International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Nannaware D et al. Int J Reprod Contracept Obstet Gynecol. 2023 Dec;12(12):3683-3686
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20233658

Case Report

Navigating mixed connective tissue disease in pregnancy: a rare case report

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Received: 17 October 2023
Revised: 11 November 2023
Accepted: 13 November 2023

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ABSTRACT

Autoimmune connective tissue diseases (CTDs) in pregnancy present a complex interplay between maternal health and fetal outcomes. While historically discouraged due to potential complications, proper preconception counselling and disease control offer the prospect of safe pregnancies. This case report focuses on mixed connective tissue disease (MCTD), a rare condition combining features of SLE, systemic sclerosis, rheumatoid arthritis, and polymyositis, presenting during pregnancy. A 29-year-old woman, gravida 2, para 1, with a history of rheumatoid arthritis, was referred at 31+4 weeks with a deranged coagulation profile, fetal growth restriction (FGR), and oligohydramnios. Extensive laboratory and imaging investigations confirmed MCTD diagnosis. Treatment involved LMWH, aspirin, hydroxychloroquine, and prednisolone. Comprehensive monitoring and multidisciplinary care were maintained throughout. Despite initial improvement, the patient faced complications at 35+3 weeks, leading to an emergency caesarean section at 36 weeks due to preterm FGR, oligohydramnios, and breech presentation. A male infant weighing 2.1 kgs was delivered, requiring neonatal intensive care due to prematurity and respiratory distress. Postoperatively, the mother resumed medication and was discharged with her baby. This case highlights successful MCTD management during pregnancy through meticulous monitoring and a multidisciplinary approach. The risk of complications necessitates informed preconception counselling, emphasizing the importance of disease remission, close surveillance, and prompt intervention in disease relapse. Comprehensive care, including medications and careful planning, contributes to improved maternal and neonatal outcomes in this rare and challenging scenario.

Keywords: Mixed connective tissue disease, Autoimmune, pregnancy, Fetal growth restriction, Management

INTRODUCTION

Autoimmune connective tissue diseases (CTDs) are more prevalent in women, particularly during their childbearing years. The relationship between autoimmune diseases and reproduction is bidirectional: the disease can impact women's reproductive health, and pregnancy can affect the disease's course.[1] Historically, women with autoimmune disorders have been discouraged from having children due to the potential risk of disease flares and adverse perinatal outcomes. However, the effect of pregnancy on the disease course and the impact of the disease on pregnancy outcomes vary depending on the specific autoimmune disorder. Women with CTDs are known to have an elevated risk of pregnancy complications, including miscarriage, preeclampsia (PE), fetal growth restriction (FGR), and preterm birth (PTB). Nevertheless, with proper preconception counselling, well-controlled disease before conception, and comprehensive medical care, safe and uneventful pregnancies can be achieved. Common CTDs encompass rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), antiphospholipid antibody syndrome (APS), systemic sclerosis (SSc), primary Sjogren's syndrome (PSS), and inflammatory myositis.[2]

Mixed connective tissue disease encompasses features of SLE, systemic sclerosis, rheumatoid arthritis, and polymyositis. It is recognized as a distinct condition primarily due to the discovery of anti-U1RNP antibodies. This syndrome often presents with antinuclear antibodies (ANAs) and antibodies to ribonucleoprotein. Clinical features typically include arthritis or arthralgias, lupus-like rash, telangiectasis, Raynaud's phenomenon, gastrointestinal tract hypomotility, myalgias, and proximal muscle weakness. The severity of these symptoms varies, and corticosteroids are often effective in managing exacerbations.[3]

The risk of developing mixed connective tissue disease (MCTD) appears to be higher after initial disease manifestations and in patients with multiple autoantibody positivity, such as anti-double-stranded DNA (dsDNA), antiphospholipid antibodies (aPL), anti-Ro/SSA, and anti-La/SSB.[4] Regular follow-ups of these patients, especially during pregnancy, is crucial. This case report illustrates such an instance of MCTD during pregnancy.

CASE REPORT

A 29-year-old, G2A1 woman at 31+4 weeks' gestation was referred to our facility from a private hospital. She exhibited a deranged coagulation profile (prothrombin time: 22.7 seconds, international normalized ratio: 1.8, activated partial thromboplastin time: 52.37 seconds), fetal growth restriction (FGR), and oligohydramnios. On evaluation at the antenatal outpatient department (OPD), she reported symptoms of arthritis and presented with hypopigmented skin lesions on her body and face. She had a previous diagnosis of rheumatoid arthritis, supported by a positive family history. Laboratory investigations revealed several significant findings: anti-U1 ribonucleoprotein (U1RNP) antibodies, positive rheumatoid factor (RF), and positive anti-phospholipid antibodies (APLA) for both immunoglobulin M (IgM) and immunoglobulin G (IgG). Furthermore, her antinuclear antibody-immunofluorescence, 1:1000 dilution (ANA-IF-1:1000) was positive, as well as antinuclear antibody blot with specific reactivity to nRNP/sm (ANA blot-nRNP/sm) and anti-cyclic citrullinated peptide (anti-CCP). Complement levels C3 and C4 were notably reduced. While her complete blood counts, liver function, and kidney function tests yielded normal results, electrocardiogram (ECG), two-dimensional echocardiogram (2D-ECHO), and ultrasonography of kidneys, ureters, and bladder (USG-KUB) scans also showed no abnormalities. An early obstetric scan performed at 12+2 weeks indicated a normal nuchal translucency (NT) measurement of 1.7 mm with nasal bone ossification. An anomaly scan at 18+4 weeks revealed left-sided intraventricular echogenic foci. Upon admission to our facility, an obstetric scan showed a single live intrauterine gestation at 29+6 weeks with an amniotic fluid index (AFI) measuring 7.2 cm and an estimated fetal weight of 1.465 kg. The patient's management included daily subcutaneous injections of low molecular weight heparin (LMWH) 0.4 mg, daily oral aspirin (75 mg), daily oral hydroxychloroquine (200 mg), and daily oral prednisolone (20 mg). Additionally, she received iron and calcium supplements and was advised to apply local sunscreen by the dermatologist. The patient's condition improved significantly, and she was discharged while maintaining the same medications. She continued to receive regular follow-up care from both the obstetrician and the general physician at our hospital.

However, at 35+3 weeks of gestation, the patient was readmitted due to decreased fetal movements. An obstetric scan indicated a single live intrauterine gestation at 33+2 weeks, showing severe oligohydramnios (AFI: 3.4 cm), an estimated fetal weight of 2 kgs, breech presentation, and pathological cerebroplacental ratio (CPR). Importantly, the laboratory investigations and coagulation profiles remained within normal limits. At 36 weeks, she underwent an emergency caesarean section due to preterm fetal growth restriction (FGR), oligohydramnios, breech presentation, and non-reassuring NST. She successfully delivered a male child weighing 2.1 kgs with APGAR scores of 6/6/8. The baby was initially transferred to the neonatal intensive care unit (NICU) due to prematurity and respiratory distress but was later reunited with the mother. Postoperatively, she resumed injection LMWH, hydroxychloroquine, and prednisolone and was discharged with her baby. This case highlights the successful management of mixed connective tissue disorder during pregnancy with close monitoring and a multidisciplinary approach.

Table 1: General guidelines for managing mixed connective tissue disease (MCTD) in pregnancy.

S. no.	Guidelines
1	Inform patients about the risks of pregnancy
2	Plan pregnancy during disease remission
3	Regular multidisciplinary monitoring during pregnancy and postpartum
4	Recommend appropriate treatment for disease relapse
5	Close clinical surveillance for severe prognosis cases

DISCUSSION

The physiological adaptation of the immune system to pregnancy can influence the course of all connective tissue disorders. Conversely, the autoimmune processes inherent in these conditions can impact fetal outcomes.[5] The course of mixed connective tissue disease during pregnancy is akin to that in systemic lupus erythematosus (SLE) patients. While some patients may experience disease exacerbations, most do not experience significant worsening of their condition. In present case, the patient presented with SLE-predominant features in the backdrop of rheumatoid arthritis at 31 weeks of gestation. This presentation, coupled with FGR, severe oligohydramnios, and required preterm delivery, demonstrates that this

condition may elevate the risk of medical and obstetric complications for both the mother and her fetus. Therefore, it is advisable to counsel patients about the increased risk of maternal and fetal complications.[6]

Following the established guidelines for autoimmune rheumatic diseases, a set of key recommendations has been outlined to guide the management of these conditions within the unique context of pregnancy. Firstly, an emphasis is placed on ensuring that patients are well-informed about the potential risks associated with pregnancy while managing autoimmune connective tissue diseases. This awareness is instrumental in empowering individuals to make informed decisions regarding family planning, taking into consideration the possible challenges and complications that may arise. Secondly, strategic planning of pregnancy is advised to coincide with periods of disease remission. This approach is designed to maximize the likelihood of successful maternal and fetal outcomes by minimizing the potential for disease-related complications during pregnancy. Planning conception during phases of disease quiescence is, therefore, a proactive strategy to optimize the overall well-being of both the mother and the baby. The third recommendation underscores the importance of regular monitoring throughout the entirety of pregnancy and the postpartum period. This vigilant approach involves a multidisciplinary team, including specialists such as rheumatologists, obstetricians, and neonatologists. Collaborative oversight ensures comprehensive care, early detection of any emerging issues, and timely intervention to optimize maternal and fetal well-being. In the event of a disease relapse, the fourth guideline advocates for the prescription of appropriate treatment, even if it involves aggressive measures. This recommendation is grounded in the understanding that active disease poses a potentially greater risk to the fetus than the medications used for management. Swift and effective intervention during a relapse is deemed essential to mitigate potential adverse outcomes and safeguard the health of both the mother and the baby. Lastly, pregnancies complicated by the onset of rare autoimmune rheumatic diseases are acknowledged to carry a particularly severe prognosis. The fifth guideline underscores the importance of prompt treatment and close clinical surveillance in such cases. Timely and vigilant management becomes paramount to navigate the unique challenges posed by these rare conditions during pregnancy, aiming to improve overall outcomes for both the mother and the baby. Table 1 succinctly summarizes these general guidelines for managing mixed connective tissue disease (MCTD) in pregnancy, providing a quick reference for healthcare professionals involved in the care of these patients.[7]

During pregnancy, close attention should be given to both the mother and the fetus. Early assessment of baseline blood pressure, renal function, complement levels, and serologic tests, such as anti-double-stranded DNA antibodies, is crucial. Exacerbations of SLE are more likely if the disease is active at the time of conception, with an increased frequency occurring in the second half of pregnancy and the early postpartum period. Fetal complications, including prematurity, intrauterine growth restriction (IUGR), and perinatal mortality, are elevated but similar to other rheumatologic diseases in pregnancy.[8] Neonatal lupus was frequently observed in pregnant women with MCTD (28.6%), similar to the rates for offspring from mothers' positive for anti-Ro or La antibodies, displaying cutaneous (10–20%) or hematologic and hepatic (27%) manifestations.[9]

CONCLUSION

MCTD in pregnancy, being rare and variable, lacks comprehensive data. Pregnancy can exacerbate MCTD, elevating risks like preeclampsia, fetal growth issues, and preterm birth. Regular monitoring is crucial, especially for active disease and multiple antibodies. Careful planning and close rheumatological and obstetric oversight are essential. Medications like NSAIDs, corticosteroids, and antimalarials can manage the disease and reduce pregnancy complications. Consider vitamin D supplementation and low-dose aspirin for those at risk, aiming for improved maternal and neonatal outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Nannaware D, Kamath A, Gangane N, Yadav A. Navigating mixed connective tissue disease in pregnancy: a rare case report. Int J Reprod Contracept Obstet Gynecol 2023;12:3683-6.