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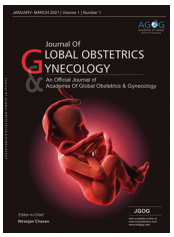
Case Report



An Interesting Case of Pregnancy in a Known Case of Adult Onset Still's Disease

Niranjan N. Chavan, Vaibhavi Iyer*, Deepali Kapote, Swara Patel, Madhura Mandlik, Radhika Bhutada

Department of OBGYN, LTMMC and GH, Sion, Mumbai, Maharashtra, India

ABSTRACT

Adult-onset Still's disease (AOSD) is a clinical syndrome with an unclear etiology and pathogenesis. Its main symptoms include fever, erythema, arthralgia, and muscle pain. Diagnosis is challenging due to the lack of specific auxiliary tests, and it can sometimes first appear during pregnancy. The onset of AOSD is closely related to pregnancy, and that pregnancy is one of its predisposing factors. A 27-year-old primigravida registered under our center with regular follow-up delivered preterm dichorionic diamniotic twins by Cesarean section at 35 weeks of gestation. The disease is usually diagnosed through the process of exclusion, which can frequently lead to misdiagnosis and delays in treatment.

Key words: Adult-onset Still's disease, Diagnosis, Pregnancy

INTRODUCTION

Adult-onset Still's disease (AOSD) is an autoinflammatory disorder marked by the activation of macrophages and neutrophils in response to inflammatory cytokines such as tumor necrosis factor-alpha, interleukin (IL)-6, and IL-18.[1] It is characterized by spiking fever, arthralgia or arthritis, and evanescent rash. Although AOSD flares during pregnancy have been documented, they most commonly occur in the first or second trimester, with fewer cases reported in the third trimester.

An estimated prevalence of one to 34 cases per million people predominantly affects females at a young age.[2]

Previous research has shown that CMV infections, increased neutrophil extracellular traps, and several other factors play a role in the development of AOSD.[3]

At present, the relationship between pregnancy and AOSD, including disease onset, relapse, and pregnancy outcomes remains unknown. There are only a few studies published, mostly as case reports or brief literature reviews, so conclusive interpretations are not yet available.

Correspondent Author:
Dr. Vaibhavi Iyer, Junior Resident, Department Of OBGYN, LTMMC & GH, Sion, Mumbai, Maharashtra, India. Phone: 9702477138.
E-mail: vaibhavi.iyerapple@gmail.com

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CASE REPORT

A 27-year-old female primigravida with a known case of Still's disease came to the outpatient department (OPD) at a tertiary center hospital in November 2023 for ANC registration at 18.2 weeks of gestation with dichorionic diamniotic twins. The patient conceived on ovulation induction and planned relation in October 2023. The patient had regular follow-up visits. Antenatal investigations were within normal limits during her follow-up.

In June 2015, the patient was diagnosed with Still's disease after presenting with symptoms including fever, joint pain, and rashes. Despite multiple follow-up visits to the medicine OPD, her symptoms did not improve with treatment. The autoimmune disease panel, which tested for rheumatoid arthritis, systemic lupus erythematosus (antinuclear antibodies), and ankylosing spondylitis, came back negative.

Inflammatory markers such as erythrocyte sedimentation rate and C-reactive protein were elevated, and the symptoms persisted despite earlier treatments. After excluding other potential diagnoses, Still's disease was confirmed through a process of elimination. The patient was subsequently started on a tablet of prednisolone 5 mg once daily and a tablet of cyclosporine 50 mg twice daily. The treatment was effective, leading to the gradual resolution of the symptoms. The patient continued these medications until October 2023. During her pre-conceptional counseling, her rheumatologist changed her medication from cyclosporine to azathioprine as cyclosporine is associated with premature delivery and low birth weight infants.

During her antenatal period, the patient experienced no worsening of her symptoms and adhered to her medication regimen, attending regular follow-up appointments. On June 13, 2024, she came to the emergency department with complaints of abdominal pain at 35 weeks of gestation. Her blood pressure was recorded at 150/100 mmHg, for which she was given a tablet of labetalol 100 mg. Urine albumin was traced, and there were no premonitory symptoms; bilateral knee jerks were normal. Her complete blood count, liver function tests, and renal function tests were normal.

Abdominal examination revealed a full-term-sized uterus, with multiple fetal parts palpable and two distinct fetal heart sounds detected. Mild uterine contractions were presented, indicating irritability. On per vaginal examination, the patient was found to be in latent labor. A diagnosis of pre-eclampsia with dichorionic diamniotic twins in preterm labor was made. A diagnosis of pre-eclampsia with dichorionic diamniotic twins in preterm labor was made. A decision was taken to terminate the pregnancy with an emergency lower-segment cesarean section.

On June 13, 2024, the twins were delivered: Twin A, a male weighing 2354 g, was born in a vertex presentation, whereas Twin B, also a male, weighed 2020 g and was delivered breech. Both infants cried immediately after birth and had an APGAR score of 9/10.

Postoperatively, the patient's blood pressure was stable at 110/70 mmHg, there was no abdominal distension, urine output was adequate, and no warning signs were present.

The rest of the postnatal period was uneventful.

DISCUSSION

AOSD can significantly impact pregnancy and childbirth, as the condition may intensify during pregnancy due to hormonal changes and immune system dysregulation. The elevated incidence of AOSD diagnoses during and after pregnancy suggests that sex hormones might increase the risk of developing new-onset AOSD. However, if AOSD is well-managed, it generally does not worsen significantly during pregnancy.

Patients with AOSD are at a higher risk for spontaneous abortion and preterm birth. In a study of 40 pregnant women with AOSD, 25% experienced spontaneous abortion, and 35% had preterm deliveries.[4] A case-based review of 19 AOSD cases during pregnancy revealed that nearly 50% of patients encountered obstetric complications. These included prematurity (10/20), preterm premature rupture of membranes (3/20), intrauterine growth restriction (IUGR) (3/20), oligohydramnios (2/20), and neonatal death (1/20).[5] In addition, patients with AOSD may face an increased risk of pre-eclampsia and gestational diabetes. Adverse pregnancy outcomes in these patients can include preterm labor, fetal growth restriction, premature rupture of membranes, oligohydramnios, and pre-eclampsia.

Therefore, it is essential to closely monitor and manage AOSD during pregnancy to ensure the best outcomes for both the mother and the child. Table 1 depicts Yamaguchi Criteria used for the diagnosis of Still's Disease.

Table 1: The major and minor Yamaguchi Criteria

Major Criteria	Minor Criteria
Fever >39° for more than 1 week	Sore throat
Arthralgia/arthritis >2 weeks	Lymphadenopathy
WBC >10,000 with 80% PMNs	Increased LFTs
Typical rash	RF and ANAs negative

WBC: White blood cell, LFT: Liver function test, RF: Rheumatic Factor, ANA: Antinuclear antibodies

The precise pathogenesis of AOSD is not completely understood, but it is well-established that macrophage activation plays a central role, leading to the activation of T helper 1 cell cytokines. Pro-inflammatory cytokines such as IL-1, IL-6, and IL-18 are crucial in the onset and progression of the disease. Common clinical manifestations linked to this pathogenesis include fever, rashes, arthritis, muscle pain, throat pain, and lymph node enlargement. In rare instances, AOSD may cause kidney damage, central nervous system abnormalities, and peripheral nerve damage. In addition, some patients may experience acute respiratory failure, congestive heart failure, or disseminated intravascular coagulation.

Yamaguchi criteria[6]

A diagnosis of AOSD can be confirmed when more than five indicators are present, including at least two main ones, and after excluding infectious diseases (such as septicemia and infectious mononucleosis), malignant tumors (such as malignant lymphoma and leukemia), and other rheumatic conditions (especially multiple aneurysms and rheumatic vasculitis with extraganglial manifestations).

Adding the Yamaguchi criteria and serum ferritin levels (specifically levels above 1250 μg/L) further enhances the specificity of the diagnosis from 92.1% to 99.2%.

Management of AOSD during pregnancy involves both pharmacological and surgical approaches:

Drug therapy

While there is no cure for AOSD, medication can help manage symptoms. Common treatments include non-steroidal anti-inflammatory drugs, glucocorticoids, and disease-modifying anti-rheumatic drugs (DMARDs) such as azathioprine. However, DMARDs may pose risks to the fetus, such as malformations and growth restrictions, so their use must be carefully balanced against the benefits of controlling the disease. Glucocorticoids are a primary treatment option despite potential risks such as gestational diabetes, high blood pressure, IUGR, and preterm premature rupture of membranes.

Surgical treatment

Plasma exchange is also considered a viable treatment option for AOSD.

The hereditary aspects of AOSD are not fully understood, but there is evidence suggesting that genetic factors might contribute to its development. A study of 11 AOSD patients revealed that five

had a family history of rheumatologic diseases, hinting at a possible genetic predisposition. Genetic variants such as human leukocyte antigen-DRB1 and IL1 polymorphisms have been associated with AOSD. While the precise hereditary risk is not well-defined, it is likely that AOSD results from a combination of genetic and environmental factors. Consequently, genetic predisposition, along with environmental influences such as infections and stress, may impact the risk.

Furthermore, managing AOSD during pregnancy with medications such as glucocorticoids and immunosuppressants could affect the fetal immune response. This case underscores the complexity of AOSD pathogenesis and highlights the importance of understanding both genetic and environmental factors in managing the disease.

CONCLUSION

Our findings indicate that pregnancy in patients with AOSD is linked to a higher risk of complications, which should be monitored by both rheumatologists and obstetricians. AOSD is first identified during pregnancy and seems to represent a distinct subset of the disease with a systemic progression, flares occurring in the first and second trimesters, and obstetric complications such as prematurity and IUGR, which can sometimes lead to severe situations necessitating parenteral corticosteroids and intravenous immunoglobulins.

If AOSD is well-controlled before pregnancy, its activity generally does not increase during pregnancy. This highlights the importance of assessing and managing the disease before conception.

REFERENCES

1. Rettew JA, Huet YM, Marriott I. Estrogens augment cell surface TLR4 expression on murine macrophages and regulate sepsis susceptibility in vivo. Endocrinology 2009;150:3877-84.
2. Giacomelli R, Ruscitti P, Shoenfeld Y. A comprehensive review on adult onset Still's disease. J Autoimmun 2018;93:24-36.
3. Chi H, Liu D, Sun Y, Hu Q, Liu H, Cheng X, *et al*. Interleukin-37 is increased in adult-onset still's disease and associated with disease activity. Arthritis Res Ther 2018;20:54.
4. Filipovich AH. Hemophagocytic lymphohistiocytosis (HLH) and related disorders. Hematology Am Soc Hematol Educ Program 2009;127-31.
5. Placais L, Mekinian A, Bornes M, Poujol-Robert A, Bige N, Maury E, *et al*. Adult onset still's disease occurring during pregnancy: Case-report and literature review. Semin Arthritis Rheum 2018;47:575-7.
6. Yamaguchi M, Ohta A, Tsunematsu T, Kasukawa R, Mizushima Y, Kashiwagi H, *et al*. Preliminary criteria for classification of adult Still's disease. J Rheumatol 1992;19:424-30.

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