Oncological emergency (SIADH)
February 19, 2003

Harmesh R. Naik, MD.
Oncologic emergency

SIADH
SIADH: Actual case-1

- 70 year old female
- Lethargy, weakness
- On Lasix
- CT head: negative
- Sodium: low
- Chest x-ray: Lung mass
- E. Coli UTI
SIADH: Actual case-1

- CT Chest (11-17-03):
  - 1.5 cm left lung mass
  - 5.5 x 3 cm mediastinal mass

- Biopsy: Small cell lung cancer
SIADH: Actual case-1

- Sodium, serum: 117
- Urine sodium: 52
- Serum osmolality: 238 mmol
- Urine osmolality: 361 mmol
- U. Osm > S. Osm
- Urine is inappropriately concentrated compared to serum
SIADH: Actual case-1

CT Chest (11-17-03):

- 1.5 cm left lung mass
- 5.5 x 3 cm mediastinal mass

CT Chest (1-14-03 post 3 cycles of chemotherapy):

- 1 cm left lung mass
- 2 cm mediastinal mass
SIADH: Actual case-1

Pre-treatment

Small cell, lung cancer-lung mass

Post-treatment
SIADH: Actual case-1

Pre-treatment

Post-treatment

Small cell lung cancer-mediastinal adenopathy
SIADH: Actual case-1

Pre-treatment

Small cell lung cancer-liver metastases

Post-treatment
SIADH: Actual case-1

- 11-16-2002: Na 117
- 11-19-02: Na 126
- 11-20-02: Na 125
- 11-22-02: Na 119
- 11-25-02: Na 122
- 12-09-02: Na 133
- 12-16-02: Na 146
- 1-27-03: Na 140 (post 3 cycles)
SIADH: Actual case-1

![Graph showing Na level changes during chemotherapy](image-url)
SIADH

Syndrome of inappropriate secretion of anti-diuretic hormone
SIADH

- First described in two lung cancer patients in 1957
- Hypothesis: Abnormal production of ADH or ADH like substance
- In 1968 ADH was extracted from cancers confirming the hypothesis
SIADH

- Observed in 1-2% of cancer patients
- 3-15% of small cell lung cancer patients have the syndrome
**SUBCLINICAL SIADH**

- Ectopic production of ADH is more common (without SIADH) in up to 40% of lung cancer patients
- Majority of small cell cancers stain positive for ADH (Arginine Vasopressin)
ADH (anti-diuretic hormone, Arginine Vasopressin)

- Released by posterior pituitary in response to increase in plasma osmolality or decrease in plasma volume
- It increases water resorption from renal collecting tubules and concentrates the urine
- Volume repletion inhibits ADH secretion
SIADH: Mechanism

- Inappropriate secretion of anti-diuretic hormone of central origin

  OR

- Ectopic production of anti-diuretic hormone (or ADH type substance)
Unregulated ADH production results in

- ADH binds to receptors in renal collectiong ducts and ascending loop of henle
- Increased sodium delivery to distal nephron
- Water retention by kidney
- Increase in renal perfusion
- Decreased resorption of sodium in proximal tubule
SIADH: Pathophysiology

- End result
  - Increased total body water
  - Increase in plasma volume
  - Inability to excrete maximally dilute urine in presence of low serum osmolality
  - ADH secretion continues despite low plasma osmolality
SIADH: Patterns of ADH concentration

- Erratic ADH release
- In 37% case
- ADH release is independent of osmotic control
SIADH: Patterns of ADH concentration

- Reset Osmostat
- In 33% case
- Abnormally low threshold for ADH release
- At very low sodium level, patients can produce maximally dilute urine
SIADH: Patterns of ADH concentration

- ADH leak pattern
- In 16% case
- Sustained ADH production below the threshold
- Normal ADH release in response to osmotic challenge
SIADH: Patterns of ADH concentration

- Normal ADH level
- 14% patients Failure to dilute urine despite normal ADH levels
- Mechanism not understood
SIADH: Patterns of ADH concentration

- Normal
- Erratic ADH
- Reset osmostat
- ADH leak
Ectopic ANP induced hyponatremia

- Atrial natriuretic peptide is released by atria
- Excess ANP may produce syndrome similar to SIADH
- Small cell cancer may have excess levels of ANP producing hyponatremia (with normal ADH levels)
SIADH: Symptoms

- Asymptomatic
- Neurological changes: memory loss, apathy, loss of thinking, lethargy, confusion, focal findings (Na level 120-125 meq)
- Fatigue, anorexia, myalgia
- Seizures and coma and death if Na is <115 (medical emergency).
SIADH: Symptoms

Factors determining the symptoms:

- Level of sodium
- Rapidity of sodium decline
SIADH

- Diagnosis is suspected because of low sodium level
Hyponatremia

- Hypervolemic
- Euvolemic
- Hypovolemic
SIADH: Differential diagnosis of hyponatremia (Hypervolemic)

- Excess sodium and water
- Excess ECF volume (edema)
  - Liver disease-cirrhosis
  - Congestive heart failure
  - Nephrotic syndrome
  - Renal failure
### SIADH: Differential diagnosis of hyponatremia (Hypovolemic)

- **Deficit of sodium and water-volume depletion**
- **Renal losses**
  - Diuretic excess
  - Salt losing nephritis
  - Osmotic diuresis (mannitol, glucose, urea)
- **Extra-renal losses**
  - Vomiting, diarrhea, pancreatitis
SIADH: Differential diagnosis of hyponatremia (Euvolemic)

- Hypothyroidism
- Adrenal insufficiency
- SIADH
- Drugs
- Pain
SIADH: Physical exam

- Determine volume status (fluid overload, euvolemic or volume depletion)
- Neurological findings sometimes focal
- Signs of primary cancer
SIADH

- Establish the diagnosis
- Lab work is the key to diagnosis
SIADH: Diagnostic tests

- Serum and urine electrolytes and osmolality
- Less than maximally dilute urine with low p. osmolality (water intoxication)
SIADH: Diagnostic criteria

- Euvolemic status
- Normal renal, thyroid, pituitary and adrenal function
- Serum hyponatremia (< 135 meq)
- Urine sodium > 20 mmol/L
- High urine Osm (> 500 mosm)
- Low plasma Osm (< 280 mosm)
SIADH: Laboratory features

- Low sodium and low uric acid are almost only abnormalities in electrolytes.
- Suspect additional complications for any additional electrolyte abnormalities (e.g., Hypokalemia—ACTH production, Hypercalcemia—bone mets or ectopic PTH like).
SIADH: Etiologic work up

- Determine the etiology of SIADH
- Chest x-ray
- Many times cancer diagnosis is obvious
- Sometimes cancer is diagnosis of exclusion
SIADH: Causes

- Malignancy
- CNS disease (CNS metastases, infections, trauma, bleeding)
- Pulmonary diseases (cancer, TB, abscess, pneumonia)
- Drugs (Cytoxan, Morphine, Vincristine, diuretics, Amitriptyline etc.)
SIADH: Common cancers

- Small cell lung cancer (60%)
- Carcinoid tumors
- Pancreatic, esophageal, colon cancers
- Prostate cancer
- Bladder cancer
- Adrenal carcinoma
- Hodgkin’s disease, AML
SIADH and Cancer prognosis

- Not an indicator of poor outcome
- Not an indicator of disease burden
SIADH: Acute therapy goals

- Slow correction at 0.5-1 meq/l/hr
- Increase sodium to no more than 20-25 meq/48 hours from the baseline
- Target sodium level 125-130 meq/L
- Na needed = (desired serum Na - measured Na) x kg body weight x 0.6
SIADH: Acute therapy

- Induced diuresis (N. Saline with Lasix)-replace electrolytes
- 3% Hypertonic saline-for coma or seizures
- Central pontine Myelinolysis if correction is >2meq/l/hr
- Acute therapy for CNS or other cancer
Central pontine Myelinolysis

- Symmetrical focal myelin destruction in basal central pons
- Follows 1-3 days of hyponatremia followed by rapid correction over 20 meq/L
- Flaccid or Spastic quadriparesis
- Meticulous maintenance of electrolytes may reverse it
SIADH: Chronic therapy

- Treat the underlying tumor
- Fluid restriction (<0.5-1 L/day)
- Demeclocycline PO 300-600-1200 mg/day
- Induces renal resistance to ADH and allows free water excretion (reversible nephrogenic diabetes insipidus)
- Lithium salts-less reliable
SIADH and Status of cancer

- Hyponatremia correlates with the activity of cancer
- May serve as a marker
SCLC and SIADH-case-2 (lung, adenopathy, liver mets)

Diagnosis

Chemotherapy completed

Local chest recurrence

Radiation

Recurrent Liver mets

Hospice