

Severe coughing during captopril and enalapril therapy

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Captopril and enalapril maleate are angiotensin-converting-enzyme inhibitors used in the treatment of hypertension.¹ The following case illustrates the apparently causal relation between both of these drugs and severe coughing.

Case report

A woman with renovascular hypertension due to occlusion of the left renal artery and mild stenosis of the right, along with essential tremor and rheumatoid arthritis, first had respiratory problems in 1980, at the age of 61 years, when a diagnosis of gold-induced interstitial pneumonitis was made. She recovered completely when gold therapy was stopped.

Although her renal artery disease was not amenable to balloon angioplasty and her hypertension had proved resistant to a variety of treatment regimens, the patient remained opposed to surgical intervention. She responded to captopril when this medication became available. About the same time she also began treatment with penicillamine for her arthritis. Within a few weeks urticaria developed; it cleared when the penicillamine was withdrawn.

After about 1 year of captopril and propranolol therapy a severe cough developed. It was usually worse at bedtime and was sufficiently severe that it interfered with sleeping and caused emesis. There was no history of wheezing or dyspnea. Examination by a specialist in chest diseases and standard tests of respiratory function (measurement of the forced expiratory volume in 1

second, forced vital capacity, peak expiratory flow rate and diffusing capacity of the lung for carbon monoxide) revealed no significant abnormality.

Because of concern about possible nocturnal airways reactivity related to the use of a β -blocker, the propranolol therapy was stopped. The coughing persisted and the tremor worsened, so propranolol therapy was reinstated; the coughing was unaltered. Early in 1985 the captopril therapy was stopped, and the coughing resolved within 3 to 4 weeks.

When other medications failed to control the patient's blood pressure, emergency release was requested for enalapril, a new inhibitor of angiotensin converting enzyme devoid of the sulfhydryl group thought to be responsible for some of the adverse effects of captopril.¹ The patient conducted three separate challenges with enalapril. She reported that she could tolerate the drug for about a month before coughing recurred and that the coughing resolved within 7 to 10 days of stopping enalapril therapy. In May 1985 this outcome and the probable association were reported to the manufacturer.

Comments

In August 1985 a report from Japan described a single case of a persistent dry cough associated with captopril therapy.² Five months later a series of four cases, one associated with captopril and three with enalapril therapy, was reported from Scotland.³ The difficulty in recognizing coughing as an adverse effect of these drugs is highlighted by the long duration of coughing before diagnosis in each of these cases.

Although a common mechanism related to the inhibition of angiotensin converting enzyme was postulated in both of the previous reports, my patient is the first with documented coughing after exposure to both captopril and enalapril. The speculation of Semple and Herd³ that accumula-

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tion of kinins, whose breakdown is also inhibited by these drugs, promotes coughing or bronchospasm in susceptible individuals is nevertheless difficult to accept given the relative frequency with which these drugs are used in patients for whom β -blockers are contraindicated because of airways reactivity, along with the apparent rarity of the adverse effect. Furthermore, kinins are thought to be cleared quickly, and accumulation of either drug is unlikely in view of their usually short half-lives.¹

In my patient the development of pneumonitis with gold therapy, urticaria with penicillamine therapy and coughing with both captopril and enalapril therapy may have been coincidental, but

one is certainly tempted to speculate that a common toxicologic mechanism was responsible.

References

1. Douglas WW: Polypeptides — angiotensin, plasma kinins, and others. In Gilman AG, Goodman LS, Rall TW et al (eds): *Goodman and Gilman's The Pharmacological Basis of Therapeutics*, 7th ed, Macmillan, New York, 1985: 639-659
2. Sesoko S, Kaneko Y: Cough associated with the use of captopril. *Arch Intern Med* 1985; 145: 1525
3. Semple PF, Herd GW: Cough and wheeze caused by inhibitors of angiotensin-converting enzyme [C]. *N Engl J Med* 1986; 314: 61

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Date

Title

Place and city

Contact person and telephone number

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September

Sept. 8-12, 1986

Organ Imaging Review — Toronto 1986

Four Seasons Hotel, Toronto

Dr. Edward Kassel, program coordinator, Department of Radiology, University of Toronto, 139 FitzGerald Bldg., Toronto, Ont. M5S 1A8; (416) 978-6801

Sept. 15-19, 1986

Annual Conference of the Canadian Society of Forensic Science

Sheraton Brock Hotel, Niagara Falls, Ont.

Mrs. JoAnne Cottingham, executive secretary, Canadian Society of Forensic Science, 215-2660 Southvale Cres., Ottawa, Ont. K1B 4W5; (613) 731-2096

Sept. 21, 1986

Community Approaches to High Blood Pressure Prevention and Control
Toronto

Dr. Karen Mann, Hypertension Unit, Camp Hill Hospital, 1763 Robie St., Halifax, NS B3H 3G2; (902) 423-1371

Sept. 21-25, 1986

Royal College of Physicians and Surgeons of Canada annual meeting

Harbour Castle Conference Centre and Westin Hotel, Toronto

Royal College of Physicians and Surgeons of Canada, 74 Stanley Ave., Ottawa, Ont. K1M 1P4; (613) 746-8177

Sept. 24-26, 1986

Canadian Psychiatric Association 36th annual meeting
Westin Bayshore Hotel, Vancouver

Mrs. Lea C. Métiévier, chief administrative officer, 103-225 Lisgar St., Ottawa, Ont. K2P 0C6; (613) 234-2815

Sept. 25-27, 1986

Physician Manager Institute 1986: Leadership Skills Development

Fern Resort Ltd., Orillia, Ont.

Mr. Chuck Shields, Canadian College of Health Service Executives, 201-17 York St., Ottawa, Ont. K1N 5S7; (613) 235-7218 or Mr. Joe Chouinard, Canadian Medical Association, 1867 Alta Vista Dr., Ottawa, Ont. K1G 3Y6; (613) 731-9331

Sept. 28-30, 1986

Tri-Disciplinary Conference for the Senior Management
Team: Physician, Nurse & Administrator

Delta Airport Inn Resort, Vancouver

Canadian College of Health Service Executives, 201-17 York St., Ottawa, Ont. K1N 5S7; (613) 235-7218

Sept. 28-Oct. 1, 1986

Sixth International Seminar on Terminal Care
Montreal

Dr. Balfour M. Mount, director, Palliative Care Service, Royal Victoria Hospital, 687 Pine Ave. W, Montreal, PQ H3A 1A1; (514) 842-0863