Cancer Chemother Pharmacol (1982) 8:253–254

Cancer Chemotherapy and Pharmacology

Letter to the Editor

Syndrome of Inappropriate ADH Secretion Secondary to Vinblastine

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Sir,

It is well recognized that vincristine in high doses can cause the syndrome of inappropriate ADH secretion (SIADH) [3]. We wish to report the occurrence of this syndrome in an adult patient after a vinblastine overdose.

A 35-year-old male with testicular carcinoma and advanced retroperitoneal disease was admitted for chemotherapy because of an elevated alpha-fetoprotein level 1 month after undergoing resection of residual retroperitoneal disease after induction chemotherapy. The only abnormality noted on admission was a slightly dilated right renal pelvis without evidence of an ureteral obstruction on abdominal ultrasound and IVP. Serum creatinine was 88 μmol/l. The patient was given *cis*-platinum 35 mg IV on day 1 through 4, bleomycin 30 mg IV on day 2, and vinblastine 35 mg instead of 10 mg on day 1 and 2, representing a total dose of vinblastine of 1.0 mg/kg. After the mistake was noted the patient was transferred to the laminar flow unit on day 6. At that time he complained of severe muscle pain necessitating large amounts of narcotics. He was febrile and a spontaneous urinary fistula had developed in the surgical wound on his right side. The laboratory tests showed hyponatremia (120 mmol/l) and a blood urea level of 2.8 mmol/l.

The patient was not dehydrated and the serum creatinine level was unchanged. The estimated serum osmolality was 251 mosmol/kg. Treatment was instituted with oral decontamination, parenteral nutrition, cefoxitine, and netilmycine. From day 6 to day 10 the intake of free water was restricted to a mean of 500 ml per day. Urinary loss (mean 1,675 ml/day) and other losses (mainly sweating) during that time were replaced by normal saline (mean 1,870 ml/day), and the central venous pressure was kept at a low normal range. During the treatment stomatitis, subileus and hypertension of maximally 170/120 mm Hg were noted. The temperature remained over 38° C from day 5 to day 12, and no infection was identified. The patient became delirious on day 8, and this continued to day 11. A lumbar puncture was normal. Granulocytopenia of less than 100/mm^3 lasted from day 5 to day 11. Thrombocytopenia with a nadir of 24,000/mm^3 was observed. The courses of serum sodium, urinary sodium, and blood urea levels are depicted in Fig. 1, the hatched area representing the time when fluid was restricted. During that time the serum creatinine remained at

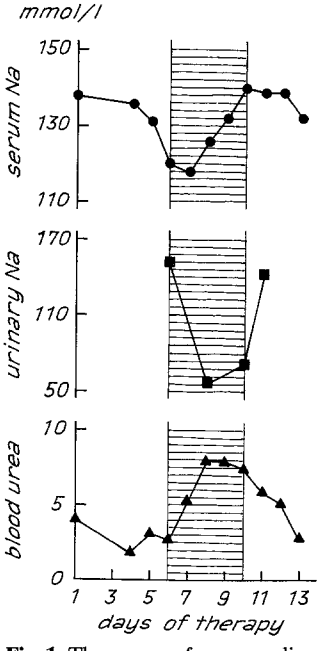

Fig. 1. The course of serum sodium, urinary sodium and blood urea after a vinblastine overdose on days 1 and 2. The *hatched area* represents the time when fluid intake was restricted

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0344-5704/82/0008/0253/$ 01.00

88 μmol/l or less and the creatinine clearance ranged from 93 to 147 ml/min.

This case of SIADH secondary to a vinblastine overdose is well substantiated by the normal electrolytes at the beginning of therapy, the high urinary sodium at a time of severe hyponatremia in a well-hydrated patient, the low blood urea, the normal renal function as measured by serum creatinine and creatinine clearance, and the excellent response to fluid restriction, with a return to a normal serum sodium on day 10. So far there have been three reports of this sydrome secondary to vinblastine with total doses ranging from 0.4 mg/kg [2] to an overdose of 2.1 mg/kg in a child [3]. In a third case, after 0.8 mg/kg the patient showed a similar clinical picture to that seen in our patient [4].

Physicians treating patients with high doses of vinblastine or confronted with a vinblastine overdose should be aware of this complication and its relatively simple treatment by fluid restriction.

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Received December 11, 1981/Accepted Jannuary 26, 1982