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Monoarticular rheumatoid arthritis in pregnancy: A case report

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Abstrac

Rheumatoid arthritis (RA) is a lifelong, systemic autoimmune disease that affects women three times more frequently than men, often in their most productive and childbearing years. This chronic inflammatory disease occurs mainly due to immunological dysfunction and infiltration of T cells secreting cytokines causing inflammation and arthritis due to cartilage destruction and systemic symptoms. The primary feature being inflammatory synovitis which usually involves the peripheral joints.

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.

In our case, A 28 year old female, Primigravida with 26 weeks of gestation came to the OPD of department of Obstetrics and Gynaecology, MGM hospital with complaints of pain in the left knee joint for the past one year, aggravated two weeks back and diffuse swelling over the joint since 1 month. A diagnosis of monoarticular Rheumatoid arthritis was formed after ruling out other pathologies like reactive arthritis, tuberculosis of knee joint, referred pain due to pathologies in the neighbouring joints. Since the patient was pregnant, a decision based on level five evidence, was taken to avoid the DMARDs due to their potential teratogenicity and she was managed with an intra-articular injection of corticosteroid which showed no improvement in the patient's symptoms. Hence it was followed by an intra-articular injection of 8ml of Platelet rich plasma (PRP) which resulted in an improvement in VAS scores from 8 to 2, 4weeks after injection along with a clinical reduction in joint swelling and pain even at extremes of movements. The clinical benefits of PRP in RA can possibly be explained by its anti-inflammatory effects.

Keywords: monoarticular, platelet rich plasma (PRP), pregnancy, rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a lifelong, systemic autoimmune disease that affects women three times more frequently than men, often in their most productive and childbearing years ^[1]. 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 ^[2]. There is an association with the class II major histocompatibility complex molecule HLA-DR4 and HLA-DRB1 alleles ^[3].

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 [4].

The remission of this disease can be attributed to the shift of Th1 mediated immunity to Th2 which occurs during pregnancy. Thus, with the suppression of Th1 cells and upregulation of Th2 cells promote humoral and antibody based immunity.

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Case Report

A 28 year old female, Primigravida with 26 weeks of gestation came to the OPD of department of Obstetrics and Gynaecology, MGM hospital with complaints of pain in the left knee joint for the past one year, aggravated two weeks back and diffuse swelling over the joint since 1 month. No complaints of spotting or bleeding per vagina or pain in abdomen.

She was referred to department of Orthopaedics for further evaluation, where it was concurred that the pain was insidious in onset, gradually progressive, not radiating proximally to the upper thigh or hip joint or distally to the ankle joint. Patient also gave a history of increased stiffness in the left knee joint, experienced maximum in the morning and relieved gradually after movement of the left knee. Patient gives no history of trauma, lower back pain, contralateral knee or ipsilateral hip pain, no other joints including the small joints of the hands and feet were involved, fever, cough, evening rise of temperature. No past history of any other systemic illnesses or comorbidities.

On examination of the left knee joint, on inspection there was visible effusion of the joint obliterating the medial and lateral parapatellar gutters, no visible scars, sinuses or vessels were noted. On palpation, there was local rise of temperature as compared to the right knee joint and moderate medial joint line tenderness. There was no fixed deformity at the left knee joint and the patient had a complete but painful range of movements. She had a VAS score of 8 on 10. There were no limb length discrepancies noted and no distal neurological deficit was noted and all the distal pulses were well felt.

Based on the history of the patient, a weight bearing X Ray radiography of the bilateral knee joint in the antero-posterior and lateral views were taken [Figure 1, 2], abdominal shield was used to protected the foetus from radiation exposure, X ray findings were suggestive of minimal medial joint line

narrowing of the left knee joint as compared to the right knee. Since the symptoms of the patient outweighed the X ray findings, a decision was taken to run blood investigations *viz*. CBC, ESR, CRP, RA Factor and Sr. Creatinine, arthrocentesis of left knee joint for acid fast bacilli and an MRI of the left knee joint was carried out.

Blood investigation reports were as follows: ESR -65mm/hr, CRP 23mg/dl and RA Factor- 23mg/dl.

Joint aspirate was negative for acid fast bacilli.

MRI Knee was done which showed narrowing of joint space and synovial hypertrophy and edema.

Based on the history, X Ray, Blood investigations and MRI findings a diagnosis of Monoarticular Rheumatoid arthritis was formed.

Patient was started on low dose oral prednisone 7.5mg/day and NSAIDs and followed up weekly for 2 weeks but there was no relief of symptoms, her VAS score continued to be 8. Intra articular steroid 2ml of 40mg Triamcinolone diluted with 0.5% Bupivacaine was given, patient was followed up after 1 week, the pain was still persistent with a VAS score of 7. Decision to give intra articular platelet rich plasma (PRP) was made. Patient and relatives were explained regarding persistent pain and refractory inflammation in spite of oral and intra articular steroids, consent for intra articular PRP was taken. 8 ml of PRP was administered [Figure 3] and patient was followed up after 4 weeks, she had a significant amount of reduction in pain even at extremes of movements with a VAS score of 2, there was also a significant reduction in effusion and stiffness.

Patient was followed up every weekly till 36weeks of gestation and then twice weekly till 39weeks. She went into spontaneous labour at 39 weeks and delivered vaginally, a male baby of 2.8kgs. Patient was explained regarding the possibility of postpartum flare and immediate follow up if necessary.



Fig 1-2: Weight bearing X ray Antero-posterior and lateral views.



Fig 3: Platelet Rich Plasma administration under sterile conditions.

Drug class	FDA category	Clinical recommendations
Symptom-modifyi	ng drugs	
NSAIDs	В	First part of pregnancy
	C	After 30 weeks of gestation. Increased risk of premature closure of the ductus arteriosus
CSs	С	Use during the first trimester is associated with increased risk of oral cleft in the newborn
		Increased risk of adrenal insufficiency
DMARDs		
SSZ	В	No increased risk of congenital malformations
		Combine with folate supplements
AZA	D	Can be continued to maintain remission during pregnancy
MTX	X	Contraindicated in pregnancy
		Discontinue 3-6 months before conception
LEF	X	Contraindicated in pregnancy
		Discontinue 2 years before pregnancy or use cholestyramine washout procedure until plasma levels are <0.02 μg/ml on two measurements spaced at least 2 weeks apart
Anti-malarials	C	HCQ is compatible with pregnancy
		Risk for retinal toxicity and ototoxicity higher for chloroquine than for HCQ
Biologicals		B Production (1974 - 1
Anti-TNF	В	Anti-TNF antibodies are not transferred to the embryo/fetus in first trimester of pregnancy
Abatacept	C	No human pregnancy data available
		Discontinue 10 weeks before planned pregnancy
Rituximab	C	Reversible B-cell depletion or lymphopenia in the neonate
		Long half-life. Discontinue 1 year before planned pregnancy
Tocilizumab	C	No human pregnancy data available.
		Discontinue 10 weeks before planned pregnancy

Fig 4: FDA Categories of disease modifying anti-rheumatoid drugs DMARDs

Discussion

Rheumatoid Arthritis is a chronic inflammatory disease that involves damage to the joint cartilage. Most cases show a dramatic improvement during pregnancy, however a quarter of them have no improvement and a small proportion of cases worsen during pregnancy.

Several RA medications are contraindicated during pregnancy leaving only a limited number of medications available for treatment. The drug safety information for use mainly relies on the Food and Drug Administration (FDA) category for drug use in pregnancy.

The following table summarises the drugs used in the treatment of RA and the current recommendations of their use

in pregnancy.

[Figure 4]

RA shares features with osteoarthritis (OA), such as cartilage matrix degradation and progressive joint remodelling, while OA joints exhibit predominant inflammation. This suggests a shared underlying pathology in RA and OA ^[5]. RA also shares features such as articular erosion and inflammation with OA, a condition where benefits of PRP are reported ^[6,7].

Platelet rich plasma (PRP) is a concentrate of autologous cell growth factors and highly concentrated platelets which has shown pain relief in patients with OA. PRP may help to restore cartilage morphology and microarchitecture due to its action on synovial cell proliferation and differentiation and

inhibition of inflammatory factors in joints [8-10].

The application of PRP in wound healing and tissue regeneration can be attributed to various growth factors and cytokines such as platelet-derived growth factor, epidermal growth factor (EGF), connective tissue growth factor (CTGF), platelet factor-4, vascular endothelial growth factor (VEGF), transforming growth factor- β , insulin-like growth factor-1, interleukin 1β , and IL6 [11].

PRP has shown good effectiveness in OA, however its use in RA has limited experience.

Conclusion

In our case, intra-articular injection of 8ml of PRP resulted in improvement in VAS scores from 8 to 2, 4weeks after injection along with a clinical reduction in joint swelling and pain even at extremes of movements. The clinical benefits of PRP in RA can possibly be explained by its anti-inflammatory effects. Also, no adverse reactions were noted over the 14week follow-up period.

The precise mechanism of action of PRP is not clearly known. However, autologous plasma rich in platelets is believed to be a rich source of growth factors from the harvested platelets that have been activated by endogenous thrombin due to the added calcium chloride in the PRP preparations [12]. Platelet activation results in growth-factor release [13]. These growth factors accelerate healing and improve functional outcomes in intra-articular pathologies.

Our findings in this case suggest a beneficial role of PRP in patients with RA, especially in patients who have a failed therapy with one or more of the drugs used for management of RA in pregnancy. However, these findings should be confirmed in well-planned clinical studies for RA.

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