Preeclampsia

Preeclampsia is characterized by the new onset of sustained hypertension (blood pressure ≥140/90 mm Hg) and proteinuria (>300 mg/day) that develops after 20 weeks' gestation in a previously normotensive woman. Although hypertension and proteinuria are the principal features of preeclampsia, it is a systemic vascular disease that may also cause central nervous system symptoms (e.g., visual disturbances, headache, altered mental status), abdominal pain, nausea and vomiting, liver dysfunction, thrombocytopenia, pulmonary dysfunction, impaired fetal growth, nephrotic-range proteinuria, and AKI. If grand mal seizures develop without other explanation, a diagnosis of eclampsia is made. The HELLP syndrome, characterized by *h*emolysis, *e*levated *l*iver enzymes, and a *l*ow *p*latelet count, may be a manifestation of severe preeclampsia, although some consider it to be a separate disorder. It is also associated with increased maternal and fetal mortality.

Preeclampsia should be distinguished from other hypertensive conditions that can occur during pregnancy, including preexisting hypertension that occurs before 20 weeks' gestation and persists after delivery, preeclampsia superimposed on preexisting chronic hypertension, and gestational hypertension (i.e., new-onset hypertension after 20 weeks' gestation without proteinuria or other related manifestations).

Progress has been made in understanding the pathogenesis of preeclampsia, and maternal and placental or fetal factors have been implicated. Abnormal development of placental vasculature in early pregnancy is thought to lead to some degree of placental hypoperfusion that releases antiangiogenic factors into the maternal circulation, disturbing the delicate balance of angiogenic and antiangiogenic factors. This causes systemic endothelial dysfunction in the mother that leads to hypertension, proteinuria, and other manifestations of the disease.

Soluble FMS-related tyrosine kinase 1 (sFLT1) is a placenta-derived circulating antiangiogenic factor that appears to play a central role in the pathogenesis of preeclampsia. It antagonizes the proangiogenic effects of vascular endothelial growth factor (VEGF) and placental growth factor (PGF) by binding to them and preventing interaction with their receptors. Soluble endoglin (sENG), another antiangiogenic factor that is widely expressed on vascular endothelium, is thought to be an important mediator of preeclampsia. Endothelial dysfunction in preeclampsia is associated with increased sensitivity to vasopressor agents, including angiotensin II, systemic vasoconstriction, and reduced fibrinolytic function.

Kidney biopsy findings include glomerular endothelial cell swelling (i.e., endotheliosis) and occlusion of the capillary lumen with ischemia. These findings are also seen with other microangiopathic disorders, although fibrin thrombi in glomerular capillaries are less commonly seen than with other causes. Foot process effacement is not usually seen.

The only effective treatment for preeclampsia is delivery of the fetus and placenta. The timing of delivery must take into account gestational age, severity of preeclampsia, presence or absence of systemic features, and status of the fetus and mother. Proper obstetric care is essential to balance the risk to the mother against the risk for prematurity of the fetus.

Treatment of mild hypertension in women with preeclampsia should be avoided because it does not treat the underlying disease process, alter the course of disease, or reduce clinical sequelae. In the absence of clinical manifestations other than proteinuria, it is usually unnecessary to start antihypertensive medications unless the systolic blood pressure is greater than 150 mm Hg or the diastolic blood pressure is higher than 100 mm Hg. Labetalol and hydralazine, both of which can be given intravenously or orally, are often recommended as first-line therapy for acute management. For chronic treatment, methyldopa or labetalol are often recommended initially, with extended-release nifedipine added if necessary. Diuretics and dietary sodium restriction usually are avoided unless the patient has pulmonary edema.

The risk profile of these medications is poorly defined in pregnancy. ACE inhibitors, ARBs, and direct renin inhibitors are contraindicated during pregnancy because of the risk of fetal abnormalities. Magnesium sulfate is used in severe cases of preeclampsia to reduce the risk of seizures, but it does not treat other manifestations of the disease or reduce maternal or fetal mortality rates.

Most manifestations of preeclampsia begin to improve shortly after delivery, but in some women, hypertension, proteinuria, and other manifestations may persist for several weeks or months before resolving completely. Because preeclampsia is a risk factor for future hypertension, kidney disease, and cardiovascular events, continued medical follow-up is essential.

Scleroderma Renal Crisis

Systemic sclerosis (i.e., scleroderma) is an idiopathic connective tissue disorder associated with deposition of collagen and other extracellular matrix proteins that produces inflammation and fibrosis of the skin and internal organs. Proliferative endovascular lesions may lead to obliteration of the vascular internal lumina and renal ischemia, with hypertension, increased renin activity, and elevated levels of angiotensin II and aldosterone.

AKI and rapidly worsening hypertension in patients with scleroderma is called *scleroderma renal crisis*. It occurs in approximately 5% to 10% of patients with scleroderma, typically within the first few years after onset and primarily in those with systemic rather than localized cutaneous scleroderma who also have progressive skin and cardiac involvement. Subclinical renal involvement occurs much more frequently. Scleroderma renal crisis occasionally develops before the clinical diagnosis of scleroderma has been made.

Scleroderma renal crisis is often associated with rapid and severe loss of kidney function, oliguria, hypertensive encephalopathy, and heart failure. Microangiopathic hemolytic anemia may also occur. About 10% of patients with scleroderma renal crisis do not have hypertension. This occurs more commonly among patients being treated with ACE inhibitors or high-dose corticosteroids.

Anti–RNA polymerase III antibodies are strongly associated with the risk of scleroderma renal crisis and have been suggested as markers for scleroderma renal crisis. Renal biopsy may reveal interlobular artery involvement with intimal thickening, endothelial cell proliferation, and edema with obliteration of the vessel lumen with concentric onion-skinning of the wall of arterioles. Fibrinoid necrosis occurs in afferent arterioles with intravascular