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Tobis, J
Das, BN

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must be regarded as potential pathogens when isolated from patients with hematologic neoplasia. Bacteriology laboratories should be urged to evaluate these isolates fully in appropriate cases. If specific therapy seems appropriate, the initial antibiotic treatment should include gentamicin until antibiotic sensitivity testing is completed. The prognosis

for this infection seems especially poor in this population of patients.

Nonproprietary Names and Trademarks of Drugs

Cephalothin sodium—*Keflin*.
Gentamicin sulfate—*Garamycin*.
Carbenicillin disodium—*Pyopen*.

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Cardiac Complications in Amitriptyline Poisoning Successful Treatment With Physostigmine

Jonathan Tobis, MD, Bodh N. Das, MD

THE USE of tricyclic antidepressant medications is increasing as a form of self-poisoning. There have been a number of reports of the anticholinergic effects of amitriptyline hydrochloride and imipramine hydrochloride.¹ Although many cases of cardiotoxicity have been reported,² there is little information concerning the treatment of the serious cardiac complications. Physostigmine salicylate has been used successfully to treat the central effects of tricyclic antidepressants, such as agitation, seizures, and coma, as well as their peripheral effects, such as tachycardia.³ We have used this drug in treating a young woman who had a cardiac arrest subsequent to an amitriptyline overdose. To our knowledge, this is the first reported case of amitriptyline poisoning in which malignant arrhythmias and conduction defects were successfully treated with physostigmine.

Report of a Case

A 22-year-old woman ingested an estimated 750 to 1,000 mg of amitriptyline hydrochloride (Elavil) on March 25, 1975. She was brought to the Lincoln Hospital emergency room two hours later in a severely agitated state, and she became progressively obtunded. An electrocardiogram showed a wide QRS complex with a rate of

125 to 135 beats per minute (Fig 1, A). Physostigmine salicylate was given intravenously in three successive 2-mg doses. Each injection produced only minimal responses in level of consciousness, diminution of pupil size, and decrease of the

tachycardia.

The patient was transferred to the intensive care unit where an ECG showed sinus tachycardia (115 beats per minute) with some variation of PR interval, right bundle-branch block with left axis deviation.

Fig 1.—A, Initial cardiogram (March 25, 1975, 3 PM) (lead II) shows supraventricular tachycardia with wide QRS complex. B, Lead II rhythm strip taken six days after ingestion of amitriptyline (April 1, 1975) shows sinus rhythm with frequent atrial premature contractions. C, Lead V₁ rhythm strip taken seven days after overdose (April 2, 1975, 2 PM) shows atrioventricular dissociation with junctional rhythm and premature contractions. D, Lead II rhythm strip shows restoration of normal sinus rhythm following 2 mg of physostigmine given intravenously (April 2, 1975, 2:20 PM).

From the University of California at Irvine (Dr Tobis), and Lincoln Hospital, Bronx, NY (Dr Das).

Reprints not available.

Fig 2.—First 12-lead cardiogram shows supraventricular tachycardia of 115 beats per minute, right bundle-branch block with left axis deviation (-120°), and QRS complex of 0.16 sec (March 25, 1975, 6 PM).

tion (-120°), and a QRS complex of 0.16 sec (Fig 2). The rate increased to 140 beats per minute and soon thereafter the monitor showed a ventricular tachycardia, and the pulse became unobtainable. External cardiac massage was begun. Lidocaine, 100 mg given intravenously, suppressed the ventricular focus, and treatment with physostigmine was reattempted. The QRS complex began to narrow, and the rate slowed. A total of 22 mg of physostigmine salicylate was given over the following 48 hours to maintain the heart rate under 110 beats per minute. The patient was alert by the morning of March 26; an ECG demonstrated a narrow QRS complex with an axis of $+60^\circ$ and an incomplete right bundle-branch block (Fig 3).

On April 1, six days after the ingestion of amitriptyline, an ECG showed frequent atrial premature contractions, for which she was not treated (Fig 1, B), and she was discharged. On the following day, she complained of dizziness and returned to the emergency room. An ECG disclosed atrioventricular dissociation with frequent junctional premature contractions (Fig 1, C). One mg of physostigmine salicylate was given intravenously, with no response after five minutes. A repeat dose of 1 mg of physostigmine salicylate given intravenously induced a general tonic-clonic seizure, during which time her ECG converted to normal sinus rhythm (Fig 1, D). She subsequently remained in good health.

Comment

Earlier reports of physostigmine in the treatment of anticholinergic poisoning dealt predominantly with the neurologic complications or the more benign cardiac effects such as tachycardia. Our patient exemplifies some of the more severe cardiac complications of amitriptyline, such as the abnormal conduction pathways, atrioventricular dissociation, and ventricular tachycardia. These abnormalities were suppressed with conversion to sinus rhythm by physostigmine salicylate, 22 mg given over 48 hours—a higher total dose than is usually required to treat the central nervous system complications. Prolonged atrioventricular conduction disturbances can persist for an extended

Fig 3.—Cardiogram after treatment with physostigmine (March 26, 1975, 10 AM) shows sinus rhythm with incomplete right bundle-branch block and an axis of $+60^\circ$.

period and may respond to physostigmine, but the drug must be given cautiously to avoid inducing seizures.

It is believed that the tachycardia of amitriptyline poisoning occurs through competitive blockade of acetylcholine receptors, resulting in an increased sympathetic tone. It is unclear how the tricyclic antidepressants induce the high degree of

heart block and conduction abnormalities. Available experimental evidence indicates that amitriptyline may exert a direct myocardial toxic effect² and that physostigmine may be effective in reversing the cardiotoxic properties.

Alan Ross, MD, Larry Klecatsky, MD, and the Lincoln Collective provided guidance.

Nonproprietary Names and Trademarks of Drugs

Amitriptyline hydrochloride—*Elavil*.
Physostigmine salicylate—*Esromiotin*.

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Pituitary Abscess Following General Sepsis in a Diabetic Patient

Yiechul Jung, MD; Jae Dong Kim, MD; Rajagopal Chadaga, MD; Joseph Tandatnick, MD; Leonard P. Caccamo, MD

SINCE Glinski¹ and Simmonds² in 1913 and 1914 described pituitary abscesses accompanying systemic bacterial infection there have been only two such reports in the world literature.^{3,4}

We now report the case of a patient with diabetes mellitus and fatal *Escherichia coli* septicemia in whom severe hypoglycemic reactions developed. An abscess of the pituitary gland was found on postmortem examination.

Report of a Case

A 47-year-old woman with a ten-year history of diabetes mellitus was admitted to the hospital because of agitation and disorientation. Her temperature was 38°C, pulse rate 120 beats per minute, and blood pressure 70/50 mm Hg.

She had been taking 40 units of isophane insulin suspension daily, with good control of diabetes and without any history of hypoglycemia or ketoacidosis. On admission, blood glucose level was 400 mg/100 ml with glycosuria (3+) and albuminuria (3+), as well as many white blood cells (WBC) per high power field. No acetone was detected in either urine or undiluted plasma. The hemoglobin concentration was 9.5 gm/100 ml and the WBC count 13,400/cu mm. Several microaneurysms were noted in the ocular fundi, and there was mild atrophy

of the hand muscles. No other substantial abnormalities were found.

Initially, the patient was treated with 20 to 40 units of isophane insulin suspension daily and continuous intravenous infusions of 5% dextrose solution at 125 ml/hr. Cultures of both blood and urine yielded many *E coli*. One gram of ampicillin sodium every six hours and 80 mg of gentamicin sulfate every eight hours were given intravenously.

The patient remained relatively comfortable, though febrile, until the fourth day of hospitalization, when she lapsed into coma, with cold and clammy skin while 5% dextrose solution was running intravenously at 125 ml/hr. Her blood glucose level was 36 mg/100 ml. She responded promptly to the parenteral administration of 50 ml of 50% dextrose solution. Subsequently, there were eight additional episodes of a similar nature, with blood glucose concentrations ranging from 23 to 59 mg/100 ml while she was receiving 15 to 30 units of isophane insulin suspension a day as well as continuous infusions of 5% dextrose solution. At least two hypoglycemic reactions occurred without insulin and with glucose when needed for one week. Throughout the entire hospital course, control of the sepsis was never achieved, despite the change of antibiotics to chloramphenicol, clindamycin hydrochloride hydrate, and cephalothin sodium, according to reports of sensitivity tests.

Pituitary integrity was tested by adrenocortical function and growth-hormone responses. Plasma cortisol level on the sixth hospital day was 9.0 µg/100 ml and 7.4 µg/100 ml at 8 AM and 4 PM, respectively. The 24-hour urine 17-hydroxycorticosteroid and 17-ketosteroid levels were 13.4 and 4.0

mg, respectively, on the seventh day, and 12.6 and 5.4 mg on the tenth day. On the 11th day, however, repeated plasma cortisol determinations were 3.6 µg/100 ml and 2.2 µg/100 ml at 8 AM and 4 PM, respectively. Growth-hormone responses to 1 mg of glucagon were normal on the tenth day, and serial blood glucose levels were 358, 388, 420, 396, and 392 mg/100 ml.

The patient died on her 27th day in the hospital. Autopsy revealed widespread pituitary necrosis with massive neutrophilic infiltration. In addition, there were acute and chronic pyelonephritis and multiple abscesses in the renal parenchyma. There was bronchopneumonia in both lower lobes, with multiple septic infarctions of the upper lungs. The adrenal glands and pancreas were normal.

Comment

The severity and frequency of hypoglycemic reactions in this case are impressive. Pituitary functions in terms of growth-hormone responses and adrenocortical function were normal initially. Subsequently, however, plasma cortisol levels were very low, indicating flagging pituitary function, which ultimately ended in destruction by overwhelming infection. The patient of Brenner³ had a similar course.

Nonproprietary Names and Trademarks of Drugs

Ampicillin sodium—*Alpen*, *Amcill*, *Omnipen*, *Penbritin*, *Polycillin*, *Principen*.
Cephalothin sodium—*Keftin*.
Clindamycin hydrochloride hydrate—*Cleocin Hydrochloride*.
Gentamicin sulfate—*Garamycin*.

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From the Department of Internal Medicine, St Elizabeth Hospital, Youngstown, Ohio, and the Northeastern Ohio Universities College of Medicine, Kent, Ohio.

Reprint requests to 2111 Belmont Ave, Youngstown, OH 44505 (Dr Jung).

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