suffered respiratory arrest. Endotracheal intubation and mechanical ventilation were promptly instituted. Repeat chest radiograph showed uniformly diffuse pulmonary infiltrates without change in heart size (Fig 1). Mechanical ventilation with 100 percent oxygen and positive end-expiratory pressure of 15 cm H2O was needed to elevate the PaO2 to 67 mm Hg. Hemodynamic measurements from a flow-directed catheter revealed a pulmonary artery pressure of 32/12 mm Hg and a pulmonary capillary wedge pressure of 9 mm Hg. Cardiac output by thermodilution was 6.50 L/min (5.07 L/min/m²). Although extensive bacterial cultures later proved negative, she developed a fever of 38.3°-38.6°C 36 hours after intubation. Therapy with broad

![Figure 1. Chest radiograph shortly after endotracheal intubation showing diffuse, uniform pulmonary infiltration and a small cardiac silhouette compatible with non-cardiogenic pulmonary edema.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=data/journals/chest/21623/ on 06/22/2017)
spectrum antibiotics was begun. With continuous ventilatory support and diuretic therapy, the chest radiograph and arterial blood gas levels gradually returned to normal and fever subsided. A transient major rise in creatine kinase with negative MB isoenzyme fraction was noted with lesser elevations of total lactic dehydrogenase and alanine aminotransferase. Urine drug screens were trace-positive for barbiturates and tricyclic anti-depressants. Diltiazem was present in "massive" quantity by semi-quantitative thin layer chromatography.

**DISCUSSION**

We present a clearcut case of noncardiogenic pulmonary edema occurring in association with a massive ingestion of diltiazem. We can only speculate as to the relative effects of the drug itself and of the patient’s rather prolonged shock-like state on the genesis of the pulmonary edema. Hypotension of similar severity and duration has been reported after verapamil overdose without development of overt pulmonary edema. The pulmonary artery pressure values and normal cardiac index exclude myocardial depression as an etiologic factor. Fluid resuscitation alone probably could not explain the profound arterial desaturation and pulmonary inflation in the absence of unusual pulmonary capillary leakiness. There was no suggestion that aspiration pneumonia played a role in the patient's pulmonary deterioration.

There are few reports of diltiazem overdose in the English language. Of ten prior cases of diltiazem overdose with adequate data available, all had bradycardic rhythms (sinus bradycardia and/or heart block), nine had hypotension, and one who died had "cyanosis." Calcium infusion, anticholinergics, and catecholamine infusions have been used with variable success in restoring unstable hemodynamics in calcium channel blocker overdose, commonly failing to restore blood pressure and pulse rate adequately for some hours, as in our patient.

Pulmonary edema has previously been noted after nifedipine overdose in a patient whose clinical picture and response to initial therapy approximated our patient's but whose duration of sustained hypotension was probably somewhat less. Pulmonary edema has also been noted at autopsy after verapamil overdose and "pneumonia" requiring mechanical ventilation (for 11 days) and positive end-expiratory pressure was required on the second day of a diltiazem overdose complicated by a short period of hypotension. Arterial desaturation presumably due to ventilation-perfusion mismatch appears relatively common in the setting of verapamil overdose; the possibility that these episodes of modest desaturation may represent incipient or subclinical pulmonary capillary leak has never been addressed.

Multiple mechanisms appear to underlie the various forms of drug-induced noncardiogenic pulmonary edema. Mechanisms implicated in drug overdose pulmonary edema include inhibition of prostacyclin synthesis (aspirin) and mast cell degranulation (opioid overdose). Reported effects of calcium entry blockers on prostacyclin synthesis are contradictory. Although nifedipine has been reported to suppress calcium infusion-mediated increases in prostacyclin metabolism, diltiazem has been reported to increase vascular prostacyclin synthesis. Mast cell membranes appear to be stabilized by calcium entry blockers. Calcium entry blockers are well known to cause selective systemic pre-capillary vasodilation with associated peripheral edema. A similar mechanism may contribute to excessive pulmonary capillary transudation in calcium blocker overdose.

Serious pulmonary embarrassment may result in the course of calcium channel blocker overdose, although attention has not previously been drawn to this possibility and its potential frequency remains to be established. We recommend prompt institution of cardiac pacing if catecholamines, anticholinergics, and calcium infusion fail to quickly improve bradycardic rhythms in this setting. Hypotensive but well perfused patients probably should not be overly challenged with crystalloid in the absence of clearcut pre-existent volume depletion.

**REFERENCES**

5. Jakubowski AT, Migala HF. Effect of diltiazem overdose. Am J Cardiol 1987; 60:932-33
6. Data on file, Marion Laboratories, Kansas City, Missouri