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Case Report

A Pregnant Patient with Sjögren's Syndrome and non-Hodgkin Lymphoma: A Case Report

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Abstract:

Background: Sjögren's syndrome is an autoimmune disease primarily affecting women around the age of 50, but can also occur in women of reproductive age, leading to serious maternal-fetal complications during pregnancy. The exact cause of this condition is not entirely understood, however, it is assumed to attack the exocrine glands, leading to impairment of their function. Additionally, an increased risk of developing lymphomas, particularly non-Hodgkin lymphoma is recognized among affected patients.

Objective: To illustrate the management of pregnancy in a patient with Sjögren's syndrome and non-Hodgkin's lymphoma and the achievement of obstetric success without maternal-fetal complications.

Case report: In the article, a 36-year-old pregnant patient with Sjögren's syndrome history, two miscarriages, and non-Hodgkin's lymphoma is presented. Due to unexpected pregnancy, the patient discontinued lymphoma treatment. Through the pregnancy, fetal well-being, blood flow, and maternal health were meticulously monitored, showcasing successful obstetric management. Due to Sjögren's syndrome, fetal atrioventricular conduction was monitored weekly from the 16th to the 30th week, showing no abnormalities. Additionally, during the course of pregnancy gestational diabetes, cervical insufficiency treated with pessary insertion, anemia and thyroid insufficiency were diagnosed. Multidisciplinary care addressed these issues, allowing our patient to give birth to a healthy child at 37 weeks via cesarean section.

Conclusion: Pregnancies in Sjögren's syndrome patients pose elevated risks due to the presence of antibodies causing tissue damage and complications. These antibodies contribute to fetal myocardial issues and congenital heart conditions. Regular fetal heart ultrasounds, especially for those positive for Ro/SS-A antibodies, are crucial between the 16th and 31st weeks. Maternal-fetal complications include a higher risk of preterm delivery and lower birth weight of the offspring, often due to fetal growth restriction. Additionally, considering the potential for oncohematologic disorders in adults, comprehensive obstetric care is essential for minimizing complications risk.

Key words: sjögren's syndrome; non-hodgkin lymphoma; pregnancy/ autoimmune diseases/ atrioventricular conduction

Introduction

Sjögren's syndrome (SS) is an autoimmune disease that may manifest independently (as primary SS) or concurrently with an underlying connective tissue disease (as secondary SS), commonly associated with systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA) [1]. Primary Sjögren's syndrome ranks as the second most prevalent autoimmune disease following RA. The condition predominantly affects females (female-to-male ratio of 9:1), exhibiting a prevalence rate of 1-4.8% among the overall female population. Although the incidence figures remain uncertain, it is established that the onset of the disease is possible at any age, with a notable predilection for affecting women primarily in their fourth or fifth decade of life. In recent years, an increased occurrence of SS has been noted among women during their reproductive period [2]. Approximately 14% of diagnoses are established before the age of 35 [3]. Taking into consideration growing population of patients deciding to conceive at the age of 30, the issue of SS complication during pregnancy might be growing and worth attention. The etiology and pathogenesis of SS are not entirely understood, however, it is assumed that the primary mechanism involves lymphocytic infiltration within the exocrine organs, with parotid glands among them, subsequently leading to impairment and inhibition of their function [4].

The clinical spectrum of SS extends from dryness of mucosal surfaces like the mouth, eyes, and vagina, to complications such as dyspareunia, edema of the parotid gland, recurrent parotitis, and extraglandular symptoms like arthritis, fatigue, vasculitis, and pain.

Pregnancies in SS patients are associated with high obstetric and neonatal risks, posing challenges to medical care that require increased surveillance in these group of patients.

We report a case of a pregnant patient with Sjögren's syndrome, who was diagnosed with non-Hodgkin lymphoma (NHL) of the right parotid gland before pregnancy. In presented case through diagnostic assessment and treatment, as well as quality obstetric care, a range of maternal-fetal complications were successfully avoided and the patient delivered a healthy newborn at 37 weeks of gestation.

Case report

In October 2023, a 36-year-old female patient at 34 weeks of gestation presented for scheduled admission to the Emergency Department of our clinic due to elevated levels of bile acids and fetal growth restriction (FGR). The patient was referred to the Department of Pregnancy Pathology. According to medical history, the patient underwent two cranial trepanation procedures following a car accident at the age of 7, which later became one of the indications to cesarean section (CS) deliveries.

Between 2001 and 2016, the patient underwent diagnostic examinations for Sjögren's syndrome due to enlargement of the right parotid gland and other clinical symptoms; however, the immunological tests did not conclusively indicate this condition. Over the years, the patient developed muscle and joint pains, xerophthalmia, a sensation of foreign body presence under the eyelids, photophobia, xerostomia, salivary viscosity, sporadic dental caries. In 2016, after 15 years, during hospitalization at the Institute of Rheumatology in Warsaw, a diagnosis of SS was eventually established and treatment with hydroxychloroquine and methylprednisolone was initiated. In adulthood, gynecological symptoms such as vaginal xcerosis, dyspareunia and difficulties in conceiving were observed. The patient had a 3-year long history of infertility and sought consultation at the Fertility Treatment Clinic. Genetic tests were conducted, revealing the presence of MTHFR heterozygotic mutation, moreover hypothyroidism was diagnosed and treatment with levothyroxine was initiated.

In 2017 and 2018, the patient experienced two spontaneous miscarriages, and following the first one she underwent a surgical hysteroscopy with removal of intrauterine adhesions due to secondary amenorrhea. Later, in the same year, the patient successfully managed to conceive again. During the pregnancy gestational diabetes mellitus (GDM) was diagnosed and managed with dietary measures. At 29 weeks, cervical insufficiency was identified, and a pessary was inserted. Additionally, FGR and oligohydramnios were observed. At 36 weeks of gestation a decision on labor was made. Cesarean section was performed due to maternal neurological indications. A hypotrophic female infant was born, weighing 2070 g and measuring 55 cm, with a 10 Apgar score points. The newborn presented with pneumothorax and breastfeeding difficulties, but no morphological or developmental abnormalities, particularly heart conditions, were detected.

In 2019, a palpable mass in the right salivary gland, which did not decrease in size, led to three fine-needle biopsies, raising suspicion of non-Hodgkin lymphoma. Methylprednisolone therapy was discontinued. In 2022, a diagnosis of non-Hodgkin lymphoma was confirmed, and rituximab treatment was implemented. In February 2023, the first dose of radiotherapy was administered, but quickly discontinued due to early pregnancy confirmation.

In the current pregnancy, in the first trimester, drug-induced elevation of transaminases (ALT 314 U/L AST 141 U/L) with biliary acids (BA) within normal limits occurred and was managed with phospholipidum essentiale. Transaminases levels were continuously increasing and at the 20th week of gestation were as follows: ALT 457 U/L AST 200 U/L, while BA levels remained within the normal range (BA 5.7 umol/L). In addition, at the 26th week, gestational diabetes mellitus was diagnosed and managed through dietary measures. At 29th week cervical insufficiency was identified and a pessary was inserted. Bening anemia of pregnancy was also detected and oral iron supplementation was implemented. The patient was treated with levothyroxine for thyroid insufficiency and also progesterone 2x50mg. Additionally, acetylsalicylic acid 75 mg and enoxapariunum natricum 40 mg was also taken. During the hospitalization patient reported detection of node in her left armpit. Controlled USG confirmed presents of normal lymph glands measuring up to 8,5mm. Additionally, USG examination of the right parotid gland revealed changes typical of SS, while no alterations suggestive of lymphoma were observed.

At the time of admission to the Department of Pregnancy Pathology at 34th week of gestation, cholestasis of pregnancy was conclusively diagnosed with BA 24 umol/L, ALT 286 U/L AST 204 U/L and treated with ursodeoxycholic acid. During the hospitalization the hydroxychloroquine dose was reduced by half (from 2x200mg to 1x200mg) and methylprednisolone treatment was replaced by prednisone treatment. Control examination after 2 weeks of hospitalization showed value of BA 17 umol/L, ALT 113 U/L AST 87 U/L.

Due to the positive anty-Ro (SS-A) and anty-La (SS-B) antibodies, fetal atrioventricular conduction was monitored weekly from the 16th to the 30th week of pregnancy, and each result was within normal limits. Additionally, fetal well-being was monitored, including the assessment of fetal growth. The flows in crucial fetal arteries- middle cerebral artery (MCA) and umbilical artery (UA) remained within normal limits, but an amniotic fluid index (AFI) decreased from 8 to 4 cm. According to above results, the decision of labor via CS was made.

The patient gave birth on 17.10.2023 at 37th week via CS due to maternal neurological indications. The delivery date was scheduled based on an elevated BA levels. A planned CS was performed due to fetal breech presentation and maternal neurological indications. The fetal membranes exhibited meconium staining, prompting a sample collection for analysis, which revealed no abnormalities. Apart from these observations, a healthy son was born, weighing 2800 g and measuring 54 cm, with a 10 Apgar score points. The newborn experienced feeding difficulties and bilateral pleural effusion post-delivery.

Discussion and conclusions

Sjögren's syndrome is the second most common autoimmune disease, following RA, with the peak incidence around the age of 50. However, it is important to acknowledge that the disease can also impact women of reproductive age, leading to significant complications during pregnancy and the postpartum period, so preconception counseling is recommended for women with SS. Data shows that the disease often goes undiagnosed in over half of affected adults [5].

The antibodies presented in SS mediate the tissue damage and contribute to impaired fertility and complications during pregnancy. Since the beginning, pregnancies of patients with SS are considered with higher risk compared to those without SS. Elevated risk of spontaneous miscarriages is observed in these diseases [3]. The patient described in the case had a history of difficulties conceiving and had experienced two spontaneous miscarriages. Meta-analysis by Yang et al. has reported that the occurrence of adverse pregnancy outcomes is significantly higher in patients with autoimmune diseases when compared to the general population [6]. Antibodies characteristic for SS cross the placenta since the 12th week of gestation, and precipitate myocarditis and arrhythmias by targeting fetal myocardial tissue. They also increase the risk of congenital heart conditions, including congenital heart block in the fetus [7]. Therefore, it is crucial to monitor atrioventricular conduction of the fetal heart. For women with a positive result for Ro/SS-A antibodies, including patients with SS, it is recommended to undergo weekly fetal

heart ultrasound examinations from the 16th to the 31st week of pregnancy to assess the fetal cardiac rhythm [8]. In the case of our patient, this examination was conducted weekly according to recommendations, and each result was normal.

In addition, when it comes to maternal-fetal complications, there remains an increased risk of preterm delivery and lower average birth weight, often caused by fetal growth restriction, as in presented case. The study by Yang et al. showed also a heightened susceptibility to gestational hypertension and preeclampsia [6], which were not demonstrated in the case of our patient.

In adults, considering potential expansion of diagnostics, oncohematologic disorders should be taken into consideration due to the fact, that the risk of developing conditions such as lymphomas increases 10-44-fold in patients with SS [9]. NHL is the most frequently observed type of lymphoma in patients with SS [10], particularly in those with positive Ro/SS-A and anti-SS-B antibodies [11]. In the case described by the authors, the salivary gland, an organ affected by autoimmune disease, also became a target of neoplastic disease. It is essential to note that autoimmune diseases frequently have a negative impact on maternal-fetal obstetric outcomes, while the severity of the disease or risk of relapse may be reduced during pregnancy [12, 13]. In presented case, the tumor in the right parotid gland has undergone remission, which may be attributed to a single dose of radiotherapy administered prior to pregnancy. However, it is important to note that the patient should continue oncological follow-up.

In conclusion, in case of our patient, both pregnancies were associated with high risk of wild range of aforementioned complications, most of which are characteristic for SS and might have been a result of the disease. Proper obstetric care allowed to reduce maternal-fetal complications associated with the disease, which resulted in delivery of healthy infants in both pregnancies. At the time of publishing this case, the woman did not report any symptoms related to SS, nor any issues with the parotid gland.

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Conflict of interest

The authors declare that they have no conflict of interest regarding the publication of this case report.

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