Scleroderma renal crisis in pregnancy associated with massive proteinuria

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ABSTRACT

Scleroderma renal crisis is a well-recognized complication of systemic sclerosis (SSc) usually occurring early in the course of the disease in patients with diffuse skin involvement. We report the diagnostic challenge of a case of scleroderma renal crisis associated with massive proteinuria at approximately 20 weeks gestation in a pregnant patient with diffuse cutaneous systemic sclerosis.

Introduction

Scleroderma renal crisis, first described by Auspitz in 1863, is an abrupt onset of renin-mediated hypertension and renal failure usually seen in patients with diffuse cutaneous systemic sclerosis. The inciting factors that trigger the onset of this entity remain unknown. Recognition and treatment of renal crisis in the pregnant patient presents several unique challenges.

Case report

A 27-year-old primagravida Filipino female was admitted at 20 1/7 weeks gestation with a 5-day history of headache, visual changes, and a 3-pound weight gain. One week prior to admission, at a routine obstetrical followup, she was asymptomatic, blood pressure was 100/60 mmHg, and dipstick urinalysis showed 4+ protein. A 24-hour urine collection for protein and creatinine was initiated that time. Approximately one month prior to admission, as part of a high-risk pregnancy evaluation, a 24-hour urine collection was notable for 96 mg of protein, and serum creatinine was 0.5 mg/dl. Antinuclear antibodies were positive at a titer of 1:1280 in a homogenous pattern; lupus anticoagulant, anti-phospholipid antibodies, and anti-Ro antibodies were absent. Complete blood count (CBC) demonstrated a hematocrit of 40.6% and the platelet count was 175,000/mm³.

Past medical history was significant for the onset of Raynaud’s phenomenon 54 months prior to admission and the skin changes of scleroderma 52 months prior to admission. In addition, there was a history of major depressive disorder with previous suicide attempts. She had no prior history of hypertension. A chest radiograph was normal 16 months prior to admission; echocardiogram was normal 4 months prior to admission. Medications at the time of admission were felodipine 2.5 mg once a day and prenatal vitamins; there were no known drug allergies. She denied the use of tobacco, ethanol, or illicit drugs. Family history was unremarkable for connective tissue disease.

On physical examination at the time of admission, the patient’s temperature was 37.7°C, pulse was 85 bpm and blood pressure was 160/100 mmHg. Fetal heart tones were recorded at a rate of 160 bpm. Funduscopic exam revealed no evidence of papilledema, hemorrhage, or exudate. The neck was without jugular venous distention and heart sounds were regular in rate and rhythm with an S4 gallop present. The chest was clear to auscultation and the abdomen was gravid, soft, and nontender; the fundal height was 20 cm. Examination of the extremities revealed 2+ pitting edema in the lower extremities extending to the thighs; the hands were puffy and no evidence of digital pitting or arthritis was noted. Skin changes typical of scleroderma were present on the face, upper extremities, chest, abdomen, and thighs. The modified Rodnan skin score was 19 (0-51) (1).

Laboratory data on admission revealed a serum creatinine of 0.9 mg/dl; the remainder of the electrolytes were normal. CBC demonstrated a hematocrit of 39.5% and a platelet count of 120,000/mm³ with a few schistocytes noted on the peripheral smear. Serum aspartate transaminase and lactate dehydrogenase levels were elevated at 59 IU/L (normal 14-36 IU/L) and 1277 IU/L (normal 313-618 IU/L), respectively; the remainder of the liver-associated enzymes were normal and the serum uric acid level was 6.0 mg/dl. Microscopic examination of the urine sediment revealed 5 red blood cells and 6 white blood cells per high powered field, and a 24-hour urine collected the day prior to admission was remarkable for 18 grams of protein.

A diagnosis of scleroderma renal crisis versus preeclampsia was made, and...
therapy was initiated with oral captopril. A repeat 24-hour urine collection on the second hospital day demonstrated 26 grams of protein. Subsequent laboratory testing revealed undetectable levels of serum haptoglobin; antibodies to double-stranded DNA were absent. Serum complement levels were notable for C3 and C4 of 96.5 mg/dl (normal 86-184 mg/dl) and 13.3 mg/dl (normal 20-59 mg/dl), respectively. A DTPA renal scan showed normal renal blood flow without evidence of renal artery or renal vein thrombosis, or obstructive uropathy. Renal ultrasound examination was notable for edematous, slightly enlarged kidneys with no evidence of renal vein thrombosis. The blood pressure was difficult to control, necessitating escalating doses of captopril, labetalol, and felodipine.

Fetal heart tones were monitored regularly, and on the fourth hospital day, fetal heart tones were absent; ultrasound confirmed an intrauterine fetal demise and vaginal delivery was induced. The serum creatinine peaked at a level of 1.2 mg/dl on the fourth hospital day. Pathologic examination of the placenta noted extreme small size, with extensive infarction and accelerated villous maturation.

Marginal control of the blood pressure was achieved on a regimen of captopril 100 mg three times a day, labetalol 100 mg twice a day, and felodipine 5 mg every day. The postpartum course was complicated by endometritis, and the patient was discharged on the tenth hospital day. At the time of a follow-up visit 3 weeks later, the blood pressure was controlled on a regimen of lisinopril 40 mg and felodipine 10 mg once daily. The serum creatinine was 0.6 mg/dl, and a 24 hour urine collection was notable for only 3.9 grams of protein. The visual changes persisted, but the patient was otherwise asymptomatic.

Six weeks after discharge, serum C3 was 116 mg/dl (normal 54-178 mg/dl) and serum C4 was 29.6 mg/dl (normal 10-42 mg/dl).

Discussion

Pregnancy during the course of SSc is not an uncommon event, as the disease is up to five times more prevalent in females, with a mean age of onset at approximately age 40 (2). No differences in the age of onset of menopause (3) or ability to conceive (4) have been found in women with SSc, as compared to statistical controls. Although early case reports and case control studies report high rates of negative outcomes of pregnancy in SSc patients (2), a more recent prospective study demonstrated no increase in the rate of miscarriage (5). However, small full-term infants (6) and preterm births (5) have been shown to be more common outcomes of pregnancies in SSc patients than in control groups. SSc has not been shown to be a risk factor for the development of preeclampsia (6).

Scleroderma renal crisis (SRC), defined as “the new onset of accelerated arterial hypertension and/or rapidly progressive oliguric renal failure during the course of systemic sclerosis,” has been reported to occur in 10% of all SSc patients (7). The greatest risk of developing SRC appears to be found in patients with early onset of diffuse skin disease (8). Some authors have reported pregnancy to be a precipitant of SRC (9), while others maintain that early, diffuse disease is a more important risk factor (5) in such cases. Prior to the late 1970’s, fatality was a nearly universal outcome following the onset of SRC. However, with the advent of treatment with angiotensin-converting enzyme inhibitors (ACEI), marked improvement in survival rates is now noted (10), even though the patient’s blood pressure may not always be controlled by ACEI (11).

SRC does not appear to occur with increased frequency during pregnancy (5). Although there are great concerns with the use of ACEI in pregnant patients, SRC has been successfully treated in pregnancy with these agents (12). In addition, five successful pregnancies have been reported in patients with a history of SRC, all of whom continued therapy with ACEI for the duration of the pregnancy (5). Preeclampsia has been defined as the triad of hypertension, proteinuria, and edema occurring after 20 weeks gestation in a previously normotensive woman (13). Our patient did not fulfill this definition. In addition, the persistence of symptoms long after delivery of the fetus is not consistent with the usual course of preeclampsia (14, 15). The improvement in symptoms without specific therapy other than treatment with antihypertensive agents suggests that an immune complex-mediated nephritis, such as that seen in systemic lupus erythematosus, was not the etiology of this presentation. Additionally, there were no serological or physical exam findings to suggest the possibility of an overlap connective tissue disease. Complement activation has been shown to occur and reflect clinical severity in SSc patients (16). Renal biopsy was not pursued, due to the fact that her clinical condition improved after the institution of antihypertensive therapy, and without the need for immunosuppression.

There are reports of atypical presentations of renal disease associated with antibodies to myeloperoxidase; these reports have consistently described an association with normotensive renal failure (17-21). Our patient was not tested for antineutrophil cytoplasmic antibodies or antibodies to myeloperoxidase; however, her clinical course was consistent with that of classic scleroderma renal crisis.

In summary, we present a difficult diagnostic and therapeutic challenge of a second trimester onset of malignant hypertension in a pregnant SSc patient. We believe that the onset of symptoms in the 19th week of gestation, as well as both the requirement for aggressive antihypertensive therapy and persistence of nephrotic-range proteinuria 3 weeks postpartum, are diagnostic of SRC. To our knowledge, the amount of proteinuria seen in this episode of SRC has not been previously reported, even in large, prospective SSc databases (Steen VD: Personal communication.)

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