azole mixture plus colistin, titers were consistently greater than 1:4. The serum concentration of amikacin one hour after infusion was 12.0 μg/ml; however, levels of gentamicin and carbenicillin were not determined.

**DISCUSSION**

Endocarditis due to Pseudomonas is now a well-recognized complication of intravenous drug abuse, primarily heroin addiction. The tricuspid valve is most commonly involved. The case reported herein was not dissimilar from the usual case of heroin-associated endocarditis due to Pseudomonas.

Medical therapy for endocarditis due to this pathogen has been disappointing, as noted by Carruthers and Kanokvechayan and by Saroff et al. Most recently, despite the availability of chemotherapeutic agents effective against Pseudomonas, the two largest series of cases of heroin-associated endocarditis due to Pseudomonas reported by Reyes et al. and Archer et al. had medical cures in 23 and 33 percent of their patients, respectively. Our patient failed to respond to the agents usually effective against Pseudomonas, i.e., gentamicin, carbenicillin, and amikacin. Continued bacteremia and refusal of surgery by our patient necessitated a search for an alternative therapeutic regimen.

A recent report suggested that the combination of sulfonamides, trimethoprim, and a polymyxin drug demonstrated enhanced activity to gram-negative bacilli, including some strains of *P aeruginosa*. Therefore, it was elected to initiate therapy with a trimethoprim-sulfamethoxazole mixture plus colistin. The patient's fever rapidly abated, and cultures of blood became sterile. Because progressive azotemia ensued, therapy was discontinued, and the patient relapsed with fever and bacteremia. In *in vitro* studies of susceptibility performed in our laboratory demonstrated synergism when all three agents were tested in combination against the pathogen. Therefore, following improvement of renal function, therapy with the trimethoprim-sulfamethoxazole mixture and colistin was reinstituted. An open cardiotomy was subsequently performed, which confirmed the diagnosis of endocarditis but showed that the active infection had resolved. Subsequently, the patient was treated with the trimethoprim-sulfamethoxazole mixture plus colistin for 11 weeks.

To the best of our knowledge, there have been no previous reports of endocarditis due to *P aeruginosa* that was successfully treated with the combination of a trimethoprim-sulfamethoxazole mixture and a polymyxin drug. Rosenblatt et al. described two patients treated with a trimethoprim-sulfamethoxazole mixture and polymyxin B, one of whom had endocarditis due to *P aeruginosa*. That patient initially responded and remained without bacteremia for 19 days but subsequently relapsed while receiving therapy. The *in vitro* testing for susceptibility suggested that the three-drug combination was effectively bactericidal against the Pseudomonas.

In conclusion, endocarditis due to *P aeruginosa* continues to be a major therapeutic problem. Medical cures have been disappointing, even with the availability of several chemotherapeutic agents effective against Pseudomonas. Consideration of administering a trimethoprim-sulfamethoxazole mixture with a polymyxin drug may be warranted when clinical and bacteriologic cure is not achieved with standard chemotherapeutic agents known to be effective against *P aeruginosa*. Moreover, a trimethoprim-sulfamethoxazole mixture is given orally, whereas colistin is generally administered intramuscularly, which may be advantageous in heroin addicts who lack accessible venous sites for intravenous medication.

**ACKNOWLEDGMENTS:** We thank Ms. Lorraine Fugita for typing the manuscript and Ms. Sharon Shibata for performing the studies of antibiotic susceptibility.

**REFERENCES**


**Putrid Pulmonary Abscess and Empyema with Inappropriate Secretion of Antiuretic Hormone**

Joel C. Seidman, M.D.

The syndrome of inappropriate secretion of antidiuretic hormone has been associated with many pulmonary inflammatory diseases. The origin of the hormone in these cases is the neurohypophysis, although the afferent stimulus has not been adequately characterized. A previously unreported association of this syndrome with putrid pulmonary abscess and empyema is documented.

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Since the syndrome of inappropriate secretion of antidiuretic hormone was elucidated by Schwartz et al., numerous reports have described its role in diverse clinical settings, notably seizure disorders. Good evidence indicates that oat cell bronchogenic carcinoma produces the syndrome by aberrant secretion of arginine vasopressin or a like substance by the tumor itself, while the inappropriate release in chronic obstructive pulmonary disease, aerobic pyogenic pneumonitis, pneumonitis due to Mycoplasma, viral pneumonitis, advanced pulmonary tuberculosis, cavitary aspergillosis and during continuous positive-pressure ventilation is neurohypophyseal in origin. The following is a report of a case of the syndrome of inappropriate secretion of antidiuretic hormone (by the criteria of Bartter*) in a patient with putrid pulmonary abscess and empyema.

CASE REPORT

A 50-year-old man was admitted to Wayne County General Hospital, Eloise, Mich, on July 13, 1976, following a week of remittent fevers and sweats and a cough productive of foul-smelling sputum. He had been well previously, except for an idiopathic seizure disorder treated with phenytoin (Dilantin) sodium (100 mg orally thrice daily); no convulsions had occurred recently. Symptoms of hyponatremia were absent.

The patient appeared ill but well hydrated. The blood pressure was 148/90 mm Hg, the pulse rate was 140 beats per minute, the respiration rate was 36/min to 40/min, and the oral temperature was 40°C (104°F). There was no edema. Severe periodontitis was observed. Pulmonary examination revealed signs of consolidation over the middle posterior right lung. No other abnormal findings were noted.

On the day of admission, the white blood cell count was 15,200/cu mm, and the specific gravity of the urine was 1.030. The blood urea nitrogen level was 12 mg/100 ml, the serum level of creatinine was 0.9 mg/100 ml, and the random serum glucose level was 170 mg/100 ml. Serum levels of lipids, bilirubin, and transaminases were normal. The results of other pertinent biochemical studies appear sequentially in Table 1. A chest x-ray film demonstrated an 11-cm cavity with an air-fluid level in the right lower lobe (Fig 1). Reactivity to reference-standard purified protein derivative of tuberculin (PPD-S) was absent, despite a significant response to Candida antigen. Cultures of sputum obtained by transtracheal aspiration produced a few organisms of Hemophilus parainfluenzae by aerobic and anaerobic techniques. Cultures of blood were sterile. The patient was treated with clindamycin (Cleocin) phosphate (300 mg intravenously every six hours). Therapy with phenytoin was continued as before.

On the fourth day of hospitalization, a right hydropneumothorax developed. Drainage with a large-bore chest tube yielded 1,200 ml of feculent-smelling pus. Aerobic and anaerobic cultures were negative.

On the eighth day of hospitalization, asymptomatic hypotension was noted (Table 1), and the patient’s intake of fluids was restricted to 1 L/day. The level of cortisol in a sample of plasma drawn in the morning was 21.8 μg/100 ml.

On the 13th day of hospitalization, the fever abated, and the cavity evidenced closure, although the bronchopleural fistula remained patent. The serum level of sodium rose to 128 mEq/L, and restrictions on the intake of fluids were relaxed. Four weeks after admission, the fistula spontaneously sealed, and the serum level of sodium rose almost to normal (Table 1). Antibiotic treatment was completed, and the chest tube was withdrawn after seven weeks, with no further evidence of hyponatremia with unrestricted intake of fluids.

TABLE 1—Biochemical Studies of Serum and Urine

<table>
<thead>
<tr>
<th>Day of Hospitalization</th>
<th>Measurement 1</th>
<th>8</th>
<th>31</th>
<th>Normal</th>
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<tr>
<td><strong>Serum values</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mEq/L</td>
<td>124</td>
<td>117</td>
<td>134</td>
<td>131-145</td>
</tr>
<tr>
<td>Chloride, mEq/L</td>
<td>88</td>
<td>81</td>
<td>95</td>
<td>93-107</td>
</tr>
<tr>
<td>Potassium, mEq/L</td>
<td>4.0</td>
<td>4.1</td>
<td>4.3</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>Carbon dioxide, mEq/L</td>
<td>21.0</td>
<td>27.0</td>
<td>28.5</td>
<td>22-30</td>
</tr>
<tr>
<td>Osmolarity, mOsm/L</td>
<td>...</td>
<td>251</td>
<td>273</td>
<td>275-295</td>
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<tr>
<td><strong>Urine values</strong></td>
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<tr>
<td>Sodium, mEq/L</td>
<td>...</td>
<td>115</td>
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<tr>
<td>Osmolarity, mOsm/L</td>
<td>...</td>
<td>382</td>
<td>421</td>
<td></td>
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</table>

Discussion

Among reports of an association between pulmonary diseases and the syndrome of inappropriate secretion of antidiuretic hormone, there is no recording of an abscess or empyema of probable or proven anaerobic etiology, for which there was strong presumptive evidence in this patient. It seemed clear that the hyponatremia and hypopomolality of the serum could be explained only by the inappropriate secretion of antidiuretic hormone when it appeared simultaneously with hypertonicity of urine containing appreciable amounts of sodium. This conclusion was supported further by the presence of clinically normal hydration and the absence of cardiac, hepatic, renal, and adrenal insufficiencies.

It has been proposed that the syndrome of inappropriate secretion of antidiuretic hormone in inflammatory pulmonary disease is neurohypophyseal in origin, with the exception of one report, which hypothesized the source of hormone as tuberculous pulmonary parenchyma. Others have emphasized parasympathetic afferent...
circuits arising in pulmonary, mediastinal, or particularly left atrial receptors. Finally, some have suggested discharge of a humoral mediator to act at the hypothalamo-neurohypophyseal level. The characteristics of the pulmonary pathologic findings in this patient do not serve to define an underlying mechanism but broaden the scope of association.

A peculiar circumstance was the history of medication with phenytoin, which is known to suppress central secretion of vasopressin. The daily dosage likely was insufficient for complete suppression, although it was not increased to prove this. Other medications prescribed have not been reported to alter the effect of vasopressin on the renal concentrating mechanism or to induce the syndrome of inappropriate secretion of antidiuretic hormone. Finally, the delayed appearance of maximal hyponatremia is speculative; it is probable that its association with the pneumothorax was coincidental.

While it is known that obtundation may be associated with anaerobic pulmonary infection, an electrolyte disturbance should be considered; unexplained alterations of mental status may be secondary to the syndrome of inappropriate secretion of antidiuretic hormone. In addition, since it is common practice to vigorously induce hydration in patients with pulmonary suppuration, the clinician should be wary that such therapy may exacerbate a preexisting hyponatremic state.

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Prolonged Administration of Bleomycin without Clinical Toxicity*
Therapy with 2,700 Units over Four Years

John E. Kurnick, M.D.

A 26-year-old white man with stage 4-B Hodgkin's disease resistant to conventional chemotherapy obtained complete remission with administration of bleomycin. Maintenance of this remission required continued therapy with bleomycin. The patient received a total of 2,700 units of bleomycin over a 51-month period without signs or symptoms of pulmonary toxicity. Serial studies of pulmonary function have shown a stable forced vital capacity and minimally decreased total lung volume and pulmonary diffusing capacity. This case demonstrates the ability of a patient to tolerate massive cumulative doses of bleomycin over a protracted period without severe loss of pulmonary function.

We have been observing a patient whose continued complete remission of stage 4-B Hodgkin's disease has been dependent upon maintenance therapy with bleomycin for the past three years. In this time, he has received a total of 2,700 units of bleomycin without serious impairment of pulmonary function or changes in chest x-ray films.

CASE REPORT

A 26-year-old man had Hodgkin's disease with mixed cellularity diagnosed on axillary node biopsy in February, 1972. His disease was classified as stage 4-B on the basis of fever, a 12 kg (25 lb) loss of weight, and laparotomy-proven involvement of the liver, spleen, and para-aortic lymph nodes. Combined chemotherapy with mechlorethamine, vincristine, procarbazine, and prednisone failed to produce a significant response.

On Aug 7, 1972, the patient was started on a regimen of five daily injections of 15 units of bleomycin and 240 mg of 1-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (CCNU). This was followed by 7.5 units of bleomycin twice weekly and 200 to 240 mg of CCNU every two months. Therapy with bleomycin was interrupted in February 1973 after a cumulative dose of 480 units, with a status of complete remission having been achieved. Maintenance therapy with CCNU was discontinued nine months later, when fevers, loss of weight, and recurrent adenopathy signaled a relapse of the Hodgkin's disease. Measurements of pulmonary function were normal on Nov 7, 1973, and therapy with bleomycin was resumed at a dosage of 7.5 units twice weekly, with excellent response. An attempt to reduce the frequency of administration of bleomycin to once weekly failed because of recurrence of fever. Since the patient was unresponsive to all other agents then available and his chest x-ray films and data on pulmonary function remained unaltered, the twice weekly regimen of bleomycin was resumed, and the fever abated.

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