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When listening for hoofbeats, sometimes there are zebras—an interesting case of a teenager with edema and high blood pressure: Answers

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Answers

Hospital course

There was marked improvement in her blood pressure during hospital day 1. A complete blood count did indicate significant anemia with a hemoglobin count of 5.0 g/dl. Her urinalysis showed 3+ protein and a large amount of blood by dipstick; microscopic examination of the urine showed 10–20 red blood cells per high-powered field. Urine protein/creatinine ratio was 8.0. Serologic studies were performed, and the results showed that the C3/C4 complement levels were within normal limits at 90 and 12 mg/dl, respectively and that streptococcal antibodies (anti-streptolysin O and anti-DNAse B) were negative. The serum creatinine level was 0.6 mg/dl.

By hospital day 2, the patient's edema had improved, but an abdominal mass was then palpated in the midline in the lower abdomen. An abdominal ultrasound and an ultrasound of the kidneys were ordered. The ultrasound revealed normal kidneys and urinary tract; however, a large multi-septated mass was visualized that was assumed to be a dilated uterus (Fig. 1). A serum pregnancy test was ordered and was found to be positive. At this point, a diagnosis of molar pregnancy was made, and this patient's presenting clinical signs and symptoms seemed to be most consistent with pre-eclampsia. The patient's blood pressure continued to be controlled and her edema had completely resolved.

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Following consultation with the hematology/oncology departments, the patient was transferred to an adult care facility to be treated by a gynecologic oncologist. After her transfer to another facility, a magnetic resonance imaging scan of the abdomen/pelvis was performed to ensure that the tumor had not extended into the uterus. That study revealed no such extension. As pulmonary metastasis can be found in about 5 % of complete hydatidiform moles [1], a chest X-ray was obtained to check for any metastatic lesions.

Many of her symptoms, including her tachycardia and hypertension, were consistent with hyperthyroidism. Hyperthyroidism can be a presentation of molar pregnancy, and its association often indicates malignant disease [2]. Thyroid studies and ultrasound of the thyroid were all within normal limits. The patient was taken to the operating room for a dilatation and curettage procedure to remove the hydatidiform mole. An exploratory laparotomy was also performed to ensure normal fundus, ovaries, and fallopian tubes. The final pathology of the removed specimen was consistent with a complete hydatidiform mole with no fetal parts present. The patient was discharged to home with plans for ongoing gynecologic follow-up.

Background

Gestational trophoblastic disease is a rare disorder in the USA, occurring in about 1 in 1,500 pregnancies. In addition, although research indicates that molar pregnancies are more common in women older than 40 years and younger than 15 years, little information on molar pregnancies in adolescents is available in the literature [3].

Patients with molar pregnancy (hydatidiform mole) most typically present with vaginal bleeding (95 % of patients) and excessive uterine enlargement (50 % of patients). More rarely, patients can present with hyperthyroidism (<10 % of patients), anemia (<30 % of patients), and pre-eclampsia (<25 % of patients) [3, 4].

Discussion

Our adolescent female patient presented with what seemed to be a clinical picture consistent with acute glomerulonephritis. She had microscopic hematuria, proteinuria, hypertension, and edema—all findings consistent with such a diagnosis. If it were not for the palpated abdominal mass, she may have continued to be treated for glomerulonephritis. However, the palpated mass in turn prompted an abdominal ultrasound which suggested a pregnancy. This of course was confirmed by a serum beta-human chorionic gonadotropin. Therefore, this young lady's proteinuria, hypertension, and edema were all consistent with pre-eclampsia arising from her molar pregnancy. Pre-eclampsia is a rare presentation of molar pregnancy, and its diagnosis is based on the presence of hypertension and proteinuria. Although edema was once required for the diagnosis of pre-eclampsia, this is no longer true. However, edema, as was seen in our patient, is often associated with pre-eclampsia. The typical patient with pre-eclampsia will have mild proteinuria, but nephrotic-range proteinuria and mild hematuria can be seen in more severe cases of pre-eclampsia, and this may suggest a higher risk for complications [5].

Peripheral vascular resistance and blood pressure are usually decreased in the normal pregnancy state, but the reverse occurs in pre-eclampsia, where increased peripheral vascular resistance is the primary cause of hypertension. Also seen in pre-eclampsia are sympathetic activation and a heightened response to angiotensin II and catecholamines. Generalized vasoconstriction is also universally present in pre-eclampsia which implicates endothelial dysfunction as a key mediating process. Markers of endothelial activation and dysfunction, such as endothelin, cellular fibronectin, plasminogen activator inhibitor-1, and von Willebrand factor, are altered in pre-eclampsia. The production of prostaglandin I₂ (or prostacyclin), a vasodilator produced by endothelial and smooth muscle layers of blood vessels, is usually increased in normal pregnancy but reduced in pre-eclampsia. Thromboxane A₂, a potent vasoconstrictor synthesized by endothelial cells, activated platelets and macrophages, and its metabolites, are excreted in increased amounts in pre-eclampsia. Nitric oxide, which relaxes vascular smooth muscle, is synthesized by the endothelium and allows for vasodilation during a normal pregnancy. The vasoconstriction occurring during pre-eclampsia may result from damage to the vascular endothelium and decreased nitric oxide production. Another potent vasoconstrictor released by vascular endothelial cells because of injury is endothelin-1, which may also contribute to hypertension [6].

The glomerular filtration rate (GFR) increases by 40–60 % during the first trimester of a normal pregnancy, but in pre-eclampsia, both the GFR and renal plasma flow decrease by 30–40 %. Proteinuria usually accompanies or follows hypertension in pre-eclampsia, but it may precede it, and pre-eclampsia is the leading cause of the nephrotic syndrome in pregnancy. The renal pathologic findings associated with pre-eclampsia are called “glomerular capillary endotheliosis,” and the typical pattern seen on renal biopsy is consistent with a non-specific pattern of renal injury described as thrombotic microangiopathy (TMA). The differential diagnosis of conditions linked with a pattern of TMA on renal biopsy, in addition to pre-eclampsia and eclampsia, includes thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, malignant hypertension, scleroderma, some medications (i.e., cyclosporine A), and in renal allografts, antibody-mediated rejection. Under light microscopy, the glomeruli are enlarged and the capillary lumen of the glomeruli are “bloodless” because of endothelial and mesangial cell edema and hypertrophy. These findings may be noted focally in other conditions, but in pre-eclampsia the findings are prominent. Immunofluorescence studies may show the deposition of fibrin and fibrinogen derivatives. Electron microscopy confirms endotheliosis and loss of the endothelial fenestrae, and there may be focal or widespread effacement of the foot processes of the podocytes [5, 6].

Significant weight gain with generalized edema is commonly found in pre-eclampsia, and renin and aldosterone production is suppressed compared to the normal pregnancy state. Edema related to pre-eclampsia resembles the edema associated with glomerulonephritis, as it results from a decreased GFR out of proportion to the drop in renal plasma flow. A decreased GFR, increased capillary permeability, and hypoalbuminemia are all factors that contribute to edema formation [6].

The primary treatment of pre-eclampsia is delivery or therapeutic abortion. Regarding our patient, this meant evacuation of her molar pregnancy. More than 80 % of molar pregnancies are benign, but immediate treatment is usually suggested to prevent transformation into invasive disease. As little published information is available on the treatment of molar pregnancies in adolescents, teenagers are usually treated in a similar fashion as adults. Suction curettage with oxytocin infusion is the preferred treatment to preserve fertility. As in our patient, the beta-HCG level is followed up for several weeks post-treatment to ensure complete disease remission. However, due to the poor follow-up that occasionally is observed in adolescent girls, chemotherapy is sometimes discussed [7]. Chemotherapy was felt to be unnecessary in our patient due to the family's documented understanding of the importance of follow-up. Finally, it is stressed to patients that contraceptive use in sexually active patients is necessary to prevent pregnancy in the year of follow-up so that newly elevated beta-HCG levels are not confused with a new pregnancy.

This case demonstrates the need to be open-minded when considering the differential diagnosis in an adolescent presenting with edema, elevated blood pressure, and abnormal findings on urinalysis.

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Fig. 1.
Ultrasound scan of the abdomen