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Case Report

Sonography of active rheumatoid arthritis during pregnancy: a case report and literature review

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ABSTRACT

Disease activity in rheumatoid arthritis usually subsides in pregnancy, however a subset of patients have worsened symptoms with joint pain and swelling. Monitoring and mitigating disease activity in pregnancy is important for preventing deforming structural changes which can affect the ability of the patient to care for themselves and the newborn. Ultrasound is a safe and low-cost imaging modality for detecting active changes from an inflammatory arthritis, which can help guide management. We describe a case of an acute disease flare during pregnancy, readily detected with ultrasound, and present a review of sonographic evaluation of rheumatoid arthritis in pregnancy.

Introduction

Pregnancy in rheumatoid arthritis is usually associated with a decrease in disease activity in the majority of patients, said to be secondary to hormonal protection and presence of anti-inflammatory cytokines [1]. However, approximately 40% of patients have increased disease activity [1,2]. In the presence of a flare, uncontrolled active inflammatory changes can result in deforming disease with erosions and subluxations, and development of secondary degenerative arthritis from articular cartilage damage and joint space narrowing. Postpartum disease flare is also a well described phenomenon [1]. In the pregnant patient, rheumatoid arthritis is associated with preterm delivery, increased rate of cesarean section, and reduced birth weight [3,4]. Additionally, many of the standard systemic treatments are considered feto-toxic [5]. Therefore, to prevent disease progression and mitigate negative outcomes, diagnosing and managing active changes from rheumatoid arthritis during pregnancy is critical.

Conventional radiographs, ultrasonography, and MRI are all used to detect disease activity [6]. Although conventional radiographs are ubiquitous, they have a limited role in detecting the earliest evidence of active disease including synovitis and bone marrow edema [6]. MRI with intravenous gadolinium provides exquisite soft tissue detail to detect changes of

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active disease including synovitis, bone marrow edema, and osteitis; however, in the pregnant patient, its use is limited due to the mounting evidence documenting the risk of intravenous gadolinium to the fetus [7-11]. Ultrasound, in this circumstance, provides a lower cost imaging option that is capable of detecting synovitis, tenosynovitis, and periarticular erosions [12,13].

In this report, we describe a case of active changes from rheumatoid arthritis well seen on ultrasound in a pregnant patient, and present a review of the literature on the use of ultrasonography to diagnose active disease.

Case report

The patient is a 29 year old pregnant (17 weeks) female with a history of juvenile idiopathic arthritis, diagnosed at age 4. The pattern of disease was consistent with persistent oligoarthritis (lower limb predominant); without a history of uveitis. She was Antinuclear Antibodies (ANA) positive, rheumatoid factor and cyclic citrullinated peptide (CCP) seronegative at the time of diagnosis. After initial management with infliximab (Remicade, Janseen Pharmaceuticals, Horsham, PA 19004) and methotrexate, she was maintained on etanercept (Enbrel, Immunex Corporation, Thousand Oaks, CA 91320) with good response until she made plans for pregnancy, at which time she was weaned off the TNF-α inhibitor therapy. She had discontinued taking etanercept and nonsteroidal anti-inflammatory medications 5 months prior in preparation for pregnancy. At the time of presentation, the only medication being taken was prenatal vitamin supplements.

She first communicated with the rheumatologist reporting symptoms of fluctuating asymmetrical joint swelling involving bilateral wrists and left ankle for 1 month. She denied morning joint stiffness, warmth or significant joint pain. Updated laboratory data, including complete blood count, sedimentation rate and C-reactive protein level were within normal limits. Given the asymmetrical symptoms and suspicion of subclinical synovitis, ultrasound evaluation was requested for further clarification of disease activity.

Sonographic evaluation of the right hand and foot demonstrated active synovitis, characterized by marked synovial hypertrophy and hypervascularity within the imaged joints (Figs. 1, 2 and 3). There were small erosions noted at the second metacarpophalangeal joint and the second metatarsophalangeal joint. The total grayscale synovitis score was 26 out of 33, and the total Power Doppler synovitis score was 21 out of 21. Moderate hypervascular tenosynovitis was also noted involving the extensor tendons.

Based on these findings, the patient was diagnosed with a rheumatoid arthritis flare with active changes. Subsequently, she was seen in the rheumatology clinic where a physical examination revealed polyarthritis concordant with the ultrasound findings. The presence of polyarthritis including multiple small joints with radiographic erosive disease support transition from oligoarticular JIA to rheumatoid arthritis in adulthood. After rheumatologic consultation and appropriate discussion of the potential side effects to the mother and fetus from systemic therapy, the patient declined low-dose oral glucocorticoids and oral disease modifying antirheumatic drugs. She was then offered targeted steroid injections from which she reported therapeutic benefit in both the anesthetic and steroid phase.

Discussion

The management of rheumatoid arthritis in pregnancy lends itself to a complex interplay between monitoring disease activity and mitigating symptoms with nontoxic yet effective therapies. For some patients, pregnancy is not protective and results in a flare of disease activity. Therefore, detection and tight control of inflammatory changes is warranted to prevent joint destruction which can result in poor long-term prognosis with deforming changes.

MRI with intravenous gadolinium for the evaluation of rheumatoid arthritis is of limited utility in the pregnant patient. Ray et al. report an association with an increased risk of a broad set of rheumatologic, inflammatory, or infiltrative skin conditions in the fetus, and for stillbirth or neonatal death after gadolinium enhanced MRI [8]. The American College of Radiology recommendations state that MRI contrast agents should not be routinely provided to pregnant patients since gadolinium passes through the placenta barrier and stays in the amniotic space where it could dissociate from the chelate molecule, releasing the toxic gadolinium ion [10]. The American College of Obstetricians and Gynecologists committee opinion states that gadolinium use should be limited to situations in which the benefits clearly outweigh the possible risks [14].

The utility of diagnostic ultrasound for inflammatory arthritis has significantly grown over the past two decades [6,12,13,15-17]. Ultrasound is able to assess active inflammatory changes such as synovitis, tenosynovitis, and enthesitis. Several studies have demonstrated comparable rates of detection of synovial inflammation between ultrasound and MRI [18-20]. Ultrasound can also evaluate for chronic structural changes such as erosions. In a meta-analysis which included 913 patients, Baillet et al. concluded that ultrasound has comparable efficacy to MRI for erosion detection [21]. Given the untoward side effects of MRI with intravenous gadolinium, ultrasound plays a welcomed role in the evaluation of disease activity as it is easily accessible, cost-effective and allows multiple joints to be imaged concomitantly.

The definitions for the sonographic findings associated with active rheumatoid arthritis are outlined by the OMERACT7 group [12]. The hallmark of an inflammatory arthritis is synovitis which is readily detected on ultrasound as synovial thickening which can be hypervascular in its acute and subacute stages, while a more chronic fibrous pannus can present without hypervascularity. Effusions may also represent a part of the inflammatory response at the level of the joint and is well visualized on ultrasound. While synovial fluid and synovial thickening are both hypoechoic (synovial fluid may be also be anechoic), an effusion will be displaceable and compressible, while synovial hypertrophy is not. Synovial fluid is hypovascular while synovial hypertrophy, along with color Doppler signal constitutes the imaging hallmark for syn-

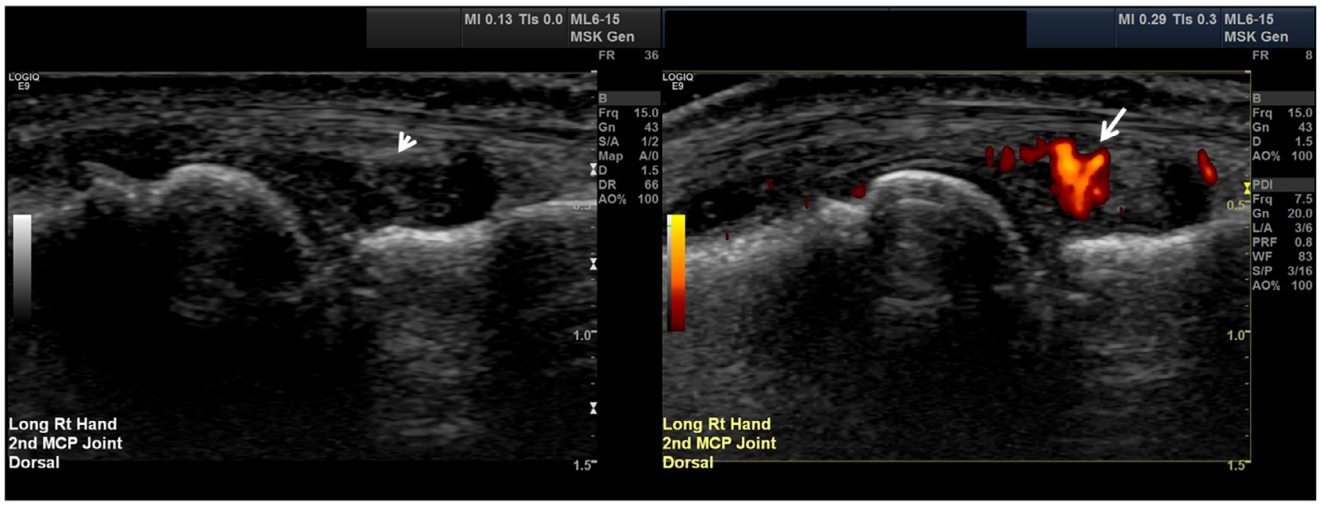

Fig. 1 – Grayscale and color Doppler sagittal images of the right hand second metacarpophalangeal joint demonstrates marked synovial hypertrophy (arrowhead) with associated significant hypervascularity on color Doppler analysis (arrow). These findings are consistent with active synovitis.

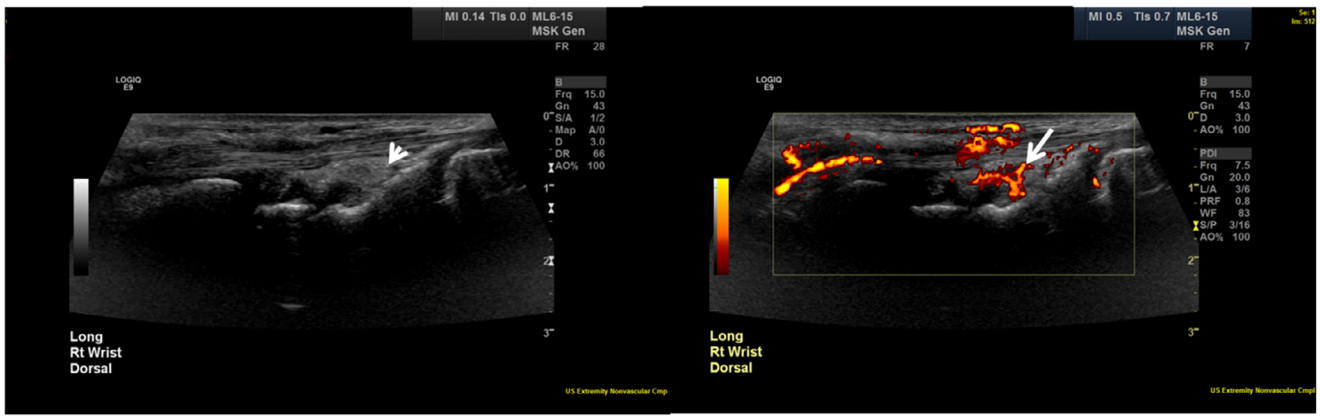

Fig. 2 – Grayscale and color Doppler sagittal images of the right wrist dorsally demonstrate synovial hypertrophy (arrowhead) with associated hypervascularity on color Doppler analysis (arrow). These findings are consistent with active synovitis.

ovitis [22]. Tenosynovitis can also represent active changes from inflammatory arthritis manifesting as thickening of the tenosynovial sheath, with or without significant effusion, and with or without increased vascularity [12]. Structural changes can also be detected on ultrasound, with erosions being defined as intra-articular cortical discontinuities visible in two perpendicular planes [12].

The German US7 score [23] and its modified version [24] are ultrasound grading criteria that were developed to monitor rheumatoid arthritis disease activity. These evaluate 7 joints of the clinically dominant hand and foot of patients with inflammatory arthritis [23,24]. These include palmar and dorsal scanning of the 2nd and 3rd metacarpophalangeal joints, the 2nd and 3rd proximal interphalangeal joints, and the 2nd and 5th metatarsophalangeal joints. Grayscale findings of synovitis are reported semiquantitatively on a 4 point scale (0-3; absent to severe synovitis). Doppler findings are also reported on a 4 point scale (0-3; no intraarticular color signal to ≥50% of the intraarticular area filled with color signal). Tenosynovitis and erosions are graded on a 2 point scale as present (0) or absent (1). The sum of the synovitis scores is then reported [23]. Both of these scoring symptoms have been validated and correlate with clinical symptoms [23-26].

Limitations for ultrasound evaluation of inflammatory arthritis are few, predominantly being a relatively high learning curve for detailed evaluation, with operator technique being paramount. Also, not all parts of the joint will be visualized on ultrasound, precluding evaluation of the entire articular surface for erosions and chondromalacia [15,16]. In addition, ultrasound cannot visualize bone marrow edema, which is considered an important sign of inflammatory changes at the level of the joint, and also a predictor of erosive changes, with a significantly high NPV of 99% [27]. While sonography can be time consuming depending on the number of joints evaluated,

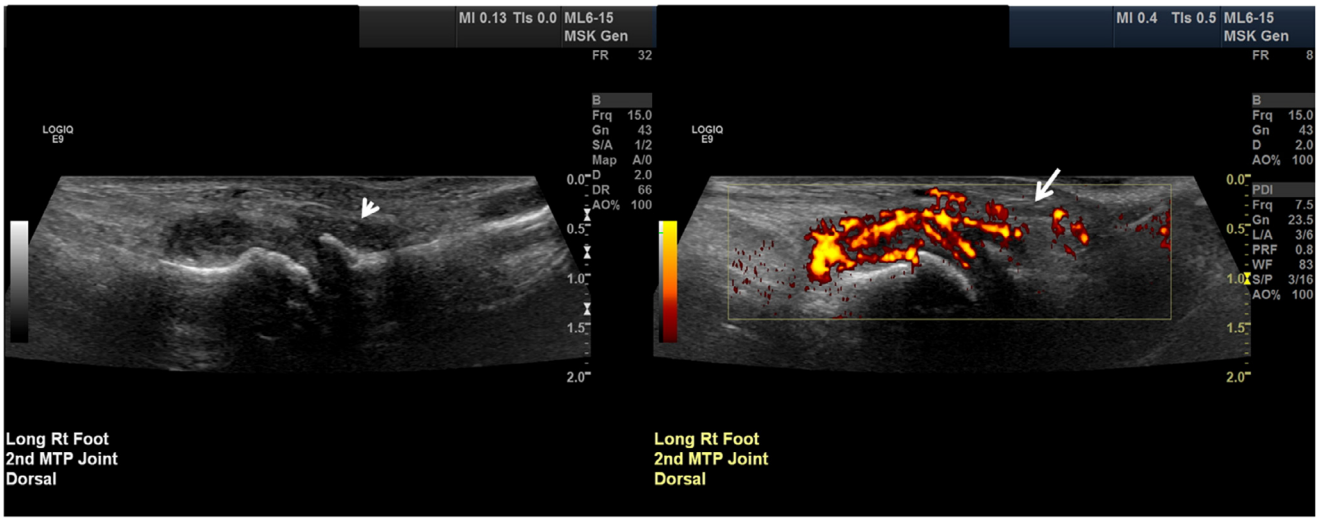

Fig. 3 – Grayscale and color Doppler sagittal images of the right foot second metatarsophalangeal joint demonstrates marked synovial hypertrophy (arrowhead) with associated significant hypervascularity on color Doppler analysis (arrow). These findings are consistent with active synovitis.

ultrasound can image both hands and feet concomitantly if needed, in a fraction of the time compared to MRI. In addition, logistics of gadolinium timing would preclude evaluation of both hands and feet in one imaging setting.

In conclusion, we describe a case of active acute changes from rheumatoid arthritis in a pregnant patient readily detected with ultrasound. When MRI with intravenous gadolinium cannot be used, ultrasound is as effective in the diagnosis and monitoring of disease activity in rheumatoid arthritis.

REFERENCES

[1] Barrett JH, Brennan P, Fiddler M, Silman AJ. Does rheumatoid arthritis remit during pregnancy and relapse postpartum? Results from a nationwide study in the United Kingdom performed prospectively from late pregnancy. Arthritis Rheum 1999;42(6):1219–27.

[2] de Man YA, Dolhain RJ, van de Geijn FE, Willemsen SP, Hazes JM. Disease activity of rheumatoid arthritis during pregnancy: results from a nationwide prospective study. Arthritis Rheum 2008;59(9):1241–8.

[3] de Man YA, Hazes JM, van der Heide H, Willemsen SP, de Groot CJ, Steegers EA, et al. Association of higher rheumatoid arthritis disease activity during pregnancy with lower birth weight: results of a national prospective study. Arthritis Rheum 2009;60(11):3196–206.

[4] Bharti B, Lee SJ, Lindsay SP, Wingard DL, Jones KL, Lemus H, et al. Disease severity and pregnancy outcomes in women with rheumatoid arthritis: results from the organization of teratology information specialists autoimmune diseases in pregnancy project. J Rheumatol 2015;42(8):1376–82.

[5] Krause ML, Amin S, Makol A. Use of DMARDs and biologics during pregnancy and lactation in rheumatoid arthritis: what the rheumatologist needs to know. Ther Adv Musculoskelet Dis 2014;6(5):169–84.

[6] Vasanth LC, Pavlov H, Bykerk V. Imaging of rheumatoid arthritis. Rheum Dis Clin North Am 2013;39(3):547–66.

[7] Webb JA, Thomsen HS, Morcos SKMembers of Contrast Media Safety Committee of European Society of Urogenital R. The use of iodinated and gadolinium contrast media during pregnancy and lactation. Eur Radiol 2005;15(6):1234–40.

[8] Ray JG, Vermeulen MJ, Bharatha A, Montanera WJ, Park AL. Association between MRI exposure during pregnancy and fetal and childhood outcomes. JAMA 2016;316(9):952–61.

[9] Sundgren PC, Leander P. Is administration of gadolinium-based contrast media to pregnant women and small children justified? J Magn Reson Imaging 2011;34(4):750–7.

[10] Kanal E, Barkovich AJ, Bell C, Borgstede JP, Bradley WG Jr, Froelich JW, et al. ACR guidance document for safe MR practices: 2007. AJR Am J Roentgenol. 2007;188(6):1447–74.

[11] Chen MM, Coakley FV, Kaimal A, Laros RK Jr. Guidelines for computed tomography and magnetic resonance imaging use during pregnancy and lactation. Obstet Gynecol 2008;112(2 Pt 1):333–40.

[12] Wakefield RJ, Balint PV, Szkudlarek M, Filippucci E, Backhaus M, D'Agostino MA, et al. Musculoskeletal ultrasound including definitions for ultrasonographic pathology. J Rheumatol 2005;32(12):2485–7.

[13] Wakefield RJ, D'Agostino MA, Iagnocco A, Filippucci E, Backhaus M, Scheel AK, et al. The OMERACT Ultrasound Group: status of current activities and research directions. J Rheumatol 2007;34(4):848–51.

[14] Committee on Obstetric P Committee Opinion No. 723: Guidelines for diagnostic imaging during pregnancy and lactation. Obstet Gynecol. 2017;130(4) e210–e2e6.

[15] McNally EG. Ultrasound of the small joints of the hands and feet: current status. Skeletal Radiol 2008;37(2):99–113.

[16] McNally EG. The development and clinical applications of musculoskeletal ultrasound. Skeletal Radiol 2011;40(9):1223–31.

[17] Tan YK, Ostergaard M, Conaghan PG. Imaging tools in rheumatoid arthritis: ultrasound vs magnetic resonance imaging. Rheumatology (Oxford) 2012;51(Suppl 7) vii36-42.

[18] Terslev L, Torp-Pedersen S, Savnik A, von der Recke P, Qvistgaard E, Danneskiold-Samsoe B, et al. Doppler ultrasound and magnetic resonance imaging of synovial inflammation of the hand in rheumatoid arthritis: a comparative study. Arthritis Rheum 2003;48(9):2434–41.

[19] Backhaus M, Kamradt T, Sandrock D, Loreck D, Fritz J, Wolf KJ, et al. Arthritis of the finger joints: a comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. Arthritis Rheum 1999;42(6):1232–45.
[20] Brown AK, Quinn MA, Karim Z, Conaghan PG, Peterfy CG, Hensor E, et al. Presence of significant synovitis in rheumatoid arthritis patients with disease-modifying antirheumatic drug-induced clinical remission: evidence from an imaging study may explain structural progression. Arthritis Rheum 2006;54(12):3761–73.
[21] Baillet A, Gaujoux-Viala C, Mouterde G, Pham T, Tebib J, Saraux A, et al. Comparison of the efficacy of sonography, magnetic resonance imaging and conventional radiography for the detection of bone erosions in rheumatoid arthritis patients: a systematic review and meta-analysis. Rheumatology (Oxford) 2011;50(6):1137–47.
[22] D'Agostino MA, Terslev L, Aegerter P, Backhaus M, Balint P, Bruyn GA, et al. Scoring ultrasound synovitis in rheumatoid arthritis: a EULAR-OMERACT ultrasound taskforce-Part 1: definition and development of a standardised, consensus-based scoring system. RMD Open 2017;3(1):e000428.
[23] Backhaus M, Ohrndorf S, Kellner H, Strunk J, Backhaus TM, Hartung W, et al. Evaluation of a novel 7-joint ultrasound score in daily rheumatologic practice: a pilot project. Arthritis Rheum 2009;61(9):1194–201.
[24] Mendonca JA, Yazbek MA, Costallat BL, Gutierrez M, Bertolo MB. [The modified US7 score in the assessment of synovitis in early rheumatoid arthritis]. Rev Bras Reumatol 2014;54(4):287–94.
[25] Ohrndorf S, Halbauer B, Martus P, Reiche B, Backhaus TM, Burmester GR, et al. Detailed joint region analysis of the 7-joint ultrasound score: evaluation of an arthritis patient cohort over one year. Int J Rheumatol 2013;2013:493848.
[26] Zavada J, Hanova P, Hurnakova J, Szczukova L, Uher M, Forejtova S, et al. The relationship between synovitis quantified by an ultrasound 7-joint inflammation score and physical disability in rheumatoid arthritis - a cohort study. Arthritis Res Ther 2017;19(1):5.
[27] Mundwiler ML, Maranian P, Brown DH, Silverman JM, Wallace D, Khanna D, et al. The utility of MRI in predicting radiographic erosions in the metatarsophalangeal joints of the rheumatoid foot: a prospective longitudinal cohort study. Arthritis Res Ther 2009;11(3):R94.