Clinical Presentation
A 23-year-old G2P1A0 woman was admitted to an obstetrics unit at 32 weeks of gestation after a routine outpatient laboratory workup revealed severe hypokalemia that failed to resolve despite potassium replacement. She reported some nausea and loose stools but denied vomiting or frequent watery diarrhea. She denied ingestion of licorice and family history of hypertension or hypokalemia. Her medical history was significant for hypokalemia and gestational hypertension leading to induction of labor and delivery at 37 weeks of gestation during a previous pregnancy approximately 2 years earlier. A review of her medical records indicated potassium levels ranging from 2.6 to 3.4 mmol/L during her first pregnancy. It was noted that her potassium level was normal after her first pregnancy.

On admission, physical examination revealed an elevated blood pressure of 138/81 mm Hg and trace peripheral edema. The patient appeared well nourished. Pertinent laboratory measurements are shown in Table 1. While she was an inpatient, serum potassium levels continued to be in the low-normal range despite supplementation of both potassium and magnesium. Eventually she was discharged on treatment with oral potassium supplements. Her potassium level continued to be in the low-normal range during outpatient follow-up visits. At 37 weeks of gestation, she was admitted to the hospital for induction of labor due to gestational hypertension. Her blood pressure and potassium level returned to normal after delivery without the need for antihypertensive medications or further potassium supplementation.

Discussion
What is the differential diagnosis of hypertension and hypokalemia observed in this patient?
The differential diagnosis for a patient presenting with hypertension and hypokalemia is broad and includes congenital adrenal hyperplasia (CAH), Liddle syndrome, primary hyperaldosteronism, syndrome of apparent mineralocorticoid excess (AME), Chrousos syndrome, Gordon syndrome (pseudohypoaldosteronism type 2), glucocorticoid remediable aldosteronism (GRA), and Geller syndrome.

CAH is due to a deficiency of 11β-hydroxylase causing an excess of 11-deoxycortisol and deoxycorticosterone (DOC) due to reduced conversion to cortisol and corticosterone, respectively. Similarly, deficiency of 17α-hydroxylase increases DOC and corticosterone levels. As a result, CAH manifests as hypertension, hypokalemia, low aldosterone levels, and low renin levels.

Liddle syndrome is due to a gain-of-function mutation of the renal epithelial sodium channel, leading to constitutive sodium reabsorption and consequently resistant hypertension and hypokalemia. Renin and aldosterone levels are suppressed.

Primary hyperaldosteronism, due to either an adrenal adenoma or adrenal hyperplasia, manifests as hypertension, hypokalemia, and metabolic alkalosis with suppressed renin levels.

AME syndrome is due to deficiency of 11β-hydroxysteroid dehydrogenase, which normally inhibits the conversion of cortisol to cortisone. Consequently, elevated cortisol levels activate mineralocorticoid receptors, causing sodium retention and potassium wasting. The syndrome can be hereditary or acquired. Certain types of licorice root contain the compounds glycyrrhizic acid and glycerrhitinic acid, which can inhibit 11β-hydroxysteroid dehydrogenase and manifest as acquired AME syndrome.

Chrousos syndrome is caused by an inactivating glucocorticoid receptor gene mutation causing resistance of tissues to glucocorticoids. Subsequently increased corticotropin secretion results in hypersecretion of corticosterone and DOC and eventually manifests as hypertension and hypokalemic alkalosis.

Gordon syndrome is caused by a gain-of-function mutation in the WNK1 or WNK4 genes and manifests as hypertension, hyperkalemia, and metabolic acidosis with low-normal aldosterone level.

GRA is a condition that disrupts regulation of aldosterone synthesis by the renin-angiotensin system. In GRA, aldosterone synthesis is under corticotropin control secondary to a mutation in the CYP11B1 and CYP11B2 genes. This manifests as hypertension, hypokalemia, and hyperaldosteronism with suppressed renin levels.

Geller syndrome is a rare disease caused by a gain-of-function mutation in the mineralocorticoid receptor resulting from the substitution of leucine for serine at amino acid 810, which is in the hormone-binding domain. It manifests as hypokalemia, low levels of
aldosterone and renin, and increased blood pressure secondary to the effect of progesterone on the mutated receptor.

**What is the most likely cause of this patient’s clinical condition and what additional diagnostics should be obtained to support the diagnosis?**

A clinical history of 2 separate pregnancies complicated by severe hypokalemia and gestational hypertension necessitating early delivery with normalization of potassium levels and blood pressure postdelivery strongly supports Geller syndrome. The high progesterone state in pregnancy activates the mutated mineralocorticoid receptor, thereby causing sodium retention and potassium wasting leading to hypertension and hypokalemia, respectively. The diagnosis can be further strengthened by evaluation for laboratory values including serum aldosterone, plasma renin, urinary potassium, urinary creatinine, serum osmolality, and urine osmolality. As progesterone level increases and peaks at a later stage of pregnancy, hypertension and hypokalemia become more prominent during the third trimester, as witnessed in this patient.

This patient had an elevated random urinary potassium-creatinine ratio despite hypokalemia (supporting renal potassium wasting) in the presence of hypertension, suggesting a hyperaldosteronism-like state. However, the observed suppressed serum aldosterone level leads to the diagnosis of an activating mineralocorticoid receptor mutation.

**How should this patient be treated?**

Therapeutics and lifestyle modifications geared toward the management of hypertension and hypokalemia with close monitoring of the mother and fetus are the cornerstone of the management in patients with Geller syndrome. Because the hypokalemia and hypertension resolve postpartum, management during pregnancy is necessary but otherwise no specific treatment is warranted.