

# Management of pregnancy with diffuse cutaneous systemic sclerosis: a case report and literature review

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## Abstract

Diffuse cutaneous systemic sclerosis may occur in women of childbearing age. Pregnancies in this population are associated with a markedly increased risk of adverse obstetric and maternal outcomes even before the onset of symptoms related to sclerosis. We report a case involving the management and outcome of pregnancy in a 30-year-old woman with diffuse cutaneous systemic sclerosis. The course of her pregnancy was good and was assisted by a group consultation including obstetricians and rheumatologists. Vaginal delivery was the patient's preferred choice because she had irregular skin tightness in her lower abdominal skin. She underwent induction of labor and combined spinal-epidural analgesia, and successfully delivered. Importantly, these pregnancies need to be planned, where possible, to allow the opportunity to counsel women and their partners in advance and to decrease any risks. These pregnancies should be considered high risk, and they require close antenatal monitoring and good supervision from an expert multidisciplinary team experienced in high-risk pregnancies. The management of delivery for patients with cutaneous systemic sclerosis is challenging, and vaginal delivery with labor analgesia is an alternative option to cesarean section.

## Keywords

Diffuse cutaneous systemic sclerosis, pregnancy, vaginal delivery, labor analgesia, Raynaud phenomenon, microstomia, aspirin

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## Introduction

Systemic sclerosis (SSc) is a heterogeneous, chronic autoimmune disorder leading to progressive fibrosis of the skin and internal organs.<sup>1</sup> The incidence of SSc is 0.3 to 2.8/100,000/year with a female predominance.<sup>2</sup> The extent of skin involvement and the accompanying pattern of internal organ involvement form the basis for the classification of SSc into limited and diffuse disease. Diffuse cutaneous SSc is characterized by progressive lesions with rapid involvement of the trunk, face, and extremities, and early onset of Raynaud phenomenon.<sup>3</sup> SSc may occur in women of childbearing age, and pregnancies in this population are associated with a markedly increased risk of adverse obstetric and maternal outcomes even before the onset of symptoms related to sclerosis.<sup>4</sup> Consequently, good supervision of these high-risk pregnancies may be necessary. Additionally, appropriate management of delivery can increase the likelihood of the success of pregnancy and birth of a healthy neonate.

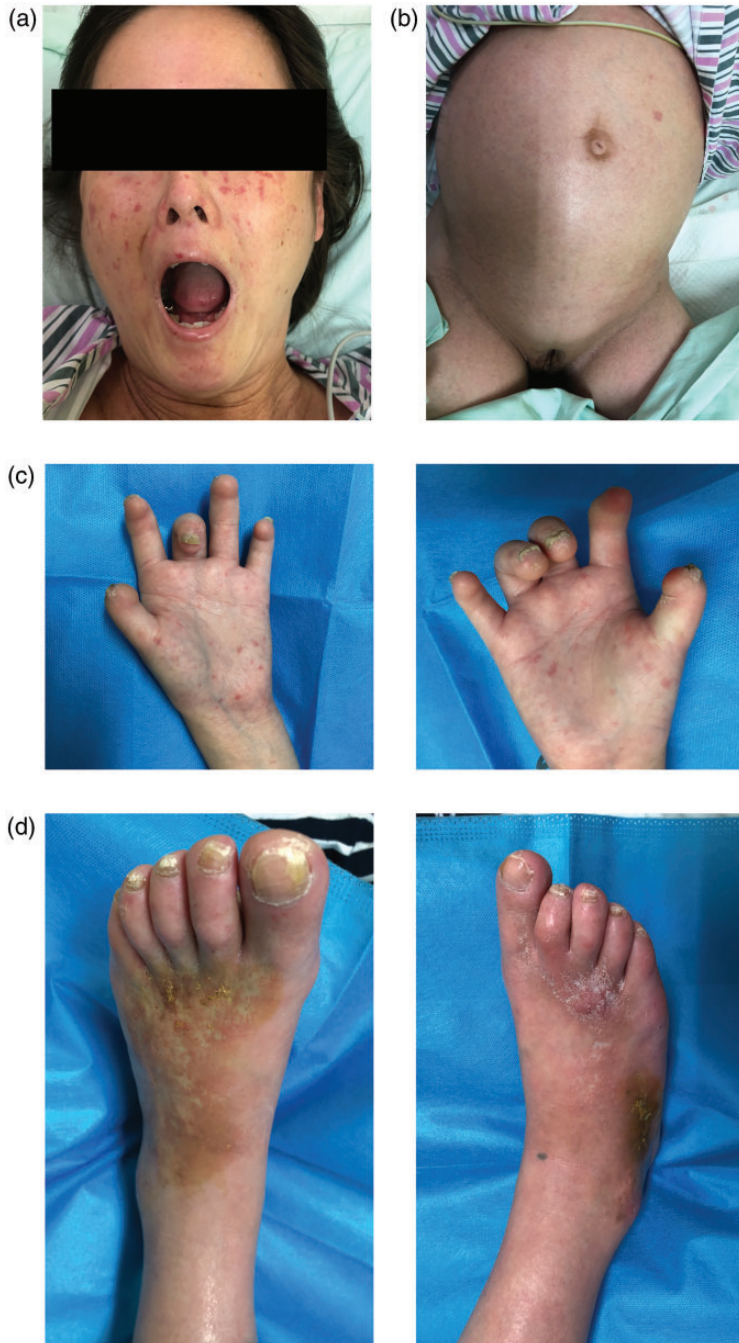
We report a case involving the management and outcome of pregnancy in a woman with diffuse cutaneous SSc. We also discuss maternal and delivery problems of SSc.

## Case report

The reporting of this study conforms to the CARE guidelines.<sup>5</sup> A 30-year-old nulliparous woman with diffuse cutaneous SSc presented to our hospital at 13<sup>+5</sup> weeks' gestation. The onset of her illness was 22 years previously. A typical Raynaud phenomenon rapidly affected her hands, feet, and body after pregnancy started, and this was easily evoked by cold exposure or emotional stress. As gestation proceeded, sclerotic changes followed, finally leading to dermatogenic contractures and sclerodactyly, perioral plication, microstomia,

and mask-like facial stiffness. Ulcers occurred on her fingertips and interphalangeal joints, accompanied by severe pruritus (Figure 1). Arthralgia and musculoskeletal pain were the most frequent complaints during her pregnancy course. The only positive autoantibody was anti-topoisomerase-1 (Scl-70). A rheumatologist prescribed aspirin with a dosage of 100 mg/day and methylprednisolone with a dosage of 4 mg/day. Her pregnancy course was good without proteinuria and hypertension, and her main complaints of arthralgia and severe pruritus slowly disappeared. At 36 weeks' gestation, her pruritus was aggravated with elevated serum aminotransferase (alanine aminotransferase: 118 U/L; aspartate aminotransferase: 106 U/L) and total bile acid (14.8  $\mu$ mol/L) concentrations, and the diagnosis of intrahepatic cholestasis of pregnancy was made. Topical emollient was provided, and ursodeoxycholic acid (1 g/day) was added to relieve the pruritus and the low bile acid and serum enzyme levels. The patient's weight increased appropriately during the pregnancy period, and an obstetric ultrasound scan showed normal fetal growth in late pregnancy.

After 2 weeks (38 weeks' gestation), she was admitted to our hospital. Electronic fetal monitoring tracing was normal, and no major abnormalities in other examinations were found. Termination of the pregnancy was decided because of diffuse cutaneous SSc and intrahepatic cholestasis of pregnancy after a group consultation including obstetricians and rheumatologists. A physical examination showed that the sclerotic lesions did not affect her perineal skin, and the vaginal birth canal was soft and elastic. Vaginal delivery was the preferred choice because of irregular sclerosis in her lower abdominal skin. Oxytocin infusion was administered after using a double-balloon device for cervical maturation. Her airway Mallampati score of III



**Figure 1.** Sclerotic changes during pregnancy. (a) Microstomia and mask-like facial stiffness. (b) Irregular sclerosis in the lower abdominal skin. (c) Dermatogenic contractures and sclerodactyly with ulcers in the upper extremities. (d) Dermatogenic contractures and sclerodactyly with ulcers in the lower extremities.

accompanied by perioral plication and microstomia were associated with increased difficulty in endotracheal intubation. Consequently, the placement of an epidural catheter with the needle-through-needle technique was performed in case of dystocia and emergency cesarean section. This catheter could also be applied for combined spinal-epidural analgesia during the induction of labor with oxytocin infusion. The patient received an intrathecal injection of 0.5% bupivacaine 2.5 mg plus fentanyl 15 mg through the pre-placed epidural catheter, and labor pain was rapidly relieved. As labor progressed after 8 hours of induction, her cervical dilatation was 10 cm, and descending of the fetal head proceeded well with the head position at the +1 station. As the fetal head began to crown, a lateral episiotomy incision was performed, and the neonate was rapidly delivered. The Apgar score was 10 at 1 and 5 minutes, and the neonate weighed 3520 g. The vaginal birth canal was checked, and the perineal incision was sutured carefully.

The patient was transferred to the Rheumatology Department on her third postpartum day without any complications. Subsequent follow-up confirmed that the perineal incision had healed and that the neonate was in good condition.

## Discussion

In reports from 10 to 20 years previously, adverse outcomes of pregnancy in women with SSc were discouraging. Among 42 pregnant women with SSc, 50% had an adverse outcome, and there were nine maternal deaths, seven neonatal deaths, and five cases in which the mother and neonate died.<sup>6</sup> Additionally, women with SSc had twice the rate of spontaneous abortions. As a result, physicians usually encourage patients with SSc to avoid or terminate the pregnancy. However, several case-control studies in the 80s and 90s

showed a low risk of maternal death (1%–2%) and neonatal death (2%–2.4%) in patients with SSc.<sup>7,8</sup> Other more recent reports showed no increase in the frequency of miscarriage, while the frequency of pre-term birth, intrauterine growth restriction (IUGR), and low-birth-weight infants was slightly increased in patients with SSc.<sup>4,9–11</sup> In our case, the use of low-dose aspirin (100 mg/day) after 12 weeks' gestation and close monitoring of fetal growth were performed. Fetal growth proceeded well without any complications, which suggested that our patient had an acceptable pregnancy outcome.

Diffuse cutaneous SSc is rare in child-bearing years, but in some women with pre-existing SSc, pregnancy is associated with negative maternal outcomes.<sup>4,9,10</sup> Pregnancy itself is associated with increased immunization caused by the micro-chimerism phenomenon, which can be significantly affected by ischemic changes, fibrosis, and inflammation that occur in SSc.<sup>12</sup> Determining the changes that pregnancy has on SSc is difficult because many pregnancy symptoms are similar to SSc symptoms. Therefore, at the onset of pregnancy, determination of the duration of this disease and the extent and severity of visceral involvement is necessary. One retrospective study showed no changes in disease-related symptoms during pregnancy in 88% of patients with SSc, an improvement in 5%, and worsening in 7%.<sup>13</sup> Disease-related symptoms included Raynaud' phenomenon, finger ulcers, arthralgias, and skin thickening.<sup>13</sup> Symptoms related to scleroderma, particularly Raynaud phenomenon, have been shown to improve during pregnancy.<sup>14</sup> Another report showed that SSc remained stable in most patients, but 20% and 32% of women noticed an improvement in Raynaud phenomenon and digital ulcerations during pregnancy, respectively.<sup>9</sup> All of these women were Scl-70 positive. A renal crisis has been singled out as the

most serious complication, occurring in 5% to 20% of patients with SSc, and most patients have early diffuse cutaneous SSc.<sup>13,15</sup> Pregnancy itself has been hypothesized to be a precipitant of a renal crisis, but the appearance of preeclampsia can be confused with a renal crisis.<sup>13</sup> In our case, as gestation proceeded, Raynaud phenomenon and sclerotic changes improved, accompanied by improvement in digital ulcerations, arthralgia, and severe pruritus.

Previous studies have shown that there are significantly more small full-term infants born to women with SSc, and an increase in preterm birth and small full-term infants occurs with equal frequency before and after the onset of this disease.<sup>7</sup> The overall preterm delivery rate is 39%, and small for gestational age infants are found in 50% of pregnancies associated with SSc. In a previous report, fetal loss complicated two pregnancies in women with severe diffuse cutaneous SSc and antiphospholipid antibody syndrome.<sup>16</sup> The high rates of prematurity and small for gestational age infants underscore the risk for growth restriction, which is consistent with the vasculopathy associated with these conditions. Another study reported that women with SSc can have successful pregnancies, despite a higher prevalence of preterm delivery and IUGR. Diffuse cutaneous SSc and Scl-70 positivity may predispose women with SSc to a failure of pregnancy.<sup>17</sup> A recent systematic review reported that pregnancies involving SSc had a higher risk of miscarriage, fetuses with IUGR, preterm birth, and newborns with a low birth weight.<sup>18</sup> Additionally, patients with SSc had a 2.8 times higher chance of developing gestational hypertension. As a result, more frequent evaluation of blood pressure, urinalysis, and renal function is required, and management should be provided in a specialized center, with a multidisciplinary team capable of identifying and promptly treating complications.<sup>19</sup> Prophylactic

aspirin with a dosage of 100 mg/day has been used before 16 weeks' gestation.<sup>20</sup> This dose proved to be effective in our patient because her pregnancy course was good without proteinuria, elevated serum creatinine concentrations, hypertension, or IUGR.

The management of delivery for patients with SSc is challenging and requires a careful discussion from an expert multidisciplinary team. Physical difficulties from a thick skin can potentially complicate the delivery. Patients with SSc have a 2.3 times higher chance of cesarean delivery.<sup>18</sup> In this case, vaginal delivery was preferable because there was no vaginal constriction or contractures. We warmed the delivery room and intravenous fluids to prevent any problems related to Raynaud phenomenon during delivery. Care should be taken with the mediolateral episiotomy incision. Combined spinal-epidural anesthesia not only provided adequate analgesia, but also provided peripheral vasodilatation and increased skin perfusion of the lower extremities. General anesthesia was abandoned because of the difficulty in intubation of this patient who had an airway Mallampati score of III and microstomia. In patients with SSc, cesarean section should be routinely prepared for in case of dystocia and an emergent situation.

In summary, the different rates of complications of pregnancies with SSc probably relate to the heterogeneity of the underlying disease severity. Stratifying women with SSc into those at a high risk of complications and those in whom pregnancy may not be risky is important. To achieve the best outcomes, these pregnancies should be planned, where possible, to allow the opportunity to counsel women and their partners in advance and to decrease any risks. These pregnancies should be considered high risk, and they require close antenatal monitoring and good supervision from an expert multidisciplinary team



experienced in high-risk pregnancies. Treatment should be limited to drugs with no teratogenic potential, except when renal crises or severe cardiovascular complications develop. Additionally, the management of delivery for patients with SSc is challenging and requires careful discussion from an expert multidisciplinary team. Vaginal delivery with labor analgesia is an alternative option to cesarean section.

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### Declaration of conflicting interest

The authors declare that there is no conflict of interest.

### Ethics statement

Verbal patient consent from the patient was acquired before submission of this manuscript. All ethical approval and consent procedures were approved by the Medical Ethical Committee of West China Second University Hospital, Sichuan University (approval number: 2020168).

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