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Still'S Disease and Pregnancy: a Case Report and Review of the Literature.

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Abstract

Adult-onset Still's disease (AOSD) is a rare systemic disorder of unknown etiology and pathogenesis **[1,2]**, with an estimated prevalence ranging from one to 34 cases per million inhabitants **[3]**, and affecting predominantly young women **[4,5]**. Yamaguchi's criteria **[6]** are commonly used, as they suggest the main clinical symptoms and laboratory findings of this disease. Typical manifestations include a remittent fever above 39 °C lasting more than one week, arthralgia or arthritis, the characteristic rash, leukocytosis, elevated liver enzymes, and splenomegaly. In addition, some cases of AOSD may present with abdominal pain and nausea **[2]**. If such findings as elevated liver enzymes and abdominal pain occur during pregnancy, AOSD may be misdiagnosed as hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome or acute fatty liver of pregnancy (AFLP). To date, although the association between disease onset and pregnancy has been extensively studied **[7,8]**, this relationship remains unclear. Moreover, only a few cases of AOSD flare-ups during the third trimester have been reported, and neither the management nor the features of this condition, which resembles HELLP syndrome and AFLP, during late pregnancy have yet been described. First-line treatment consists of high-dose corticosteroid administration **[2,9,10]**. However, some cases are refractory to corticosteroids, and Tocilizumab (TCZ), an interleukin-6 inhibitor, has proven effective in such situations **[11]**. At present, the relationship between pregnancy and AOSD, including disease onset and relapse, remains uncertain. Only a limited number of studies have been published, mainly in the form of case reports or small case series, and therefore no conclusive interpretation is available **[8,12-14]**. Here, we report the rare case of a 5-month-pregnant woman with Still's disease, who had recurrent thrombocytopenia since the first trimester, and we review previous reports on pregnancy-related AOSD flares. The patient provided written informed consent for publication of this case report.

Keywords: Still, Pregnancy, Autoimmune, Treatment

Abbreviations: AFLP: Acute fatty liver of pregnancy; AOSD: Adult onset Still's disease; HELLP: Hemolysis, elevated liver enzymes, and low platelet count; IVIG: Immunoglobulin; TCZ: Tocilizumab

Case Report

A 27-year-old primigravida, primiparous woman with a history of Still's disease for two years, followed up in the Department of Internal Medicine, had been hospitalized during the first trimester for severe thrombocytopenia with hemorrhagic manifestations and was started on corticosteroid therapy. The patient, however, discontinued treatment on her own. She was later admitted to the maternity ward for threatened preterm la-

bor associated with severe thrombocytopenia at an estimated gestational age of 22 weeks.

On admission, clinical examination found a conscious patient with a Glasgow Coma Scale score of 15/15, in good general condition, blood pressure 110/70 mmHg, respiratory rate 18 cycles/min, heart rate 80 beats/min, negative urine dipstick, capillary blood glucose 0.99 g/dL, and afebrile at 36.5 °C. She presented with widespread maculopapular lesions on the chest and ecchymotic patches on the lower limbs. Uterine contractions were noted, with a cervix dilated to fingertip size and intact membranes.

Obstetric ultrasound revealed an ongoing singleton pregnancy with fetal biometrics consistent with gestational age, a fundal placenta, shortened cervical length of 21 mm, and a large cisterna magna measuring 50 mm.

Laboratory investigations showed hemoglobin 12.3 g/dL, leukocytes 15,460/mm³, and severe thrombocytopenia at 13,000/mm³, confirmed on citrate tube and smear review. Other tests were unremarkable, including coagulation profile, renal and liver function. Urine culture and vaginal swab were sterile. The 24-hour proteinuria was negative, and infectious serologies were negative. Bone marrow aspiration revealed thrombocytopenia of peripheral origin with inflammatory features. Immunological work-up was negative, including protein S, activated protein C resistance, antithrombin, and antiphospholipid antibodies.

The patient was treated with corticosteroids and azathioprine, with improvement in both clinical symptoms and thrombocytopenia. She delivered at 39 weeks of gestation by cesarean section a live male newborn, Apgar 9/10 and 10/10, birth weight 2900 g, with no evidence of thrombocytopenia on complete blood count.

In the postpartum period, the patient maintained platelet counts between 40,000/mm³ and 100,000/mm³ over six months of follow-up.

Discussion

A flare of adult-onset Still's disease (AOSD) during pregnancy was first reported in 1980 by Stein et al **[15]**. The relationship between the development of AOSD and pregnancy remains unclear. Moreover, cases of AOSD with onset during the perinatal period are rare. The clinical course of AOSD during pregnancy has been classified into three types: the de novo type, referring to first onset of the disease in relation to pregnancy; the recurrent flare type, referring to pregnancy-related recurrence in patients with a previous diagnosis of AOSD; and the non-flare type, referring only to complications without pregnancy-related flare **[7,8,15]**. In the literature, reported cases have been divided into these three types, and our case belongs to the second type.

The onset of AOSD during pregnancy remains rare **[15]** but can compromise maternal and fetal outcomes, including preterm delivery **[14]**. It has been noted that the gestational age at onset is typically in the first or second trimester (8 to 26 weeks of amenorrhea) according to published reviews **[14]**. The median maternal age at pregnancy was reported to be 30 years **[16]**. With respect to parity, AOSD flares occur mainly in primiparous women **[8]**, as was the case in our patient.

AOSD is highly heterogeneous in its clinical manifestations **[17]**. Fever is considered the cardinal feature, followed by arthritis, while rash represents the third cardinal sign. Typically, the cutaneous eruption consists of small, salmon-pink macules or maculopapules, non-pruritic, often localized to the proximal limbs, trunk, and occasionally the palms and soles **[8,17]**. Other clinical manifestations may include arthralgia, neurological or ophthalmic involvement. In our case, the patient presented with cutaneous rash on the trunk and lower limbs.

There is no specific biological marker of AOSD. However, two laboratory features are highly suggestive: neutrophilic leukocytosis and markedly elevated serum ferritin, often with a low glycosylated ferritin fraction. Another supportive finding is the absence of autoimmunity, particularly negative rheumatoid factor and antinuclear antibodies. In contrast, abnormal liver function tests are found in up to two-thirds of patients **[17]**. Given the wide range of clinical presentations—from isolated prolonged fever to neoplastic mimicking conditions—the diagnosis of AOSD is often complex and sometimes delayed.

In 2004, Mok et al. reported new findings in 22 pregnancies in 17 women **[13]**. Disease flares were observed in 19 pregnancies, mostly during the fifth and sixth months and in the postpartum period. In 2012, Yamamoto et al. described 25 pregnancies in 19 women **[18]**, with at least one flare observed in

most cases. Disease exacerbations occurred primarily in the second trimester and postpartum. A favorable course was noted in only six pregnancies. The main complications included spontaneous abortion, intrauterine growth restriction (IUGR), preterm delivery, and one neonatal death. Maternal complications were rare but included gestational diabetes in one patient, preeclampsia in another, and macrophage activation syndrome in two cases.

A 2018 retrospective, descriptive, and analytical study **[19]**, conducted at the Internal Medicine Department of Libreville University Hospital, reviewed medical records of patients with autoimmune diseases including AOSD and pregnancy, regardless of outcome. Reported complications included two spontaneous miscarriages in the first trimester (n=1), two intrauterine deaths, one perinatal death at day 12, and two cases of eclampsia, one complicated by pulmonary embolism during a first pregnancy. The mean gestational age at delivery was 37 weeks, with most cases delivering beyond 35 weeks (n=18) compared to fewer cases before 35 weeks (n=9). Intrauterine growth restriction was observed in 10 cases, and preterm delivery in 17 cases.

In our case, the patient received corticosteroids and azathioprine, with improvement in clinical signs and thrombocytopenia. She delivered at 39 weeks of gestation, and during six months of postpartum follow-up, her platelet count remained between 40,000/mm³ and 100,000/mm³.

Based on these series and our case, pregnancy appears to favor AOSD flares, particularly at the end of the first and second trimesters and in the postpartum period. Treatment of AOSD during pregnancy can be challenging. Corticosteroids are commonly used but carry risks such as gestational diabetes, hypertension, and the need for close monitoring. Intravenous immunoglobulin (IVIG) may be considered in life-threatening cases **[20]**. Azathioprine is sometimes preferred as a steroid-sparing agent **[21]**.

Reported cases during pregnancy remain limited, and current therapeutic experience is largely derived from case reports and small series.

Conclusion

In summary, we found that pregnancy in patients diagnosed with AOSD was associated with an increased risk of complicated pregnancies, which should be anticipated by rheumatologists, internists, and obstetricians alike. However, AOSD activity was not exacerbated by pregnancy when the disease was well controlled, highlighting the importance of disease assessment prior to conception.

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