

**Case Report – Initial Presentation**

A 58 year old lady was seen by endocrinology with symptomatic hyponatraemia (Serum Na<sup>+</sup> 112mmol/L). She had chest pain, dyspnoea, lethargy, nausea and weight loss.

Past medical history included ischaemic heart disease, ischaemic stroke and chronic obstructive pulmonary disease. She had no allergies and took Aspirin, Dipyridamole, Bisoprolol, Nicorandil and Simvastatin. She smoked 20 cigarettes per day and was mobile only short distances.

Clinical examination was unremarkable and she was haemodynamically stable and clinically euvolaemic. Laboratory results (full blood count, electrolytes, troponin, liver function tests) were unremarkable aside from her hyponatraemia. Her chest x-ray was normal (Fig 1A). She was investigated for hyponatraemia and diagnosed with the syndrome of inappropriate anti-diuretic hormone (SIADH) [Box 1].

**Box 1 – Initial investigations**

<b>Serum Na<sup>+</sup> (136-145 mmol/L)</b>	112	<b>Urine Na<sup>+</sup> (mmol/L)</b>	158
<b>Serum Osmolality (275-295 mOsm/kg)</b>	247	<b>Urine Osmolality (mOsm/kg)</b>	669
<b>Short Synacthen (nmol/L)</b>	Cortisol 305 → 715 → 835		
<b>TSH (0.4-5.0 mu/L)</b>	0.71		

Day	Sodium mmol/l	Other Events
1	112	<b>Fluid restriction 1 Litre / day</b>
3	120	<b>Started demeclocycline 150mg BD</b>
6	111	US Abdomen - R adnexal cyst, benign appearance
7	117	OGD showed gastritis, started ranitidine
10	121	Ranitidine changed to omeprazole (ongoing nausea)
11		CT Thorax / Abdomen / Pelvis - Right apical lung nodularity (Fig 1B), emphysema, right adnexal cyst and no lymphadenopathy. CT Head - old infarct, no acute pathology <b>Demclocycline stopped, tolvaptan 7.5mg stat dose</b>
12	135	Acute drop in eGFR (76→42 ml/min) - <b>tolvaptan ceased</b>
13	129	<b>Demclocycline 300mg BD restarted</b>
14	127	<b>Demclocycline increased to 300mg TDS</b>
15	120	<b>Demclocycline increased to 300mg QDS</b>
18	124	<b>Stopped demeclocycline, restarted tolvaptan 7.5mg daily</b>
20	129	Discharged on tolvaptan 7.5mg alternate days - eGFR 56 ml/min

**Case Report – Follow up**

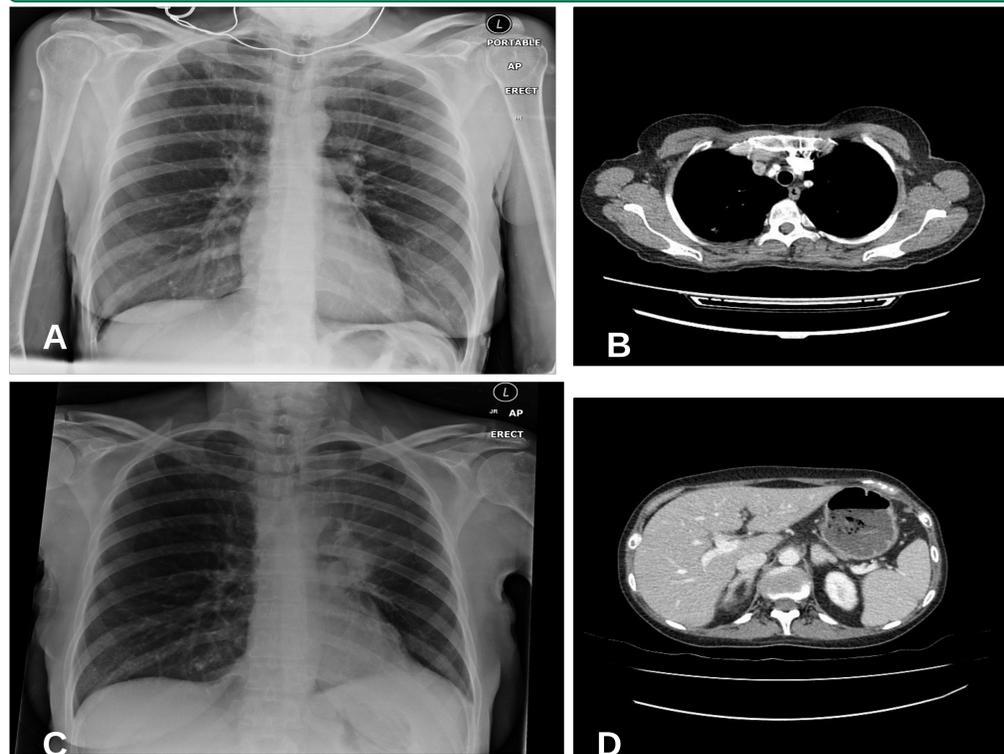
Following discharge she was seen regularly in the endocrine clinic and multidisciplinary input was obtained.

Gynaecological investigation revealed simple ovarian cysts and no sinister pathology. The respiratory MDT felt the right upper lobe nodularity was inflammatory and organised a repeat CT scan for 3 months time.

Over 2 months her tolvaptan dose was titrated to maintain her serum sodium within normal limits

Day	Sodium mmol/l	Other Events
88	121	<b>Individualised funding request (IFR) for tolvaptan rejected.</b> Re-admitted and <b>started demeclocycline 300mg TDS</b>
92	127	<b>Increased demeclocycline 300mg QDS</b> and discharged from hospital
95		Repeat CT Thorax - no change in nodule and deemed to be inflammatory
102	138	Acute kidney injury (eGFR 23), re-admitted, demeclocycline stopped, rehydrated cautiously
105	143	eGFR improved to 43 and currently off all treatment. Discharged from hospital.
133	122	Repeat IFR accepted, seen in endocrine clinic and restarted <b>tolvaptan 7.5mg alternate days</b>

**Figure 1**



**Case Report – Subsequent Events**

6 months after initial presentation she had new oral ulceration, worsening lethargy and nausea. Bloods showed sodium of 136 mmol/L, potassium of 3.2 mmol/L and thrombocytopenia (36 \* 10<sup>9</sup>/L).

Despite supplementation, her potassium dropped and she was admitted for parenteral potassium. Repeat chest x-ray showed a left hilar mass (Fig 1C). A blood film showed a leucoerythroblastic picture in keeping with marrow infiltration. A CT scan confirmed the left hilar mass with upper lobe collapse, unchanged appearances of the right upper lobe nodule and bilateral adrenal metastases (Fig 1D).

Random cortisol on admission was 2548nmol/L. Despite 16mg dexamethasone prescribed by the admission team subsequent testing showed a cortisol of 3107nmol/L and paired ACTH 561 (0 – 46ng/L) in keeping with ectopic Cushing's syndrome.

The bone marrow biopsy subsequently confirmed small cell carcinoma. The patient unfortunately deteriorated rapidly and was provided with best supportive care.

**Discussion**

Paraneoplastic endocrine syndromes are commonly associated with malignancy, particularly small cell carcinoma. 10-45% patients with small cell lung cancer will develop SIADH. <sup>1</sup> Clinically apparent Cushing's syndrome is less common and the simultaneous presence of SIADH and ectopic ACTH is rarely reported, with only 6 cases described in the literature. <sup>2,3</sup>

Hyponatraemia occurs frequently in hospitalised patients and is often underinvestigated. <sup>4</sup> Humayan et al demonstrated that hyponatraemia due to any cause but responsive only to tolvaptan was associated with increased mortality. 60% of patients had a malignancy and 90% of these malignancies were undiagnosed at presentation. <sup>5</sup> Prompt investigation of hyponatraemia may yield the opportunity for early diagnosis of malignancy.

Despite extensive investigation this lady re-presented with widespread metastatic disease. This case illustrates that SIADH may precede a cancer diagnosis highlighting the importance of exhaustive investigations and close follow-up in patients with resistant hyponatraemia, especially when responsive only to vasopressin receptor antagonists. It also highlights that multiple paraneoplastic endocrine syndromes may co-exist potentially leading to a mixed biochemical picture.

**References**

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5. Humayan M. Long-term follow-up of patients treated with tolvaptan for resistant hyponatraemia. Endocrine Abstracts (2014) 34 P84