# Case Report: Syndrome of Inappropriate Antidiuretic Hormone and Tumor Lysis in Ovarian Cancer

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Abstract

Paraneoplastic syndromes are rare disorders that are triggered by the presence of a malignancy in the body but are not directly caused by the cancer cells themselves. Syndrome of inappropriate antidiuretic hormone (SIADH) and tumor lysis syndrome (TLS) are well known paraneoplastic syndromes. Both of these syndromes are extremely rare in ovarian cancer. We present the case of a 64-year-old woman with a new diagnosis of ovarian cancer and associated SIADH. Two days after the first cycle of carboplatin and paclitaxel, the patient developed laboratory abnormalities consistent with TLS; however, the SIADH began to improve as seen by an increase in her serum sodium. The patient ultimately died 8 days after 1 cycle of chemotherapy secondary to multi-organ failure. This is a case report describing 2 rarely described paraneoplastic syndromes that not only occurred in the same patient, but also in a malignancy with which the syndromes are rarely associated—ovarian cancer.

**Key words:** syndrome of inappropriate antidiuretic hormone, tumor lysis syndrome, ovarian cancer, paraneoplastic syndrome, hyponatremia, hyperuricemia, osmolality, carboplatin, paclitaxel

## Introduction

Ovarian cancer is the most lethal of gynecologic malignancies. The American Cancer Society estimates that 22,280 women will receive a new diagnosis of ovarian cancer, in 2016, and approximately 14,240 women will die from it.[1] The signs and symptoms of ovarian cancer such as bloating, abdominal pain, early satiety, and urinary symptoms, are nonspecific, usually present late in the disease course, and can be seen in other medical conditions. The main pattern of spread is intra-abdominal, which explains why many advanced-stage patients present with these symptoms. Rarely, distant metastasis is seen in the bones, brain, distant lymph nodes, and lungs.

Paraneoplastic syndromes are clinical manifestations of a cancer that are not caused by the cancer cells themselves.[2] Although paraneoplastic syndromes are rarely associated with ovarian cancer, when they do develop, they are typically characterized by cerebellar degeneration, polyneuritis, dermatomyositis, hemolytic anemia, disseminated intravascular coagulation, acanthosis, or nephrotic syndrome. Syndrome of inappropriate antidiuretic hormone (SIADH), when occurring in the setting of a malignancy, results from the ectopic tumor production of antidiuretic hormone (ADH).[3] SIADH, as a paraneoplastic process, is commonly seen in association with small cell lung carcinoma. It results in an increase of free-water reabsorption and urinary concentration resulting in hyponatremia.[3] An extensive literature search revealed only one other case of newly diagnosed ovarian cancer with SIADH.[4]

Tumor lysis syndrome (TLS) is a serious and potentially life-threatening adverse event caused by massive lysis of tumor cells as a consequence of chemotherapy treatment, but can also occur spontaneously in certain malignancies. Although rare in solid tumors, it is more commonly associated with hematologic malignancies. Associated clinical and laboratory derangements include acute renal injury, cardiac arrhythmias, seizures, and electrolyte abnormalities such as hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia. Without prompt intervention, death may occur due to multiorgan failure.[5]

Although both SIADH and TLS are commonly associated with small cell carcinoma of the lung and hematologic malignancies, respectively, to our knowledge, this is the first case in which both syndromes, SIADH and TLS, have been seen occurring in a newly diagnosed ovarian cancer patient.

## Case Presentation

A 64-year-old African-American woman presented with complaints of worsening shortness of breath. Computed tomography (CT) of the chest and abdomen was notable for moderate-sized right pleural effusion, diffuse intraperitoneal metastatic deposits, and ascites **[Figure 1A and 1B]**. Thoracentesis was initially conducted for therapeutic and diagnostic purposes. Cytology was positive for adenocarcinoma but its origin was not elucidated. The patient subsequently underwent paracentesis and omental biopsy and resulting histological and

immunostaining were consistent with serous papillary carcinoma of the ovary. She was diagnosed with an International Federation of Gynecology and Obstetrics (FIGO) stage IVa. Baseline CA-125 was 4961.7 U/ml. Serum sodium on initial presentation was 120 mmol/L and urine studies showed an osmolality of 683 mOsm/kg, and sodium of 72mmol/L. Neoadjuvant chemotherapy was recommended prior to debulking surgery. Repeat CT angiogram of the chest was conducted due to acute onset of shortness of breath. The patient was noted to have bilateral pulmonary emboli, right pleural effusion, peridiaphragmatic lymphadenopathy, and a right pleural-based mass measuring 4.8cm. Anticoagulation was initiated and one cycle of carboplatin and paclitaxel followed subsequently.

Two days after receiving her first cycle of chemotherapy, the patient was noted to have a rise in creatinine and a mild increase in potassium. She was thought to be intrasvascularly depleted, therefore, IV fluids were administered. Hyperkalemia was initially treated with sodium polystyrene, however, her potassium levels continued to rise. On day 5, the patient was transferred to the ICU for worsening hypotension. ICU admission laboratory tests revealed hypocalcemia (7.3 mg/dL), hyperphosphatemia (7.8 mg/dL), hyperkalemia (6.1 mmol/L), elevated creatinine (2.62 mg/dL), and hyperuricemia (16.9 mg/dL). Laboratory tests were consistent with tumor lysis syndrome. Lactate dehydrogenase was increased at 1380 (IU/L). Rasburicase was administered to increase clearance of uric acid. Interestingly, the laboratory results that were consistent with SIADH began to improve. Serum sodium increased to 126 mmol/L, however, both urine sodium and urine osmolality decreased to less than 2.0 mmol/L and 354 mOsm/kg, respectively. While uric acid decreased secondary to rasburicase administration, the patient had persistent hyperkalemia, hyperphosphatemia, and a worsening creatinine. Dialysis was attempted but was repeatedly interrupted due to hypotension. The patient became increasingly somnolent.

The patient died on day 8 post cycle one of chemotherapy, secondary to multi organ failure. Laboratory studies taken on the morning of the patient's death showed a serum sodium of 130 mmol/L, its highest since diagnosis. However, other serum electrolytes showed an elevated phosphorus of 8.0 mg/dL and potassium of 6.2 mmol/L with a low calcium of 7.1 mg/dL.

**FIGURE 1A:** Coronal image demonstrating extensive omental caking, large ascites, and cirrhotic liver.

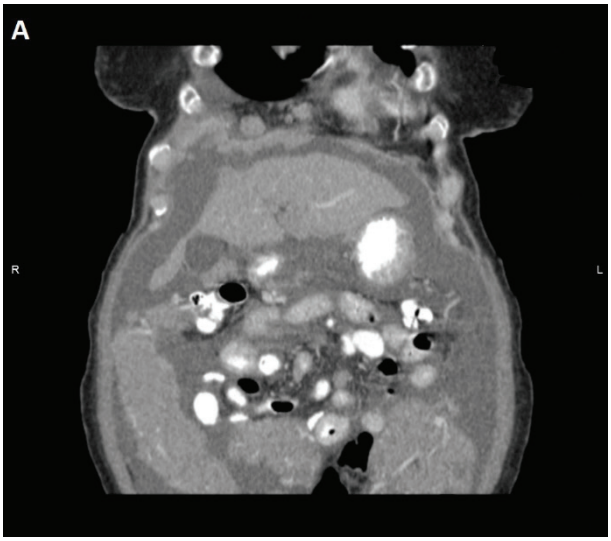
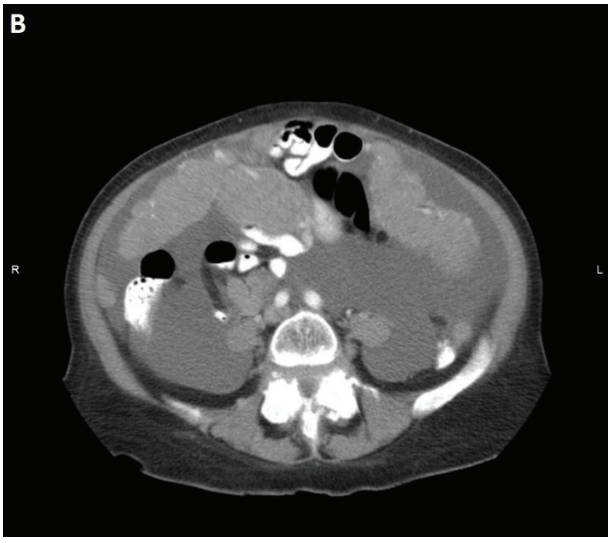



**FIGURE 1B:** Axial image demonstrating extensive omental caking and large ascites.




## Discussion

The optimal treatment for SIADH is treatment of the underlying malignancy.[6] Profound hyponatremia (serum sodium <125 mmol/L) can result in confusion, hallucination, seizures, coma, respiratory arrest, and can lead to death. Milder symptoms can include headache, poor mentation, muscle cramps, weakness, and dysgeusia.[7] If the response is suboptimal or treatment for the underlying malignancy is not possible, secondary interventions such as fluid restriction, intravenous saline infusion, vasopressin receptor antagonist, or demeclocycline are appropriate.

TLS is a potentially life-threatening complication of chemotherapy and given the high mortality associated with this syndrome, rapid recognition of the syndrome is crucial to its treatment. Risk factors for the development of TLS include large volume disease, rapid cancer growth, chemo-sensitivity of the malignancy, baseline azotemia, high lactate dehydrogenase levels, hyperuricemia, and/or hyperphosphatemia.[9-15] Treatment of TLS consists of aggressive intravenous hydration, monitoring of serum chemistries, urine alkalization, and treatment of hyperuricemia with hypouricemic agents such as allopurinol and/or rasburicase.[15] There are only a few case reports in the literature of TLS occurring with ovarian cancer after the initiation of chemotherapy.[15-21]

In summary, this case to our knowledge demonstrates the occur-

rence of both SIADH and TLS in the same patient with ovarian cancer. Both syndromes are rarely associated with ovarian carcinoma. Our patient initially presented with hyponatremia and an elevated urine osmolality and urine sodium consistent with the clinical diagnosis of SIADH. After the initiation of neoadjuvant chemotherapy, rapid cell breakdown occurred and the patient developed tumor lysis syndrome. Interestingly, as rapid tumor lysis progressed, the patient's serum sodium increased and urine osmolality and urine sodium decreased. Cytoreductive therapy with chemotherapy improved SIADH but led to TLS given the heavy tumor burden, which ultimately led to the patient's death.

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