A 59-year-old Chinese Female, active smoker 30 pack years with past medical history of HTN, T2DM, presented with generalized weakness with a background of malaise, fatigue, and diarrhea for the past two months. During this time period she noted poor BP and glucose control, despite being compliant to her prescribed medications. Her medications include glipizide, metformin, hydrochlorothiazide, Enalapril and Amlodipine.

On examination, patient was alert and anxious. Was overweight with facial puffiness. Exhibited both upper and lower limb weakness with power of 4/5. Patient had mild clubbing.

Vitals

T 37.5 HR 99 RR 16 BP 176/99 sp02 96% on RA

Initial Investigations

Hb 16 TW 10 Plt 380

Na 144 K 2.1 Cl 105 Bicarb 30 Glu 10 Cr 87 U 6 Mg 0.9

Liver panel and coagulation panel unremarkable

Besides starting immediate treatment of patient electrolyte derangement which of the following test(s) will be most useful for your workup?

Besides starting immediate treatment of patient electrolyte derangement which of the following test(s) will be most useful for your workup?

1) Thyroid panel
2) **Urine and plasma osmolarity with urine potassium**
3) Arterial blood gas
4) Urine chloride
5) 8am cortisol

Many did consider thyroid panel as an option, with periodic paralysis as a diagnosis in mind. However, there are few evidence in the history and physical examination that supports a diagnosis of hyperthyroidism. For example she has been malaise and fatigued. And there is also no weight loss. The story also did not mention any other features of hyperthyroidism like heat intolerance. I would be anxious also if I have new onset weakness and need to be hospitalized. Arterial blood gas may be useful in the approach to hypokalemia but in this case one needs to dichotomize and commit to a renal vs extra renal K loss first. Urine chloride can be used in differentiating patients with metabolic alkalosis into saline responsive and saline resistant causes, however do realize that it's not commonly used in clinical practice as clinical history and physical examination can help differentiate as well.

You calculated the TTKG based on urine & plasma osmolarity and potassium with a resultant value of 6. Patient's blood pressure was brought under control with the addition of hydralazine. As part of the workup, renal ultrasound was performed which excluded renal artery stenosis but incidentally found scattered hypodense lesions in the liver. On further history patient has had LOA although minimal change to body weight.

What is the most likely diagnosis?

1) Conn's syndrome
2) HCC
3) Congenital Adrenal hyperplasia
4) Cushing's disease
5) **Lung carcinoma**

Conn's is always the first thought we have when we think of hypertension and hypokalemia. However, do realize that the question does mention findings in the liver that you cannot dismiss as an incidental non-relevant finding. Some may argue that HCC could be the answer with paraneoplastic ACTH secretion but there are no reports of such cases. Congential adrenal hyperplasia is rarely selected as an answer as people believe it only presents in young children or in infancy but please note that this is not true.

Given the smoking history, clubbing and constitutional symptoms you suspect lung carcinoma.

A subsequent chest/abdomen/pelvis CT showed left supraclavicular and large mediastinal lymph nodes, a 13 mm left upper lobe lung lesion, and multiple mildly enhancing hepatic lesions with central necrosis.

A transbronchial fine needle aspiration of the mediastinal LNs was performed, BAL performed.

What is the most likely histology of the cancer?

1) Squamous cell carcinoma
2) Large cell carcinoma
3) **Small cell carcinoma**
4) Bronchioalveolar
5) Adenocarcinoma

This is a fairly straight forward question.

The medical student in your team is eager to understand the mechanism behind patient's initial presentation.

Given your diagnosis, which of the following combination of results would you use to explain the mechanism of the patient's hypokalemia

1) High ACTH, High aldosterone and low renin
2) High ACTH, normal aldosterone and renin
3) Low ACTH, high aldosterone and low renin
4) **High ACTH, Low aldosterone and low renin**
5) Low ACTH, high aldosterone and high renin

Everyone understands that ACTH has to be high but some argue that ACTH will result in not only the elevation of cortisol but also aldosterone. But do realize that the main mechanism that drives cortisol levels is ACTH but the main mechanism that drives aldosterone is the renin-angiotensin-aldosterone axis. Which will be underactive.

After explaining the mechanism of ectopic ACTH secretion secondary to small cell carcinoma of the lung. The eager student not convinced of your explanation asks you how does high ACTH explain hypertension and hypokalemia.

You reply confidently that

1) **Cortisol is molecularly very similar to aldosterone and is capable of binding to mineralocorticoid receptors**
2) ACTH is a stress hormone resulting in raised sympathetic drive which results in raised blood pressure and neural mechanism of diuresis
3) ACTH causes increased cortisol and vasopressin. Vasopressin results in free water reabsorption and lost of potassium.
4) Cortisol is a minor vasopressor which raises the blood pressure via increasing peripheral vasoconstriction which in reduced renal perfusion. This effect will activate the RAS mechanism which results in the low potassium
5) Hypokalemia is not related to ectopic ACTH as patient's diarrhea explains the incidental K findings.

Only option 1 is correct as the rest are simply not facts. So we classically learn that causes of hypertension and low K as primary & secondary hyperaldosteronism and non-aldosterone mediated mechanism like Cushing's. But it's important to not just memorize but to know why as well.