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Hypertension and Acute Kidney Injury During Pregnancy

CLINICAL PRESENTATION

A 25-year-old woman of South Asian ethnicity presented in the emergency department with confusion, diffuse abdominal pain, and vaginal spotting; she was 26 weeks pregnant. Gestational diabetes had recently been diagnosed, and she was started on insulin therapy. Her obstetric history was unremarkable and included one full-term pregnancy ending in an uncomplicated vaginal delivery. She had no family history of hypertension, diabetes, or kidney disease. On evaluation, the patient was found to be delirious, with blood pressure (BP) of 190/120 Hg mm. She did not have focal neurologic deficits, cardiac arrhythmia, murmur, or bruising or petechiae. Funduscopic examination revealed grade 2 hypertensive retinopathy. Laboratory testing showed the following values: total white blood cell count, $4.2 \times 10^3/\mu L$; hemoglobin, 9 g/dL; platelet count, $76 \times 10^3/\mu L$; serum creatinine, 2.4 mg/dL (corresponding to estimated glomerular filtration rate of 22 mL/min/1.73 m^2 as calculated by the MDRD [Modification of Diet in Renal Disease] Study equation); lactate dehydrogenase, 245 U/L; total bilirubin, 1.4 mg/dL; aspartate aminotransferase, 30 U/L; and alanine aminotransferase, 39 U/L. Urinalysis showed 8 to 10 red blood cells per high-power field and no casts; spot urine protein-creatinine ratio was 300 mg/g. Sepsis workup was negative, and an abdominal ultrasound confirmed abruptio placenta with intrauterine death of the fetus. Emergency evacuation of the retained products of conception was performed. The patient developed intraoperative hypotension from bleeding, requiring a multiple-unit blood transfusion. The immediate postoperative period was complicated by anuric acute kidney injury (AKI) necessitating urgent initiation of sustained slow efficiency dialysis therapy to correct pulmonary edema and hyperkalemic metabolic acidosis.

Four weeks postdelivery, the patient remained anuric with episodes of uncontrolled hypertension and flash pulmonary edema despite being on maximum doses of 4 antihypertensive medications. She required frequent rescue hemodialysis therapy and intermittent parenteral antihypertensive drugs.

- **How are hypertensive disorders in pregnancy classified?**
- **What are the causes of AKI during pregnancy?**
- **How should this case be investigated further?**
- **How should this patient be treated?**

DISCUSSION

How are hypertensive disorders in pregnancy classified?

The 2013 American College of Obstetricians and Gynecologists (ACOG) task force report recommends maintaining the current classification of hypertension in pregnancy under 4 categories: preeclampsia-eclampsia, chronic hypertension of any cause, chronic hypertension with superimposed preeclampsia, and gestational hypertension.[1]

Preeclampsia is defined as new-onset hypertension with BP ≥ 140/90 mm Hg and proteinuria with protein excretion > 300 mg/d or protein-creatinine ratio > 300 mg/g, after 20 weeks of pregnancy. Eclampsia is a severe manifestation of this syndrome characterized by convulsions. Edema often is present in preeclampsia but is no longer required for diagnosis. As stated in the current ACOG guideline and the 2014 guideline of the Canadian Hypertensive Disorders of Pregnancy Working Group, the presence of proteinuria is not essential for diagnosing preeclampsia in patients with adverse conditions and severe complications (the specific nature of which are defined in the guidelines). This recommendation is meant to facilitate early and effective interventions in such patients.[2]

Chronic hypertension in the setting of pregnancy is defined as BP ≥ 140/90 Hg mm that predates conception or is diagnosed prior to 20 weeks' gestation. When preeclampsia complicates a preexisting hypertensive disorder, it is referred to as chronic hypertension with superimposed preeclampsia. If there is evidence of concomitant target-organ dysfunction, a suffix of "with severe features" is added.

Gestational hypertension is new-onset hypertension with BP ≥ 140/90 mm Hg after 20 weeks' gestation in the absence of proteinuria that resolves after delivery.[1,2]

Secondary hypertension is diagnosed in 0.24% of pregnancies worldwide; however, it is likely under-recognized due to its rarity and because obstetricians and family physicians might lack familiarity with the entity.[3] Further, pregnancy-related changes in maternal physiology and endocrinology can pose challenges in interpreting laboratory investigations relevant to the diagnosis of secondary hypertension. Optimal use of the recommended imaging techniques in the diagnosis of secondary hypertension in pregnancy has constraints owing to the risks of radiation.

What are the causes of AKI during pregnancy?

To prevent deleterious consequences to the mother and fetus, a high index of suspicion and comprehensive knowledge of mechanisms of injury, adaptive kidney changes in pregnancy, and their implications in interpreting routine parameters used in the diagnosis of AKI are critical to early recognition of pregnancy-related AKI and subsequent intervention. The current consensus definitions of AKI are not sensitive enough to diagnose pregnancy-related AKI in the context of increased solute clearance and plasma volume expansion seen in pregnancy. The general approach to pregnancy-related AKI is guided by history, clinical setting, physical examination, urinalysis, and imaging to identify the relevant prerenal, intrinsic, and postrenal causes.[4] The current literature estimates that in the developing world, the

Table 1. Syndromes of Thrombotic Microangiopathy in Pregnancy

	Severe Preeclampsia	HELLP	TTP	aHUS
Time of diagnosis	Usually 3rd trimester	Usually 3rd trimester	2nd or 3rd trimester	Postpartum
Hypertension	100%	80%	0/+	+
AKI	Mild	Mild/moderate	Mild/moderate	Severe
Hemolytic anemia	0	+	++	++
Thrombocytopenia	0/+	+	++	++
ADAMTS-13 activity decreased to <10%	0	0	Yes	0/Mildly decreased
Recovery after delivery	<1 wk	1-2 wk	No recovery	No recovery
Treatment	Delivery and supportive	Delivery and supportive	Plasma exchange	Plasma exchange/eculizumab
High LDH:AST ratio (>22)	0	0	++	Unclear

Abbreviations and definitions: 0, absence; 0/+, occasionally present; +, sometimes present; ++, always present; aHUS, atypical hemolytic uremic syndrome; AKI, acute kidney injury; AST, aspartate aminotransferase; LDH, lactate dehydrogenase; HELLP, hemolysis, elevated liver enzymes and low platelets; TTP, thrombotic thrombocytopenic purpura.

Adapted from Machado et al[7] with permission of the Italian Society of Nephrology.

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