International Journal of General Medicine and Pharmacy (IJGMP)
ISSN: 2319-3999
Vol.1, Issue 2 Nov 2012 7-12

International Academy of Science, Engineering and Technology
Connecting Researchers; Nurturing Innovations

EARLY ONSET PRE-ECLAMPSIA IN A WOMAN WITH SCLERODERMA

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ABSTRACT

Severe Pre-eclampsia, Eclampsia and HELLP syndrome are life-threatening maternal conditions usually confined to late pregnancy. Onset before 20 weeks of gestation has historically been attributed to gestational trophoblastic disease or thrombotic thrombocytopenic purpura. We report the case of a patient experiencing all three of these pregnancy complications in the setting of Scleroderma prior to 20 weeks' gestation.

KEYWORDS: Scleroderma, Pre-Eclampsia, HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelets) Syndrome

INTRODUCTION

Scleroderma is a Rheumatologic condition defined by autoimmune attack of the skin, microvasculature, muscles and organs. Patients may exhibit all or any of the components of CREST (Calcinosis, Raynaud's Phenomenon, Esophageal Dysmotility, Sclerodactyly, Telangectasias) Syndrome. Limited data is available on the optimal management and outcomes in pregnancies complicated by Scleroderma and the prognosis for pregnancy outcome is difficult to predict. Published case reports suggest these patients are more likely to suffer severe placental dysfunction due to microvasculature effects of the disease on the developing placenta. We present a case of untreated severe systemic Scleroderma complicating a pregnancy, with disastrous results.

RESULTS

HELLP (Hemolysis Elevated Liver Enymes Low Platelets) Criteria	
Lactate Dehydrogenase	1347 U/L (normal 100-190)
Uric Acid	8.2 mg/dL (normal 2.6-6.0)
AST	452 U/L (normal 14-36)
ALT	220 U/L (normal 9-52)
Platelets	17 Ku/L (normal 129-357)
Pre-eclampsia Criteria	
Blood Pressure	177/114, 169/122, 162/126
Urinalysis protein	100 mg/dL (normal negative)
Urine Protein:Creatinine Ratio	1.6
Serum Markers of Scleroderma	
ANA Screen	Positive
SM/RNP	>200 EU (normal <25)
Scleroderma Antibody	280 EU (normal <25)
B2 Glycoprotein IgM	34 milliunits (normal <19)
Rheumatoid Factor	24.5 EU (normal 0-24)

A 26 year old G6P1-3-1-3 at 19 weeks and 4 days gestation presented as a transfer to our institution with severe pre-eclampsia and eclampsia. Laboratory studies at the referring institution were consistent with HELLP syndrome. Medical history was inclusive of chronic hypertension, gastro-esophageal reflux disease, anemia and Scleroderma.Previous laboratory studies were consistent with scleroderma and are listed in the results section.The patient's past obstetrical history included a vaginal delivery at 27 weeks complicated by chorioamnionitis, a term cesarean section, a right-sided ectopic pregnancy, a 33 week vaginal delivery and a 21 week induction of labor. This last pregnancy was complicated by severe preeclampsia and HELLP syndrome for which a previableinduction of labor was performed. Recovery was complicated by a prolonged ICU stay with congestive heart failure and pneumonia.

On arrival, the patient was in a postictal state and oriented to self only. Examination was performed confirming hyper-reflexia, confusion and clinical appearance consistent with Scleroderma. Respiratory examination revealed poor respiratory effort and fine crepitations consistent with fibrotic lung disease. Cervix was evaluated as unfavorable, with spontaneous vaginal bleeding after examination. A viable 19 week 4 day gestational age was confirmed by ultrasound. Laboratory data on presentation included a urine protein creatinine ratio of 1.6, 100mg/dL of protein on dipstick. HELLP (Hemolysis, Elevated Liver Enzymes, Low Platelets) Syndrome was confirmed by laboratory criteria. Severe thrombocytopenia was confirmed on transfer with a platelet count on 17,000/mL.

Intravenous Magnesium Sulfate was administered and cervical ripening was undertaken with Laminaria and Misoprostol, 800mcg placed per vagina. 2 Hours later, a Dilatation and Evacuation was performed without event. Vasopressin was injected circumferentially around the cervix and two 10 packs of platelets were administered at the commencement of the case. Blood loss with these measures was only 200mLs.

The patient recovered initially in the ICU. Further investigations showed a pericardial effusion, hyperdynamic right heart function with dilated pulmonary vasculature and interstitial lung disease. Laboratory values gradually improved after dilation and evacuation of the pregnancy. Pathology from the pregnancy termination specimen showed a 220 gram placenta and fetal tissues. The fetal surface of the placenta was 'cloudy and blue, with thin/translucent tan gray membranes. The maternal surface consisted of partially defined cotyledons with diffuse fibrin. The cut surface is spongy, red brown with questionable areas of infarction involving 35% of the total placental volume'. (see figures 1 and 2)

Per the patient's request, a laparoscopic left tubal ligation was performed without complication on hospital day 7. Evidence of right salpingectomy from the patient's previous ectopic was noted at this time. She was discharged home the following day.

DISCUSSIONS

Traditionally pre-eclampsia does not occur in pregnancy prior to 20 weeks of gestation. Preeclampsia is associated with term pregnancy in 75% of cases[1]. It can be seen prior to 20 weeks with gestational trophoblastic disease (molar pregnancy)[2] or in association with thrombotic thrombocytopenia purpura[3]. The current case suggests that scleroderma may be another cause of early-onset pre-eclampsia.

This patient had risk factors for pre-eclampsia including no prenatal care, chronic hypertension and history of severe pre-eclampsia. The patient did not undertake reliable contraceptionand was unaware that she was pregnant until she was evaluated for seizures and confusion.

Preeclampsia is a condition characterized by vasospasm, endothelial dysfunction and eventual organ damage. Elevated blood pressures and the presence of proteinuria are required for diagnosis. Preeclampsia becomes severe in the

presence of blood pressures greater than 160/110, oligohydramnios, fetal growth restriction, renal dysfunction, pulmonary edema, neural excitation (scotomata, seizures) and HELLP syndrome[1]. The only effective treatment is delivery of the fetus and placenta.

Eclampsia is a life-threatening condition and represents the most severe form of this condition. Unless delivery is effected, maternal mortality follows by status epilepticus, stroke or aspiration. Though much is known about this condition, the genesis is still incompletely understood. There is evidence that the placental trophoblasts are unable to invade as far into the maternal vasculature in pregnancies affected by this condition and the ensuing vascular insufficiency of the placenta causes the cascade of rising blood pressure and prothrombotic and inflammatory markers.

Patients presenting prior to 34 weeks are in fact more likely to have procoagulant disorders such asAntiphospholipid syndrome. A review of the literature indicates an association with rheumatologic disease[4].

Scleroderma, a rheumatologic condition causally related to vascular insufficiency in skin and organ systems has been linked to preeclampsia in several reports[5,6,7]. There are histological similarities between scleroderma and preeclampsia. Microvascular damage noted in scleroderma with vascular complications is reminiscent of the pathologic changes noted in the placentas delivered of gravidas with preeclampsia. Likewise the renal endotheliosis pathognomonic of preeclampsia shows similarities to the collagen deposition and histologic changes noted in rheumatologic disease.

Comparisons of placentas from normal pregnancies and pregnancies affected by scleroderma have yielded interesting results. One study compared placental biopsies from 34-38 weeks with findings of 'decidualvasculopathy, increased syncytiotrophoblast knotting, placental infarcts and villous hypoplasia' in those from scleroderma affected patients[8]. The authors also reported greater expression of VEGF and VEGFR-2, both associated with preeclampsia[8].

Much evidence now exists to support the theory that preeclampsia is an immune reaction to paternal genes in a susceptible host. We suggest that there is an underlying immune process driving preeclampsia in genetically vulnerable patients. Indeed the documented increased rate of preeclampsia in patients with systemic lupus erythematosus would support this hypothesis.

A greater body of literature exists about the related autoimmune syndrome Systemic Lupus Erythematosus. A retrospective review of a 10 year cohort revealed encouraging results[9]. 63 pregnancies in 48 women were studied. 68% of women experienced disease flares, with preeclampsia developing in 12 pregnancies (17.6%), an elevation of the estimated 2-7% risk in the general population[9]. However outcomes may be less optimistic in patients with Systemic Sclerosis.

Scleroderma is associated with prematurity in a large proportion of pregnancies and small for gestational age fetuses[7, 10]. Therapy with hydroxychloroquine, intravenous immunoglobulins and low dose steroids has been advocated by some[11].

Despite these advances there does seem to be an association of pregnancy complications with renal crisis and pulmonary arterial hypertension in the scleroderma sufferer[12]. We note that our patient did present with pulmonary fibrosis and likely would have fallen into this group. However our patient also gestatedwithout any preventive therapy.

Even in cases where patients have experienced prior severe pre-eclampsia with preceding pregnancies, treatment does seem to offer some benefit[13, 14, 15]. We note the work of Carbonne in his treatment of a 33 year old female with severe scleroderma[5]. This patient delivered a fetus at 28 weeks with severe preeclampsia and an additional 27 week fetus with HELLP syndrome in her subsequent pregnancy. She was treated with nitric oxide donors, heparin and low dose aspirin

therapy following these pregnancies and was delivered of a 37 week infant without recurrence of preeclampsia in this pregnancy.

Though too late for this patient in this pregnancy, we would be interested to observe the role of immune modulation, anticoagulation, administration of vasodilatorsand oxygen free radical scavengers in pregnancies affected by scleroderma and other autoimmune conditions.

CONCLUSIONS

Pre-eclampsia is a rare condition in early pregnancy. Known causes are Gestational Trophoblastic disease and thrombotic thrombocytopenic purpura. We have reported the case of a patient with this complication before 20 weeks of gestation in the setting of Scleroderma. Scleroderma appears to be a third disease process associated with early-onset pre-eclampsia prior to 20 week's gestation.

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APPENDICES

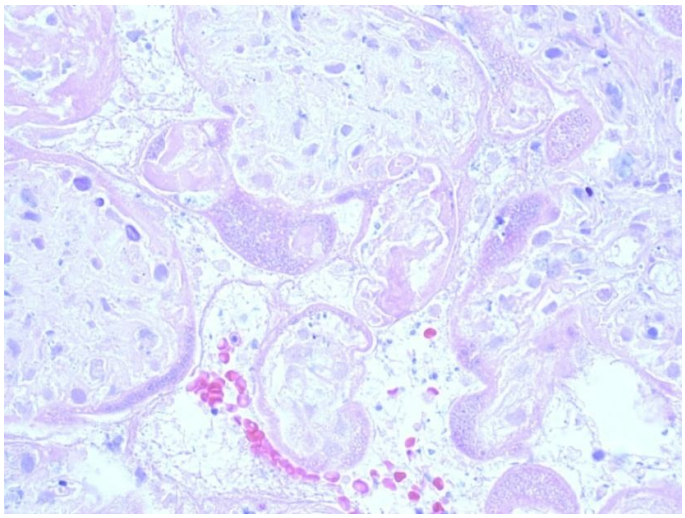

Figure 1: Placental Infarction, Courtesy of Jacqueline Emery, MD

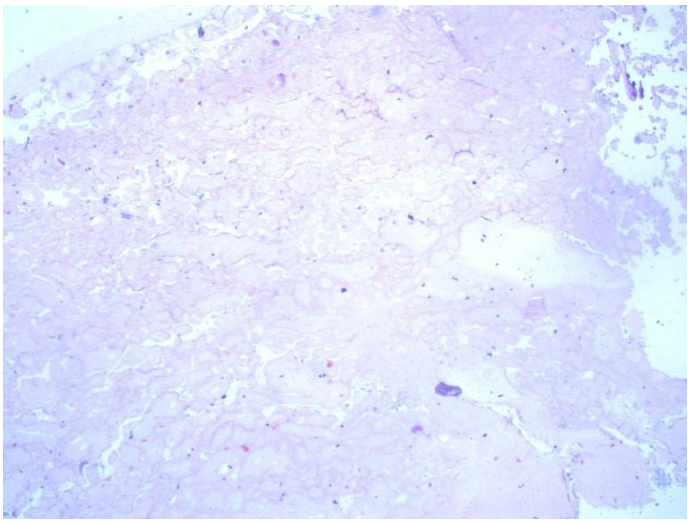

Figure 2: Diffuse Placental Infarction, Courtesy of Jacqueline Emery, MD