been beneficial in improving skin lesions in patients with sarcoidosis.11

**Patient’s treatment and course**
The patient was started on corticosteroid therapy (fluocinonide ointment) and an antibiotic (bacitracin ointment) and referred for follow-up to the pulmonary and dermatology services. Additionally, she was referred to the ophthalmology service for evaluation of possible eye complications of her disease.

**Keywords:** sarcoidosis, hilar prominence, adenopathy


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**Case Study [Chemistry]**

**Lower Abdominal Pain, Dyspnea, and Severe Shortness of Breath in a 28-Year-Old Pregnant Woman**

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**Patient**

28-year-old pregnant woman.

**Chief Complaint**

Lower abdominal pain and distention, dyspnea, and severe shortness of breath.

**Past Medical History**

Induced pregnancies (G5 P2+3) following treatment with clomiphene citrate.

**Drug History**

No current history of any medications, drugs of abuse, or therapeutic drugs, except clomiphene citrate and other agents used during ovulation induction. The induction protocol involved initial down-regulation of pituitary gonadotropin secretion and inhibition of ovarian steroid secretion with a luteinizing hormone-releasing hormone (LHRH) analogue (Buserelin), followed by stimulation with a follicle stimulating hormone (FSH) preparation, and triggering of ovulation by administration of human chorionic gonadotropin (hCG).

**Physical Examination**

She was afebrile (temperature: 36°C) with abnormal heart rate (106 beats/min), blood pressure (108/83 mmHg), and respirations (24/min). Abdominal examination revealed a large distended abdomen that was diffusely tender with positive signs of ascites. She had mild pedal edema. She was admitted to our hospital for further follow-up.

**Principal Laboratory Findings**

In addition to the laboratory data [T1], the patient’s values for all liver enzyme tests, thyrotropin (TSH), and cortisol were within normal limits; and her hemoglobin (16.7 g/dL), hematocrit (51.5%), and platelet count (599 x 10^3/µL) values were consistent with hemoconcentration. Serial measurement of serum estradiol concentration was performed during her hospital stay [F1].

**Results of Other Diagnostic Procedures**

Cardiovascular examination showed no elevation of jugular vein pressure and normal first and second heart sounds with no murmurs or added sounds. Chest examination showed dullness to percussion in the lower third of the chest posteriorly with decreased air entry and vocal sound vibration. Chest X-ray, with abdominal shield, revealed mild right-sided pleural effusion but no other abnormality.

**Questions:**

1. What is(are) this patient’s most striking laboratory result(s)?
2. How do you explain this patient’s most striking laboratory result(s)?
3. What condition(s) does this patient’s laboratory and other findings suggest?
4. What are the principal complications found in this patient’s condition?
Principal Laboratory Findings on Admission (Day 0) and During the First 10 Days of the Patient's 20-Day Hospital Stay

<table>
<thead>
<tr>
<th>Test</th>
<th>Specimen</th>
<th>“Normal” Reference Range</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
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<tbody>
<tr>
<td>Sodium (Na+)</td>
<td>serum</td>
<td>135-145 mEq/L</td>
<td>129</td>
<td>128</td>
<td>116</td>
<td>131</td>
<td>123</td>
<td>129</td>
<td>129</td>
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<td>126</td>
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<tr>
<td>Potassium</td>
<td>serum</td>
<td>3.6-5.0 mEq/L</td>
<td>4.2</td>
<td>4.8</td>
<td>6.6</td>
<td>4.5</td>
<td>4.4</td>
<td>4.7</td>
<td>5.0</td>
<td>5.1</td>
<td>4.8</td>
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<td>4.4</td>
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<tr>
<td></td>
<td>urine</td>
<td>22-31 mEq/L</td>
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<tr>
<td>CO₂</td>
<td>serum</td>
<td>3.5-5.2 g/dL</td>
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<td>3.7</td>
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<td>2.9</td>
<td>2.7</td>
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<td>2.5</td>
<td>3.4</td>
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<td>Glucose</td>
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<td>65-110 mg/dL</td>
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<tr>
<td>BUN</td>
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<tr>
<td>Creatinine</td>
<td>serum</td>
<td>0.6-1.2 mg/dL</td>
<td>0.9</td>
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<tr>
<td>β-hCG</td>
<td>serum</td>
<td>&lt;5 mIU/mL †</td>
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<td>urine</td>
<td>50-1200 mOsm/kg H₂O²</td>
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<td>Osmolal Gap ‡</td>
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</table>

*A random or spot urine sodium concentration >10 mEq/L may indicate diuretics, emesis, intrinsic renal diseases, Addison’s disease, hypothyroidism, or syndrome of inappropriate antidiuretic hormone (SIADH) secretion. †Males and non-pregnant females. ‡Depending on fluid intake. ‡Osmolal Gap = OsmoMeasured – OsmoCalculated; where, OsmoCalculated = 2[Na+] + ([Glucose]/18) + ([BUN]/2.8). BUN, blood urea nitrogen; β-hCG, beta-human chorionic gonadotropin.

5. What is(are) the most likely cause(s) of the principal complications found in this patient’s condition?
6. Which laboratory and non-laboratory test(s) are appropriate to order on this patient and why?
7. What is the most appropriate treatment for this patient?

Possible Answers:
1. Elevated serum β-hCG; hyponatremia with low serum and inappropriately high urine osmolality; and markedly elevated serum estradiol levels (ie, 4,000 to 10,000 pg/mL; normal reference range for premenopausal women: 30 to 400 pg/mL, depending on phase of menstrual cycle). Her serum sodium value decreased from an already low value of 129 mEq/L at admission to 116 mEq/L 48 hours later [**F1**].

2. The elevated serum β-hCG value is consistent with the patient being pregnant. Hyponatremia can be subdivided into 2 types: *dilutional* (due to increased secretion of antidiuretic hormone (ADH), followed by water retention, and plasma volume expansion) and *depletional* (from renal or extrarenal sodium loss). The most common cause of hyponatremia in hospitalized patients is the syndrome of inappropriate ADH secretion (SIADH); however, other conditions, including congestive heart failure, renal insufficiency, nephrotic syndrome, liver cirrhosis, hypothyroidism, and drugs that stimulate ADH secretion may also cause hyponatremia. The patient’s history (eg, the only drugs she was taking were those associated with the ovulation induction protocol), laboratory, and other diagnostic data did not support any of the aforementioned conditions. Her serum was hypo-osmolar (ie, <270 mOsm/kg H₂O). Her urine osmolality (298 mOsm/kg H₂O) was slightly greater than her serum osmolality (267 and 276 mOsm/kg H₂O). There was no significant osmolal gap, and her urine sodium concentration (91 mEq/L on day 4 of her hospital stay) was inappropriately high (ie, 40 to 80 mEq/L). These findings are typical of patients with SIADH. Her markedly elevated estradiol values are consistent with ovarian hyperstimulation syndrome (OHSS). Ovarian hyperstimulation syndrome of varying severity is seen following the use of exogenous gonadotropins for induction of ovulation. Therefore, the possibility exists that her SIADH was caused by the drugs (eg, clomiphene citrate and gonadotropins) used to induce her to ovulate. This possibility is made less likely by the fact her serum sodium concentration continued to decrease up to 3 days after admission. Thus, the cause of this patient’s hyponatremia is not clear and could be due to defects in the renin-angiotensin system or the involvement of prostaglandins and other endothelial factors. A recent report highlighted a case of severe OHSS with sodium retention,
increased plasma renin activity (PRA), and, unlike the patient described in this case study whose urine sodium concentration was inappropriately high, an undetectable urine sodium concentration. Moreover, both renin and aldosterone have been suggested to play a role in the pathogenesis of OHSS. We did not perform renin testing on a plasma sample from our patient. In deciphering the cause of this patient’s SIADH, it is interesting to note that her serum estradiol levels were negatively correlated with her serum osmolality. This finding suggests that the steroid, estradiol, and perhaps other steroids may exert an osmoregulatory effect. A recent report of hyponatremia due to SIADH in a patient with an immature ovarian teratoma lends support to this hypothesis. Although the patient’s steroid levels were not stated in this report, the serum sodium level returned to normal following resection of the patient’s tumor. Thus, it is possible that steroids such as estradiol may be involved in the pathogenesis of hyponatremia.

3. This patient’s laboratory and clinical findings are suggestive of SIADH with OHSS. This report describes a patient with SIADH in concert with OHSS. Induction of ovulation by administration of exogenous gonadotropins is frequently used in patients being investigated for infertility. Although induction of ovulation is successful in most cases, some degree of hyperstimulation occurs. The most serious is that leading to OHSS, which occurs in approximately 4% of patients undergoing ovulation induction. This syndrome occurs with most methods of ovulation stimulation, and various classifications of its severity have been suggested.

4. Complications of OHSS include fluid depletion, shock, renal failure, thromboembolism, and in some cases, thoracic involvement with acute respiratory distress and pleural effusion. Hyponatremia and sodium retention, evidenced by inappropriately low urine sodium concentration, have both been reported in patients with OHSS. Prior to this report, however, hyponatremia with the low serum osmolality and inappropriately high urine sodium concentration characteristic of SIADH had not been reported in a patient with OHSS.

5. The patient’s respiratory distress at presentation was due to the combined effects of a markedly distended abdomen compressing the diaphragm towards the chest and a pleural effusion. A culture of the ascitic fluid was negative for bacterial growth and laboratory analysis of the fluid revealed (parentheses indicate reference range for transudates): white blood cell (WBC) count, 55/mm³; red blood cell count (RBC), 101/mm³; polymorphonuclear leukocytes, 68%; lymphocytes, 32%; sodium, 130 mEq/L; potassium, 4.8 mEq/L; glucose, 101 mg/dL (>95 mg/dL); lactate dehydrogenase, 126 U/L (<200 U/L); total protein, 39 g/L; and albumin, 25 g/L. These data suggest a hypercellular exudate with transudate glucose and LD concentrations. Because only a few cases have been reported previously, the value of these laboratory findings in identifying patients with SIADH and OHSS is not clear.

6. Plasma renin activity (PRA), serum aldosterone, and abdominal ultrasound. The severity of OHSS correlates positively with PRA and measurement of both PRA and aldosterone are useful in ruling out adrenal insufficiency as a cause of hyponatremia. In the patient reported in this case study, adrenal insufficiency was ruled out by the patient’s normal cortisol level. Prostaglandins and endothelial factors are thought to have a role in the pathogenesis of OHSS; however, their measurement is not routinely available and is best reserved for research purposes. Abdominal ultrasound examination should be performed to evaluate the ovaries, the extent of ascites, and the viability of any fetuses. Ultrasound testing of our patient’s abdomen revealed markedly enlarged ovaries (left ovary, 21 x 13 cm; right ovary, 21 x 16 cm) occupying most of the abdomen in addition to the ascites and 4 intrauterine gestational sacs.

7. The clinical management of OHSS depends on the severity of the disease. Mild forms of OHSS usually resolve within 2 to 3 weeks, and the treatment is usually conservative with observation and follow-up. On the other hand severe forms of OHSS requires hospital admission and active monitoring of the patient’s electrolyte balance, ascites, and respiratory symptoms. The management of hyponatremia depends on the level of the serum sodium concentration and the clinical picture of the patient such as the presence of neurological signs or symptoms. In our patient, although the serum sodium concentration was very low, she did not have any neurological abnormalities which would require prompt administration of hypertonic saline to quickly raise the serum sodium level. Moreover, administration of hypertonic saline is contraindicated in this case because of the patient’s hemoconcentration and the possibility of thromboembolic disease. The combination of hyponatremia with low serum osmolality and hemoconcentration is unusual and difficult to explain. Ascites are treated by repeated tapping and removal of the fluid or by inserting a drain. In addition, transfusion of albumin has been used in patients with a severe form of OHSS. In patients at risk of developing OHSS, administration of albumin at the time of oocyte collection has been shown to reduce the likelihood of severe OHSS from occurring.

We applied this approach to our patient with good success in relieving her symptoms of abdominal discomfort and respiratory distress. Her hypoalbuminemia was corrected by albumin infusion, which increases plasma oncotic pressure and thus limits fluid leakage from the plasma into the intravascular space. Therefore, plasma water retention may explain our patient’s hyponatremia.

**Patient’s Treatment and Course**

Fluids were restricted and the patient was closely monitored. Although the patient’s hyponatremia was asymptomatic, normal saline was infused until her serum sodium concentration exceeded 130 mEq/L. In view of the severity of her ascites, she...
was continued on fluid restriction. Her hypoalbuminemia was corrected by multiple infusions of 20% human albumin based on her serum albumin level. Four days after admission, she became increasingly short of breath with increased abdominal pain and distension due to the accumulation of ascitic fluid. A therapeutic tap of the ascitic fluid was performed under ultrasound guidance to relieve her severe abdominal discomfort. Due to the rapid accumulation of the ascitic fluid, abdominal tapping to remove ascitic fluid and infusion of albumin was repeated 2 more times based on the patient’s symptoms. With the above management, the patient improved progressively and was discharged 20 days after admission. The patient’s condition was reviewed during outpatient follow-up visits over the next few weeks. She continued to be stable with minimum ascites and diminishing pleural effusion on ultrasound examination. Moreover, repeat ultrasound examinations during this time period demonstrated diminishing ovarian size (left ovary, 16 x 10 cm; right ovary, 13 x 5.5 cm). In addition, her pregnancy progressed; however, at 11 weeks gestation, 1 fetus had no heart sounds and was spontaneously aborted. Subsequent ultrasound examinations revealed that the remaining 3 fetuses continued to develop normally. The patient was admitted in labor at 31 weeks gestation and had an emergency Cesarean section. Three healthy male babies were delivered, weighing 3.5, 3.7, and 4.0 pounds. Ten months after delivery, she and her babies were doing well.

**Keywords:** SIADH, ovarian hyperstimulation, hyponatremia