

Hyponatremia, Cerebral Edema, and Noncardiogenic Pulmonary Edema in Marathon Runners

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Background: Noncardiogenic pulmonary edema is often associated with increased intracranial pressure and can be the initial manifestation of hyponatremic encephalopathy. Marathon runners tend to develop conditions that lead to hyponatremia.

Objective: To describe the development and treatment of noncardiogenic pulmonary edema in marathon runners that was associated with hyponatremic encephalopathy.

Design: Case series.

Setting: One university hospital and two community hospitals.

Patients: Seven healthy marathon runners who had a history of nonsteroidal anti-inflammatory drug use. The runners collapsed after competing in a marathon and were hospitalized with pulmonary edema.

Measurements: Plasma sodium levels, chest radiograph, electrocardiogram, cardiac enzyme levels, and magnetic resonance imaging or computed tomographic scans of the brain.

Results: Patients had nausea, emesis, and obtundation. The mean (\pm SD) plasma sodium level was 121 ± 3 mmol/L, and oxygen saturation was less than 70%. Electrocardiograms and echocardiograms were normal. Chest radiographs showed pulmonary edema with a normal heart. Creatine phosphokinase-MB bands, troponin levels, and pulmonary wedge pressure were not elevated. Scanning of the brain showed cerebral edema. All patients were intubated and mechanically ventilated. Treatment with intravenous NaCl, 514 mmol/L, increased plasma sodium levels by 10 mmol/L in 12 hours. Pulmonary and cerebral edema resolved as the sodium level increased. One patient had unsuspected hyponatremic encephalopathy and died of cardiopulmonary arrest caused by brainstem herniation. All six treated patients recovered and were well after 1 year of follow-up.

Conclusions: In healthy marathon runners, noncardiogenic pulmonary edema can be associated with hyponatremic encephalopathy. The condition may be fatal if undiagnosed and can be successfully treated with hypertonic NaCl.

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In a recent prospective study, 18% of 605 marathon runners developed hyponatremia; women with hyponatremia had lower plasma sodium levels and were more symptomatic than men (1). Hyponatremia in these patients resulted from substantial retention of ingested water (1). We recently reported that patients with hyponatremic encephalopathy can present with noncardiogenic pulmonary edema (2). In the present report, we describe seven marathon runners who presented with hyponatremic encephalopathy and pulmonary edema.

Case Findings

Demographic Characteristics

Seven patients were studied, six of whom survived. Five were directly cared for by one of the authors, and the authors were consulted for the other two patients. All seven had completed marathons from 1993 to 1999 in Texas, California, and Canada and had taken nonsteroidal anti-inflammatory drugs. The clinical and laboratory characteristics are given in the **Table**.

Hospital Course

All seven patients were admitted to the emergency department with nausea, emesis, copious pink frothy sputum, and pulmonary edema (**Figure, part A**). No abnormalities were seen on electrocardiography, and echocardiography showed normal ejection fractions and wall motion. The pulmonary wedge pressure was below normal in all five patients in whom this variable was measured. All seven patients had normal calcium and phosphorus levels.

Magnetic resonance imaging or computed tomography of the brain showed cerebral edema in the six patients who underwent either of these tests (**Figure, part C**). In patient 7, hyponatremic encephalopathy was not suspected, and the patient died of cardiopulmonary arrest. The autopsy showed cerebral edema with brainstem herniation, pulmonary edema, and a normal heart.

Therapy

All seven patients were intubated in the emergency department. All seven patients were supported with mechanical ventilation, and six were treated with intravenous NaCl. In these six patients,

Table. Clinical and Laboratory Characteristics of Patients*

Patient	Age	Sex	Sodium Level	Potassium Level	Chloride Level	Bicarbonate Level	BUN Level	Creatinine Level	Glucose Level†	CK-MB Bands
1	37	M	119	3.5	91	23	4.28 (12)	88.4 (1.0)	7.05 (127)	Normal
2	37	F	120	3.0	93	15	4.28 (12)	70.7 (0.8)	5.61 (101)	Normal
3	44	F	121	3.9	93	22	1.43 (4)	53.0 (0.6)	6.83 (123)	Normal
4	29	M	127	3.7	95	24	4.99 (14)	97.2 (1.1)	8.55 (154)	Normal
5	31	F	125	3.6	95	22	2.49 (7)	88.4 (1.0)	5.38 (97)	Normal
6	46	F	120	3.3	88	18	2.85 (8)	61.9 (0.7)	19.98 (360)	Normal
7	32	F	117	4.3	84	18	3.57 (10)	70.7 (0.8)	4.44 (80)	Normal
Mean ± SD	37 ± 7		121 ± 3	3.6 ± 0.4	91 ± 4	20 ± 3	3.57 ± 1.07 (10 ± 3)	79.6 ± 17.6 (0.9 ± 0.2)	8.27 ± 5.33 (149 ± 96)	

* BUN = blood urea nitrogen; CK = creatine kinase; CT = computed tomography; F = female; M = male; MRI = magnetic resonance imaging.

† No patient had a history of diabetes mellitus, and none had diabetes after recovery.

the plasma sodium level increased by 10 mmol/L in less than 12 hours (3, 4). As the plasma sodium level increased, cerebral (Figure, part D) and pul-

monary (Figure, part B) edema resolved. All treated patients recovered. No sequelae have developed after follow-up of 3 to 24 months. Magnetic reso-

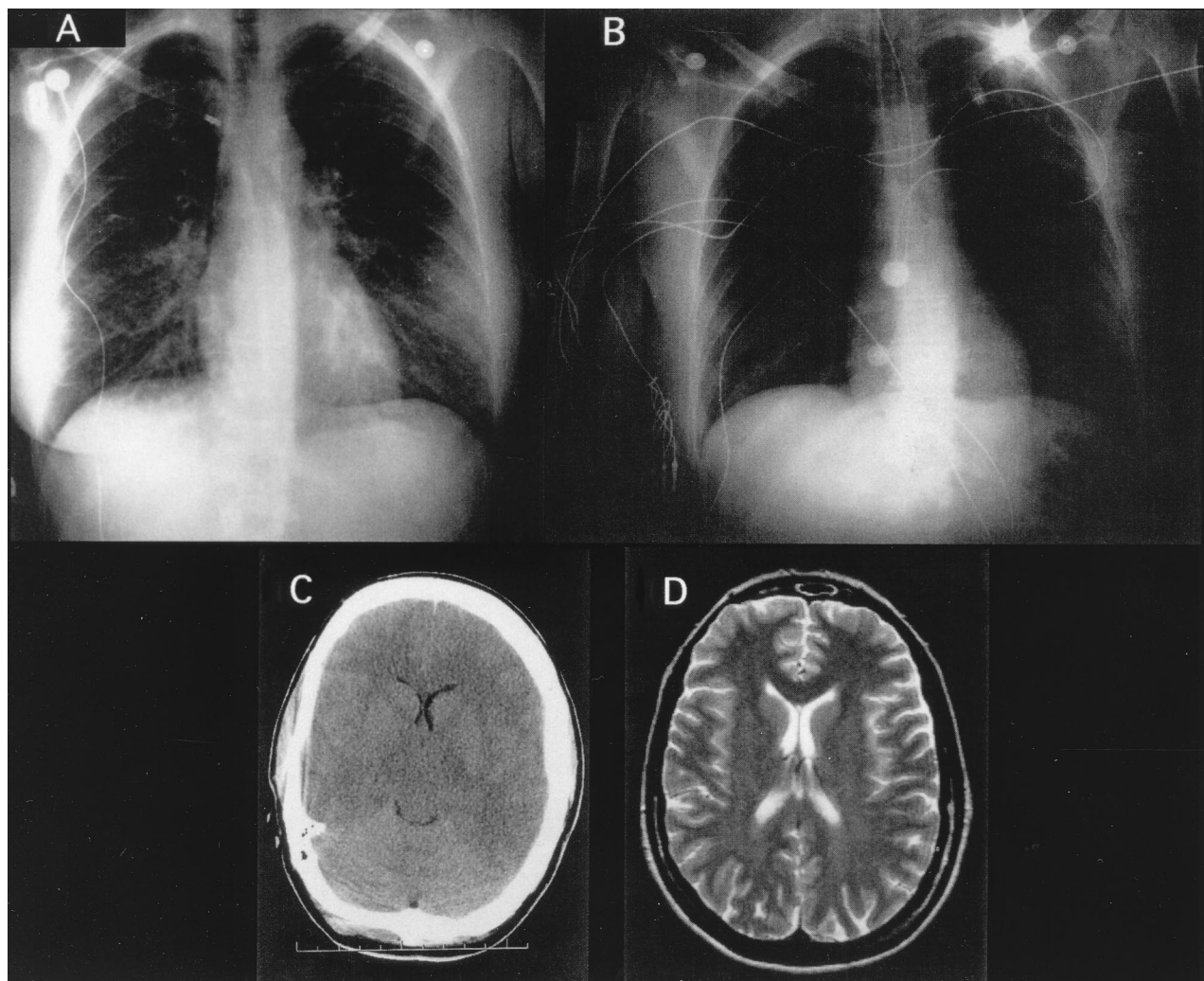


Figure. Radiographs and scans obtained from patient 3, a 44-year-old woman who was admitted to the emergency department with a plasma sodium level of 121 mmol/L and oxygen saturation of 66%. Bibasilar rales and copious pink frothy sputum were noted, and the respiratory rate was 38 breaths/min. **A.** Chest radiograph showing interstitial edema and apparent redistribution of pulmonary blood volume, with loss of distinct vascular margins. The heart size is normal. **B.** Chest radiograph obtained 24 hours after admission. The patient's plasma sodium level had been increased from 121 to 129 mmol/L in 9 hours. The patient was alert and responsive, with oxygen saturation of 97%. The chest radiograph is normal. **C.** Computed tomographic scan of the brain obtained within 1 hour of the chest radiograph shown in part A. Cerebral edema is evident, the cerebral ventricles are essentially obliterated, and the sulci are largely absent. **D.** Magnetic resonance image of the brain taken 24 hours after admission, at about the same time as the chest radiograph shown in part B. Cerebral edema has resolved, the cerebral ventricles are now clearly visible, and the sulci are more distinct.

Table—Continued

Troponin Test Results	Oxygen Saturation	Blood Pressure	Temperature	Heart Rate	Prescription Drugs	Associated Medical Illness	Findings on Chest Radiography	Findings on CT or MRI of Brain	Dose of Intravenous NaCl	Outcome
	%	mm Hg	°C	beats/min					mmol/L	
Normal	<70	120/60	37.2	72	None	None	Pulmonary edema	Cerebral edema	514	Recovered
Normal	<70	110/70	37.2	66	None	None	Pulmonary edema	Cerebral edema	514	Recovered
Normal	<70	125/77	37.0	80	None	None	Pulmonary edema	Cerebral edema	514	Recovered
Normal	<70	122/62	37.0	68	None	None	Pulmonary edema	Cerebral edema	514	Recovered
Normal	<70	120/60	37.3	70	None	None	Pulmonary edema	Cerebral edema	514	Recovered
Not done	<70	95/50	35.6	80	None	None	Pulmonary edema	Not done	514	Recovered
Not done	<70	127/50	34.4	74	None	None	Pulmonary edema	Cerebral edema	None	Died
		Systolic, 117 ± 11; Diastolic, 61 ± 10	97.8 ± 2.0	73 ± 6					514	

nance imaging scans obtained after 1 year of follow-up in five patients were normal.

Discussion

Our study demonstrates that in healthy marathon runners, noncardiogenic pulmonary edema can be a clinical manifestation of hyponatremic encephalopathy. The association between noncardiogenic pulmonary edema and hyponatremic encephalopathy was suspected in six patients. Hypertonic NaCl treatment of cerebral edema and hyponatremic encephalopathy was successful and curative in these six patients. The patient in whom the diagnosis was unsuspected died of cardiopulmonary arrest caused by brainstem herniation (Table).

All five patients in whom pulmonary capillary wedge pressure was measured had low pressure, indicating that pulmonary edema was noncardiogenic. Furthermore, through alleviation of cytotoxic cerebral edema with hypertonic NaCl, pulmonary edema also resolved (Figure, part D); this finding suggests a possible association between cerebral edema and noncardiogenic pulmonary edema. Previous reports have described pulmonary edema developing in marathon runners (5–7). However, we report resolution of both cerebral and pulmonary edema with the use of hypertonic NaCl.

Although most marathon runners are male, a recent study shows that women are more prone to develop hyponatremia and are more symptomatic (1). Five of seven patients in our study were menstruant women, suggesting that, as in other forms of hyponatremic encephalopathy, sex may be a predisposing factor (8).

Our study has some limitations. For example, the small sample precludes statistical comparisons, and we have no information on the incidence or prevalence of hyponatremic encephalopathy among marathon runners.

During heavy exercise, blood flow is diverted

from the gastrointestinal tract to skeletal muscle, and ingested water is sequestered in the gut (9). Diffuse loss of sodium and water due to sweating leads to volume contraction with stimulation of antidiuretic hormone (1, 9, 10). Vasopressin, in turn, increases retention of ingested water. When exercise ceases, blood flow may be partially redistributed to the gastrointestinal tract, leading to abrupt absorption of water into the bloodstream and resultant hyponatremia (9, 11, 12). The acute hyponatremia leads to increased intracranial pressure, with hypoxia and noncardiogenic pulmonary edema (2). Marathon runners are also likely to use nonsteroidal anti-inflammatory drugs, which can impair water excretion (13).

When people collapse in apparent shock after strenuous exercise, heat injury is usually the presumptive diagnosis (14). Some have been treated with oral administration of water or diuretics, and some have died (15, 16). The initial hospital evaluation of a marathon runner who collapses should include measurement of the plasma sodium level and chest radiography. Although counterintuitive, administration of hypertonic NaCl should be considered if pulmonary edema and hyponatremia are present. Successful therapy in such patients depends on recognition of the association between noncardiogenic pulmonary edema and hyponatremic encephalopathy.

Note added in proof: After this manuscript was accepted for publication, Dr. Sterling Huff, Director of Emergency Services at St. Joseph's Hospital, Houston, Texas, informed us of four female marathon runners who were hospitalized after completing the Houston Marathon on 16 January 2000. These women were 32 to 48 years of age and presented to the emergency department with symptoms ranging from nausea, vomiting, and headache to grand mal seizures. All had hyponatremia (plasma sodium level, 114 to 128 mmol/L). None suffered respiratory arrest. It was certain that one of the

runners had been taking nonsteroidal anti-inflammatory drugs; the history of use of these drugs was unclear in the other three. All were successfully treated with intravenous NaCl (two received hypertonic NaCl and two received normal NaCl), and all were subsequently discharged without neurologic sequelae.

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