Cancer Chemother Pharmacol (1987) 19: 163–164

Cancer Chemotherapy and Pharmacology

Amsacrine treatment of patients with supraventricular arrhythmias and acute leukemia*

Zalmen Arlin[1], Rakesh Mehta[1], Eric Feldman[1], Phyllis Sullivan[1], and Anthony Pucillo[2]

[1] Division of Neoplastic Diseases and [2] Division of Cardiology, New York Medical College, Valhalla, NY 10595, USA

Summary. Three patients with a history of supraventricular arrhythmia presented with relapse of acute leukemia. Two of the three patients were in sinus rhythm, receiving digoxin and/or verapamil daily. The third patient was in atrial fibrillation, but her heart rate was controlled with daily digoxin. All three patients received amsacrine without the occurrence of cardiac events. Although amsacrine may cause ventricular arrhythmias in the setting of hypokalemia, correction of the electrolyte abnormality permits its use in patients with a history of supraventricular arrhythmias.

Introduction

Since its introduction into clinical trials in 1978 amsacrine has proved useful in relapsed acute myelocytic leukemia (AML), [2, 6] and acute lymphoblastic leukemia (ALL) [2, 3] and has been incorporated safely into other regimens [1, 4]. Previous studies have shown that amsacrine may induce fatal cardic centricular arrhythmias in the presence of hypokalemia [7, 8]. However, amsacrine can safely be given to people with heart failure [5], and we have recommended that in the setting of heart failure an amsacrine combination may be the treatment of choice and may be safer than a regimen employing an anthracycline. Since supraventricular arrhythmias frequently indicate the presence of intrinsic cardiac disease, it suggests that amsacrine might also be preferred in this condition. However, these arrhthymias may also indicate increased cardiac irritability, which may preclude its use. We examined this question in three patients with relapse of leukemia who had a history of supraventricular arrhythmia, all of whom were undergoing remission induction therapy.

Case reports

Patient 1. A 68-year-old woman was admitted for treatment of AML in October 1982. She had a long history of hypertension, for which she was receiving metoprolol. She had complained of palpitations occurring once or twice yearly over the previous 10 years, but not therapy had been required for this. While in the hospital she received amsacrine with cytarabine (ara-C) and thioguanine, achieving a remission after one course. Several days after treatment was completed she complained of palpitations. An electrocardiogram showed atrial fibrillation, and she received digoxin 0.25 mg daily with restoration of normal sinus rhythm. At the time of relapse in April 1985 she received KCl 10 mEq/h for 12 h. After a serum potassium level of over 4.0 mEq/l had been recorded she received amsacrine 200 mg/m^2 daily for 3 days and ara-C 3 g per m^2 over 3 h daily for 5 days, and achieved remission. No arrhythmia was encountered during this period.

Patient 2. A 47-year-old woman presented with AML in May 1984. She was treated initially with mitoxantrone and ara-C, achieving a remission. She subsequently received two courses of consolidation treatment and remained in remission until February 1985. Her cardiac history included recurrent paroxysmal supraventricular tachycardia and hypertension, and she had mitral valve prolapse. She was receiving digoxin 0.125 mg daily. On relapse, the received homoharringtonine (HHT), and on the 5th day of a 9-day infusion she had a paroxysmal supraventricular tachycardia that was converted to sinus rhythm with i.v. verapamil. The HHT failed to clear the bone marrow of leukemic cells. She then received KCl 10 mEq/h for 12 h. After a serum potassium level of over 4.0 mEq/l had been recorded she received amsacrine with ara-C. She died subsequently of an intracerebral hemorrhage. There was no recurrence of the arrhythmia after amsacrine administration.

Patient 3. A 41-year-old woman presented with ALL in January 1985. She was treated initially with vincristine, daunorubicin, and asparaginase, and subsequently with mitoxantrone and prednisone. She never achieved a sustained remission. Her previous history include the presence of atrial fibrillation, for which she was receiving digoxin 0.25 mg daily. This controlled her ventricular response, but her rhythm at the time of hospitalization continued to be atrial fibrillation. On physical examination she had mitral regurgitation, and two-dimensional echocardiography showed a dilated left atrium and moderate mitral valve prolapse. Prior to receiving chemotherapy she received KCl 10 mEq/h. After a serum potassium level of over 4 mEq/l had been recorded she received amsacrine with ara-C, achieving a complete remission. No further cardiac events were noted.

* This work is supported by the Chemotherapy Foundation

Offprint requests to: Zalmen A. Arlin, New York Medical College. Munger Pavilion – Room 250, Valhalla, NY 10595, USA

Discussion

Since amsacrine given to patients with hypokalemia can lead to ventricular arrhythmias, there may be concern about giving the drug to people who have a prior history of supraventricular ectopic activity controlled by antiarrhythmic agents or who have a clinically recognized supraventricular arrhythmia. The experience reported here indicates that the drug is safe even in these patients, as long as an adequate serum potassium level (>4.0 mEq/l) is maintained at the time of drug administration.

Acknowledgement. The authors wish to thank Mary Naber for preparing this manuscript.

References

1. Arlin ZA (1983) Current status of amsacrine (AMSA) combination chemotherapy programs in acute leukemia. Cancer Treat Rep 67: 967–970
2. Arlin ZA, Sklaroff R, Gee T, Kempin S, Howard J, Clarkson B, Young C (1980) Phase I/II trial of 4-(9-acridinylamino) methanesulfon-*m*-anisidide (AMSA) in patients with acute leukemia. Cancer Res 40: 3304–3306
3. Arlin ZA, Flomenberg N, Gee TS, Kempin SJ, Dellaquila C, Straus DJ, Young CW, Clarkson BD (1981) Treatment of acute leukemia in relapse with 4-(9-acridinylamino) methanesulfon-*m*-anisidide (AMSA) in combination with cytosine arabinoside and thioguanine. Cancer Clin Trials 4: 317–321
4. Arlin ZA, Gaddipati J, Ahmed T, Mittelman A, Friedland M, Rieber E (1985) Treatment of acute leukemia with amsacrine and high-dose cytarabine (HiDac). Cancer Treat Rep 69: 1101–1102
5. Fanucchi MP, Arlin ZA (1983) Successful treatment of a patient with acute nonlymphoblastic leukemia (ANLL) and anthracycline cardiomyopathy with 4'(9-acridinylamino) methanesulfon-*m*-anisidide (AMSA). Cancer Chemother Pharmacol 10: 27–28
6. Legha SS, Gutterman JU, Hall SW, Benjamin RS, Burgess MA, Valdivieso M, Bodey GP (1978) Phase I clinical investigation of 4'-(9-acridinylamino) methanesulfon-*m*-anisidide (NSC #249992), a new acridine derivative. Cancer Res 38: 3712–3722
7. Riela AR, Kimball JC, Patterson RB, et al. (1981) Cardiac arrhythmia associated with AMSA in a child: A Southwest Oncology Group Study. Cancer Treat Rep 65: 1121–1123
8. Van Hoff DD, Elson D, Polk G, et al. (1980) Acute ventricular fibrillation and death during infusion of 4'-(9-acridinylamino) methanesulfon-*m*-anisidide (AMSA). Cancer Treat Rep 64: 356–357

Received June 18, 1986/Accepted November 7, 1986