A case report on Rheumatoid arthritis in pregnancy

Dr. Ashishkumar N Shah and Dr. Devanshi Shah

DOI: https://doi.org/10.33545/gynae.2024.v8.i4b.1483

Abstract
Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease of unknown etiology that affects women three times more frequently than men, often in their most productive and childbearing years. The disease severity of rheumatoid arthritis generally improves during pregnancy but some patients maintain active diseases. However new onset Rheumatoid arthritis during pregnancy is a rare clinical situation hence we report a case of rheumatoid arthritis that started during pregnancy.

Keywords: Rheumatoid arthritis, pregnancy, during pregnancy, chronic systemic autoimmune disease

Introduction
Rheumatoid arthritis (RA) is a lifelong, systemic autoimmune disease that affects women more frequently than men, usually starts to develop between the ages of 30 and 50. Annual incidence of 8.7 per 100,000 between the ages of 18 and 34 years further increases to 36.2 per 100,000 between the ages of 35 and 44 years. There is an association with the class II major histocompatibility complex molecule HLA-DR4 and HLA-DRB1 alleles [1]. RA is hypothesized to develop when a genetically susceptible individual (eg, a carrier of HLA-DR4 or HLA-DR1) expose to an external factor (eg, cigarette smoking, infection, trauma) that triggers an autoimmune reaction.

The course of rheumatoid arthritis (RA) often changes during pregnancy with approximately 50% of pregnant women with RA have low disease activity, and 20% to 40% achieve remission by the third trimester; however, nearly 20% will have worse or moderate-to-high disease activity during pregnancy that may require further therapeutic intervention [2]. Pregnancy provides a protection against rheumatoid arthritis development, and this may be related to HLA disparate fetal microchimerism (Förger, 2020; Guthrie, 2010) [3]. The mainstay of management of rheumatoid arthritis includes Disease Modifying Antirheumatic Drugs (DMARDs), most of which are contraindicated in pregnancy, thus causing a significant complexity in management during pregnancy.

Case report
A 40 year old female with chronic hypertension, G3P2L1D1, with 27 weeks of gestation with breech presentation and Rh negative pregnancy, and previous history of full term normal vaginal delivery presented to the antenatal OPD of GMERS General Hospital, Gotri, Vadodara for her first antenatal visit.

On general examination her vitals were stable. She had multiple deformities of joints in her limbs. The deformities of both the hands and right knee was noted. In both the hands, metacarpophalangeal joints and interphalangeal joints deformities were present which were diagnosed as swan neck deformities. In right knee, edema and stiffness with fixed flexion deformity was present.

She was further evaluated with imaging studies. X-ray of bilateral hand and knee revealed joint space narrowing, periarticular osteopenia and bony erosions. For further evaluation, laboratory test of RA factor and anti CCP antibodies were done. RA factor was >720 iu/ml and anti CCP antibodies value was 82.09 u/ml which were suggestive of rheumatoid arthritis.

Medical management was started with tablet prednisolone, tablet hydroxychloroquine 100 mg twice a day, tablet leflunomide 20 mg twice a day and tablet sulfasalazine 500 mg once a day. The decision to start medications was easy in this case as there was already Intra-uterine fetal death at the time of presentation.
On obstetric examination, she was 26 weeks pregnant with absent fetal heart sounds on auscultation. USG revealed parameters of 26 weeks pregnancy with intrauterine fetal death. The full work up for the IUFD did not reveal any apparent cause. Considering the diagnosis, induction of delivery was planned. She delivered a still born baby vaginally. Post-partum examination of the baby also did not reveal any apparent cause for IUFD.

In the postnatal period, the prednisolone was tapered. The patient was counselled properly about the importance of medication and follow up for Rheumatoid Arthritis. After appropriate postnatal care, she was discharged and advised to come for follow up after 15 days.

Discussion

Rheumatoid Arthritis is a chronic inflammatory disease that involves damage to the joint cartilage. In up to 70 percent of women with rheumatoid arthritis, disease will improve during pregnancy. Some studies suggest that this may be due to regulatory T-cell alterations. Even so, some women develop disease during pregnancy, and others become worse. A downside to this respite during pregnancy is that postpartum exacerbation occurs in 40 to 50 percent of women. This may stem from postpartum alterations in innate immunity.

In this case, diagnosis of 26 weeks pregnancy with IUFD made it easy to start medications for treatment of Rheumatoid Arthritis.

As per the available history and records of the previous pregnancy, it seems that this is the new onset Rheumatoid Arthritis. The patient has ignored the symptoms of the disease and did not seek any care for her rheumatological condition either in the pre-conceptional or the antenatal period.

In the present pregnancy, the work up for the IUFD did not reveal any other cause. It is likely that the presence of untreated Rheumatoid Arthritis has led to the IUFD.

Effect of pregnancy on Rheumatoid arthritis.

Some studies report a protective effect of pregnancy against developing new-onset rheumatoid arthritis. It is considered that pregnancy is a clinical situation of immunological tolerance induced by the semi-allogenic fetus. This is due to different factors that include several immunological processes, like:

- Thymic involution
- Decreased activity of NK cells
- Decrease in the immune response in Th1 lymphocytes with shift toward Th2 activity.
- The interference of sex hormones with several putative processes involved in arthritis pathogenesis including immunoregulation like, amelioration of rheumatoid arthritis correlated with serum levels of pregnancy-associated alpha2-glycoprotein [4]. This compound has immunosuppressive properties.

In our case report, we found patients with symptoms of inflammatory joint pain, with swollen and painful joints and with laboratory tests results compatible with rheumatoid arthritis. However, the clinical peculiarity that motivated us to publish the case lies in the fact that the patient begun her to manifest her symptoms during pregnancy, a very infrequent situation in clinical practice.

Effect of Rheumatoid arthritis on fertility and pregnancy.

Rheumatoid arthritis has an influence upon fertility and pregnancy outcome. RA patients have smaller family size due to either the patient’s choice or subfertility related to diseases activity [5].

Well controlled RA has good fetal outcome. However, women with highly active RA during pregnancy have a potential risk of maternal and neonatal complications and are considered as high-risk pregnancies. Pregnant women with RA has a higher risk of:

- Gestational diabetes
- Preeclampsia
- Infection
- Preterm premature rupture of membranes
- Small for gestational age infants and fetal growth retardation
- Preterm deliveries
- Spontaneous miscarriage
- Intra Uterine Fetal Death
- Increased cesarean section [6]

Despite all that factors, favorable outcomes remain possible with proper planning and management. This is one such case where IUFD has resulted as a complication of untreated RA.

Medical management of rheumatoid arthritis during pregnancy

The drugs most frequently used for the treatment of rheumatoid arthritis can be divided into 4 categories according to their risk for fetal development:

- moderate to high risk of fetal damage: includes methotrexate and leflunomide, with a high risk of causing
birth defects, such as congenital malformations of the central nervous system, cerebral palsy, alterations in the ossification of the cranium, extremities and palate, so they should be avoided during the conception and pregnancy. These drugs must be discontinued at least 3 months and 2 years before conception, respectively, due to their prolonged retention in the tissues [7].

- Drugs that can be used selectively during pregnancy: includes glucocorticoids such as prednisone, prednisolone and methylprednisolone, which cross the placenta in low concentrations and are relatively safe for their use in pregnancy when they are used in low doses [8]. NSAIDS can be used safely during pregnancy with certain considerations, such as being avoided during preconception and early pregnancy, since they can interfere with the implantation of the embryo; & third trimester because of the risk of premature closure of the ductus arteriosus. Inhibitors of the tumor necrosis factor can also be used electively, since it has been determined that the risk of congenital defects in patients exposed to this type of drugs is low.

- minimum risk: includes hydroxychloroquine, sulfasalazine, Azathioprine [9].

- Unknown risk: the drugs in which the tests related to the risks are insufficient, and includes certain biological agents, in which their continuity during pregnancy should be agreed with the mother, includes Rituximab, abatacept, tocilizumab and tofacitinib are [10].

In this case, due to presence of IUFD, the fetal risk was not into consideration. And so, the decision making for the choice of the drug was focused on the benefits of the combination of the drugs and maternal side effects of the drug. Hence, it was relatively easy to plan the regime of the treatment. However, long-term follow up and appropriate control of the RA is important both for general health and better outcome of the next pregnancy. The drugs must be modified whenever the patient plans to conceive again.

Conclusion
We report a case of appearance of new onset rheumatoid arthritis during pregnancy, an unusual phenomenon in clinical practice. Pregnancy planning is essential in women with rheumatoid arthritis, as it should start in the period of remission of the disease. Pregnant RA patients have higher frequency of abortion, still birth, pre eclampsia, LBW of newborn, delivery by C-section; especially with pregnancies started in the active phase of the rheumatoid arthritis, those having higher diseases activity and/or treated with potentially harmful medications. It is crucial to educate female RA patients about these risks and they should be considered as high-risk pregnancy. Treatment with low-dose glucocorticoids, hydroxychloroquine during pregnancy are considered safe for the mother and fetus, in addition to efficacy for keep the disease in remission. With appropriate counseling, correct treatment and close follow up, adverse outcomes of the Rheumatoid Arthritis and its treatment during pregnancy can be prevented.

References


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