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Review article

Medical management of wrist and hand inflammatory conditions: A literature review

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ABSTRACT

Differential diagnosis for inflammatory arthritis of the hands includes infectious processes and autoimmune conditions like rheumatoid arthritis, systemic lupus erythematosus, and crystalline arthritis, among others. As medical management of the inflammatory arthritis is (a) targeted to the specific disease and severity of the symptoms, (b) posed with diagnostic dilemmas due to overlap in presentation, and (c) adversely affected by incorrect treatment which may further complicate the diagnosis and outcomes, reaching the correct diagnosis is pivotal towards appropriate management. Medical management may span from antibiotics, corticosteroids, non-steroidal anti-inflammatory drugs, to immunosuppressive medications (conventional synthetic DMARDs and biologic agents). Herein we discuss the medical management of the most clinically relevant inflammatory arthritides involving the hand.

1. Introduction

Arthritis of the hand has a major impact not only on one's physical functioning and independence but also on one's daily quality of life. In general, prevalence estimates for arthritis of the hand are not available, except for osteoarthritis. Inflammatory arthritis is characterized by presence of synovitis. Diagnostic considerations for inflammatory arthritis are shown in Table 1. These conditions may be stratified based on onset of symptoms (acute or chronic), number of joints involved (monoarticular, oligoarticular, or polyarticular), and pattern of joint involvement. This stratification aids in establishing a specific diagnosis when combined with thorough history taking, examination, laboratory, and/or imaging work up (Table 2). Infectious arthritis remains an important differential diagnosis for arthritis of the hand and thus should be excluded in the presence of concerning signs and symptoms. The coexistence of infectious and non-infectious arthritis in the hand has been reported but is relatively uncommon. Rheumatoid arthritis is one of the autoimmune conditions that typically involves both hands and wrists in a bilateral symmetrical pattern. However, several non-rheumatoid arthritis conditions, such as crystalline arthritis (pseudogout) and systemic lupus erythematosus (SLE), may also present in a similar manner, which can pose a diagnostic challenge.[1] A review of salient features and medical management of the most clinically relevant non-infectious inflammatory arthritic conditions involving the hands is presented.

2. Rheumatoid arthritis

Rheumatoid arthritis (RA) is the most common symmetric inflammatory arthritis involving multiple joints, including the hands and wrists. The prevalence of RA has increased during the period 2004 to 2014, and the conservative estimate for RA in 2014 in the US was 1.28–1.36 million adults.[2] In a study of 200 patients with RA, 94% suffered from at least one hand or wrist related symptom within 2–4 years of disease duration, while 70% were found to have at least one impairment in the dominant hand on physical examination of the hand or wrist.[3]

Patients with RA typically present with symptoms of pain, swelling, and morning stiffness of the hands and wrists. Specific

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Table 1
Differential diagnosis for inflammatory arthritis.

Inflammatory Mono- or Oligoarthritis (<4 Joints)	
Crystalline	Gout (monosodium urate)
	Calcium pyrophosphate dehydrate deposition disease (CPPD or pseudogout)
Auto-Immune	Sarcoidosis, reactive arthritis
Infectious	Non-gonococcal septic arthritis: bacterial, mycobacterial, or fungal
	Gonococcal arthritis
	Lyme disease
Inflammatory Polyarthritis (≥4 Joints)	
Auto-Immune	Rheumatoid arthritis
	Systemic lupus erythematosus
	Seronegative spondyloarthritis (including psoriatic arthritis, ankylosing spondylitis, Behcet's Disease, enteropathic arthritis with inflammatory bowel disease, reactive arthritis), Whipple's disease, SAPHO (synovitis, active pustulosis, hyperostosis and osteitis), celiac disease
	Serum sickness, post-infectious
	Others: Still's Disease (adult and juvenile), systemic sclerosis, mixed connective tissue disease, myositis, relapsing seronegative symmetrical synovitis with pitting edema (RS3PE)
Infectious	
Bacterial	Bacterial endocarditis
	Lyme disease
	Gonococcal arthritis
Viral	Rubella
	Hepatitis B and C
	HIV
	Parvovirus

joints involved in the hands include the metacarpophalangeal (MCP) and proximal inter phalangeal (PIP) in a bilateral symmetrical pattern. In addition, radiocarpal (RC), carpal, and carpometacarpal (CMC) joints as well as ulnar styloid (US) are commonly involved. Marginal erosions followed by disfigurements may develop in the hands over time, adding to the disability. These deformities include ulnar deviation, swan neck (Fig. 1), boutonniere deformity, rheumatoid nodules, and arthritis mutilans. Tendon ruptures within the hand and wrist may also occur with extensor tendon ruptures being more common than flexor. Tendon ruptures are caused by either attrition of the tendon over bony spurs, ischemia due to hypertrophic synovium, or invasive tenosynovitis. Other secondary manifestations of RA include entrapment neuropathy secondary to synovitis (carpal tunnel syndrome, cubital tunnel syndrome), mononeuritis multiplex (wrist drop), and rheumatoid vasculitis.

Diagnosis is based on history and physical examination, along with laboratory tests and imaging that may provide supporting evidence for RA or exclude other etiologies. American College of Rheumatology (ACR)/European League against Rheumatism (EULAR) classification criteria for rheumatoid arthritis (2010) may be a helpful guide in the diagnosis of RA.[4] Rheumatoid factor (RF) is positive in 70–85% of RA patients but may also be seen in 5–10% of healthy people and in patients with SLE, mixed cryoglobulinemia (usually caused by hepatitis C virus [HCV]), and infections. Antibodies to citrullinated peptides (anti-CCP) are positive in 50–60% of RA patients and are considered more specific (>95%). Seronegative RA patients have neither RF or anti-CCP, and the diagnosis may be made based on symptoms, examination, and exclusion of other potential etiologies. Crystalline disease, SLE, viral arthritis, palindromic rheumatism, polymyalgia rheumatica, psoriatic arthritis, and osteoarthritis may mimic RA presentation.

The treatment of RA[5] is geared towards controlling joint inflammation and preventing irreversible joint damage. The therapeutic strategy is based on various factors and includes evaluation of disease activity, response to prior treatments, comorbidities, and patient preference. “Treat to target” is a proactive treatment approach directed at achieving remission or at least low disease activity in those patients with difficult-to-control disease. Treat to target approach involves careful tracking of a patient's disease activity using standardized assessment tools (e.g. disease activity score- DAS, RAPID3) and revision of management strategy to achieve the target of remission or low disease activity, thereby avoiding/limiting irreversible damage. This is attained through early institution of disease-modifying anti-rheumatic drug (DMARD) therapy and escalation or adjustment of treatment plan if necessary in order to achieve quick and sustained control of inflammation. Early involvement of a rheumatologist is recommended as it is associated with better patient outcomes in RA.[6,7] Patients should be evaluated every 3–5 weeks initially to evaluate treatment effectiveness and screen for medication related side effects. However, a coordinated team approach with active involvement of the patient's primary care provider is also required as major morbidity and mortality in RA results from cardiovascular disease, infections, and malignancy.

Non-pharmacologic interventions, such as patient education, self-management programs, nutritional and exercise counselling, cardiovascular risk screening, immunizations, and osteoporosis screening, are important adjunctive treatments. Multiple studies have shown early diagnosis, timely initiation of disease modifying anti-rheumatic drugs (DMARDs), use of treat-to-target approach, and limited use of NSAIDs and/or corticosteroidsfor flare ups have resulted in significant improvement in morbidity and mortality.[8,9] DMARDs help to achieve optimal disease control by reducing joint damage. These agents include methotrexate (MTX), hydroxychloroquine, sulfasalazine, leflunomide (Lef), and biologics (Table 3). Guidelines recommend that all patients with newly diagnosed RA should be started on DMARDs. Therapy with monotherapy DMARDs vs combination therapy DMARDs vs biologics±DMARDs is dependent on disease activity and other factors. The most common DMARD utilized in RA is low dose MTX because of its faster onset of action, similar or better efficacy, and improved long-term tolerance as compared to other non-biologic DMARD monotherapies.[10] MTX is associated with improved survival when compared to other DMARDs.[11] Its use in pregnancy is contraindicated due to teratogenic potential. Folic acid supplementation is recommended with use of MTX to reduce risk of side effects. Based on moderate to high quality evidence, a weekly dose of MTX (7.5 mg–25 mg) has shown significant clinical improvement in the majority of RA patients when compared to placebo. When MTX is not tolerated or contraindicated, other DMARDs may be used in its place.

Clinical trials conducted from 1985 to 2016 involving more than 37,000 participants aimed to evaluate the effectiveness of monotherapy with MTX vs MTX with non-biologic DMARD vs MTX with biologic DMARD. The results demonstrated that MTX with sulfasalazine and hydroxychloroquine (‘triple therapy’) was superior to MTX monotherapy but similar to MTX + biologic therapy in both MTX-naïve and inadequate-response (MTX) populations.[12] In randomized trials of patients with early RA, similar improvements in disease activity are seen with initial monotherapy with MTX as compared to initial monotherapy with TNF inhibitor; however, radiographic progression was slower in TNF inhibitor monotherapy group.[13] Although janus kinase inhibitors tofacitinib[14] and baricitinib[15] have shown superior efficacy in comparison to MTX for early RA treatment, their cost is a limiting factor. Side effects of medications should be reviewed with patients, and it is recommended most patients be screened (Table 3) with baseline blood counts, kidney-liver function tests, and for infections (Hepatitis B

Table 2
Diagnostic work-up and clinical characteristics of various forms of inflammatory arthritis involving hand and wrist.

	Diagnostics	Radiographic findings	Pattern of joint involvement	Other features
RA	- RF as screening test (positive in ~80%) - Anti-CCP is specific - Often ↑ ESR and/or CRP	- Symmetric joint space narrowing - Marginal erosions	- Often symmetric polyarthritis with significant morning stiffness that improves with joint use - Proximal distribution of hand (MCP, PIP, IP of thumb) and wrists; feet and large joints may also be affected	- Rheumatoid nodules - Lung and eye involvement may also occur
SLE	- ANA as screening test (positive in ~95%) - Anti-dsDNA and anti-Smith are specific - Complements C3 and C4 may be low - Other antibodies: anti-SSA, anti-SSB, anti-RNP	- X-rays usually appear normal with preserved joint space - Some cases may present with reducible ulnar deviation and MCP subluxation (Jaccoud's arthropathy)	- Often symmetric polyarthritis - Nearly all joints can be affected but hands and knees are most common - Tenosynovitis and tendon derangement (including rupture) are complications	Other organ systems may be involved: - Lupus nephritis - Serositis - Oro-nasal ulcers - Butterfly rash - Cytopenias
PsA	- No standard serological markers - Negative anti-CCP and RF	- Dactylitis (sausage digit) - Arthritis mutilans with progressive disease - "Pencil-in-cup" deformity - Resorption of distal phalanx tuft (acro-osteolysis) - Marginal bone erosions and bony proliferation appear as fluffy periostitis	- Varies from symmetric polyarthritis to asymmetric oligoarthritis +/- axial involvement - Often bilateral asymmetric - Distal distribution of hand with IP>MCP joints; DIP involvement is characteristic	- Psoriasis rash marked by erythematous, silvery-scaled patches - Nail changes: nail pitting, discoloration, subungual hyperkeratosis - May be associated with inflammatory back pain (sacroiliitis)
Gout	- Needle-shaped negatively birefringent crystals in synovial fluid - Normal or ↑ uric acid (can be falsely low during acute attacks)	- Typically preserved joint space - Tophi will appear as radio-opaque densities usually located in peri-articular regions - Punched-out erosions - Overhanging edges	- Often monoarticular (MTP, knee, ankle) - Most commonly involved joints of hand include the wrist, MCPs, or PIPs usually in an asymmetric pattern	- Tophi may be present - Risk factors include obesity, post menopause, alcohol consumption, hyperlipidemia, diabetes, kidney disease, medications - Coexisting infection needs to be ruled out
CPPD	- Rhomboid-shaped weakly positive birefringent crystals in synovial fluid	- Chondrocalcinosis +/- changes of OA (asymmetric joint space narrowing, subchondral sclerosis, osteophytes) - Calcification of TFCC of wrist and radiocarpal narrowing	- Often monoarticular (knee most common followed by wrist, shoulder, ankle, MTP) - Chronic CPPD may present in pseudoRA pattern with MCPs most commonly affected in hand	- Chondrocalcinosis is a common age-associated finding in asymptomatic individuals - Can co-exist with gout and OA
Erosive OA	- Negative RF, anti-CCP, and ANA	- Joint space narrowing - Subchondral "gull wing" erosions - Marginal osteophytes	- Primarily affects hand with IP>MCP joints, 1st CMC joints, STT complex	- Can mimic RA or PsA - No systemic symptoms - Predominantly affects females

Abbreviations: RF, rheumatoid factor; CCP, anti-cyclic citrullinated peptide; anti-RNP, ribonucleoprotein; ANA, antinuclear antibody; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; MCP, metacarpal phalangeal; IP, interphalangeal; PIP, proximal interphalangeal; MTP, metatarsal phalangeal; CMC, carpometacarpal; SLE, systemic lupus erythematosus; anti-dsDNA, double stranded DNA; CPPD, calcium pyrophosphate deposition; STT, scapho-trapezio-trapezoid; TFCC, triangular fibrocartilage complex; RA, rheumatoid arthritis; PsA, psoriatic arthritis; OA, osteoarthritis.

and/or C and tuberculosis) prior to starting DMARDS (MTX or Lef) or biologics. In addition, ongoing serial monitoring for medication side effects is recommended for a majority of the medications.[16]

3. Systemic lupus erythematosus (SLE)

SLE is a multisystem, inflammatory autoimmune disease that predominantly affects young women. Hallmark of the condition is the presence of anti-nuclear antibody (ANA), which is used as a screening test for patients with suspected SLE. SLE is frequently associated with unpredictable disease flares. Disease manifestations are heterogeneous, as it may affect a single organ system or any combination of organs. Arthritis and cutaneous involvement are the most common manifestations. Patients frequently seek medical care because of hand symptoms, which may be seen in 90% of patients with SLE.[17,18]

Musculoskeletal manifestations in SLE may present as an inflammatory arthritis, typically in a bilateral, symmetric distribution in the hands. Non-erosive joint disease is the most common pattern seen in SLE, but an erosive form may also occur.[19,20] In the event of poorly controlled inflammation over time, patients with SLE may develop joint subluxations (Fig. 2) (wrist, MCP joints) and/or reducible hand deformities involving the wrist (ulnar deviation), MCP, and PIP joints (flexion and extension deformities caused from ligamentous laxity, which may mimic swan neck and Boutonnière's deformities seen in RA). The latter referred to as Jaccoud's arthropathy is a visible deformity that is disabling and negatively impacts patients daily living and quality of life.[21] Tenosynovitis and rarely tendon ruptures have been reported to occur. Patients with erosive Jaccoud's arthritis usually have anti-citrullinated protein antibodies.[20] In a self-reported survey study, 73% of SLE patients reported having hand problems and up to 25% reported having hand deformities. As compared to age and gender matched health controls, 58% of SLE patients had pain and/or difficulty in performing one or several tasks on the simple hand test, compared with 8% in the healthy group. There was significant association of hand and finger function with arthritis impact measurement scales health status.[21]

Diagnosis of SLE is based on history, examination and laboratory evaluation. Various classification criteria have been developed for SLE; however, these are used more for research purposes rather than establishing a diagnosis. Laboratory studies that could support SLE diagnosis include ANA, double stranded DNA antibody, anti-ribonuclear protein antibody, anti-smith antibody, Sjogren antibodies (Ro and La), complement C3 and C4, complete blood count, basic metabolic panel, and urinalysis. When organ systems outside the musculoskeletal system are involved (e.g. renal), a tissue diagnosis of SLE may be reached through a biopsy.

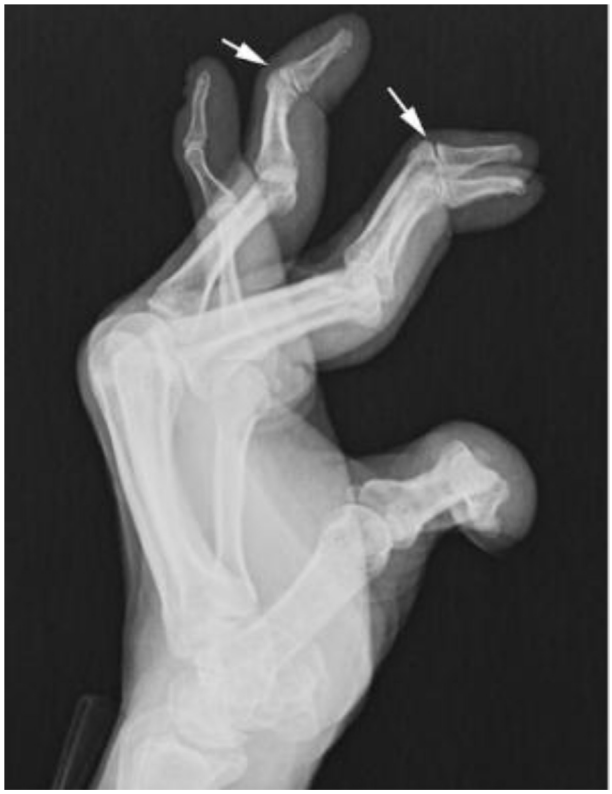

Fig. 1. Hand deformities (swan neck) in rheumatoid arthritis.

Medical management includes patient education and avoidance of known triggers (e.g. sun exposure or drugs). Treat to target approaches have recently been defined in SLE and include remission on and off medications and low disease activity state on and off medications.[22,23]

Treatment algorithms for SLE have been studied.[24] Antimalarials, specifically hydroxychloroquine (HCQ) with or without corticosteroids, are the first line treatment for SLE patients with non-erosive, non-deforming inflammatory polyarthritis. HCQ use is associated with reduced SLE flares and organ damage in the long term and improves survival.[25] NSAIDS may be used as an adjunct or as a substitute to corticosteroids for arthritis flares. Methotrexate may be added to this regimen if low disease activity state or remission is not achieved with first line treatment options, as it has been shown to be effective in controlling articular symptoms and allowing reduction in steroid dose.[26] Other therapeutic options that may be tried in the case of either intolerance or inadequate response to first- or second-line agents for arthritis include azathioprine, mycophenolate mofetil, leflunomide,[27] rituximab,[28] and belimumab.[29] Belimumab has been found to improve arthritis in patients with SLE. At 3 months, 61% of the SLE patients with arthritis showed at least 50% improvement in their arthritis.[30] Choice of agent is also based on patient preference and other factors, such as cost and plans for pregnancy. Screening for retinal toxicity with HCQ, contraceptive use with MTX and mycophenolate mofetil (MMF), and serial monitoring for medication side effects are indicated (Table 3).

4. Psoriatic arthritis

Psoriatic arthritis (PsA) is one of the seronegative spondyloarthropathies seen in association with psoriasis. Enthesopathy is the hallmark of these conditions. Nail deformities, such as pitting, may also be seen. It typically involves joints in an asymmetric and destructive pattern. In the hands, distal interphalangeal (DIP) joints are most often involved in contrast to RA, although MCP's and wrist may also be involved. Psoriatic arthritis of the hand may present with dactylitis in the form of sausage digit, a term referring to diffuse soft tissue swelling of a whole digit. The disease tends to affect peripheral joints in a "ray" distribution, in which there is inflammatory involvement of all 3 continugous joints of a digit, with sparing of other digits. Fluffy periostitis on plain radiographs (Fig. 3), especially in entheseal areas, may be seen. Other radiographic changes include bony erosions, pencil in cup deformities resulting in telescoping of digits, and arthritis mutilans, akin to that seen in RA. Patients concomitantly may have inflammatory low back pain from spinal or sacroiliac joint involvement. Diagnosis is based on history, examination, and exclusion of other conditions. Imaging and a known history of psoriasis may aid in the diagnosis.

Medical management of PsA includes similar agents to those used in RA management, such as NSAIDs, DMARDs and biologics. Treat to target approach is utilized to attain remission or low disease activity state. Early referral to rheumatologist is associated with better outcomes in psoriatic arthritis.[31] Patient education, role of exercise, and physical therapy are important in management. Patients with mild peripheral arthritis can be managed with NSAIDS alone. Patients with moderate to severe disease or mild disease (not responsive to NSAIDS) may be treated with conventional DMARDs such as MTX or Lef. Sulfasalazine or azathioprine are other options for patients intolerant or unwilling to use MTX/Lef. Patients with severe peripheral disease at presentation or patients with inadequate response to MTX/Lef may be treated with biologics, such as anti-TNF agents. Apremilast, an oral phosphodiesterase inhibitor, may be used in early non-erosive disease in patients. Other biologics like anti-IL-17 blockers (e.g. ixekizumab, secukinumab, brodalumab), anti-IL-23 (guselkumab), CTLA-4 (abatacept), anti-IL-12 and IL-23 (ustekinumab), and JAK kinase inhibitor (tofacitnib) are also alternatives for patients with TNF resistant or intolerant disease.

5. Crystalline arthritis

Several types of crystals can cause acute and chronic inflammation of the hand and wrist. Monosodium urate crystals are involved in the development of gout, whereas calcium pyrophosphate crystals are involved in calcium pyrophosphate deposition disease (CPPD), also known as pseudogout. Other forms of crystals include basic calcium phosphate crystals (BCP-calcium hydroxyapatite), whose deposition results in calcific tendinitis or calcific periarthritis.

6. Gout

Gout affects roughly 3% of US population,[32] and the prevalence varies based on body mass index. There has been an increase in the incidence and prevalence of gout over the years, which may be due to increased longevity, increased incidence of metabolic syndrome, use of medications associated with gout, increased consumption of foods associated with metabolic syndrome, and/or food additives. Risk factors for gout include age, gender, genetic variants, dietary factors including food additives (such as high fructose corn sugar), postmenopausal state, chronic kidney disease, alcohol, enhanced production of uric acid or poor excretion in the setting of renal insufficiency, medications, and metabolic syndrome. Gout tends to occur in previously damaged or osteoarthritic joints.

Acute gout flare may present with acute mono- or oligoarthritis. Joints of the hand most commonly involved include the wrist, MCPs, or PIPs, usually in an asymmetric pattern. Intense, sudden

Table 3
DMARDS (Conventional synthetic and biologic) used for management of rheumatoid arthritis.

DMARDS	MECHANISM OF ACTION	TOXICITY	MONITORING
Methotrexate (csDMARD)	Anti-inflammatory (mediated through adenosine). It also inhibits folic acid metabolism.	- Hepatotoxicity - Myelosuppression - Infection - Interstitial pneumonitis - Pregnancy category X	Baseline chest x-ray; CBC, chemistry, and LFTs every 4 weeks for the first 3 months, then every 12 weeks thereafter
Hydroxychloroquine (csDMARD)	Interferes with antigen processing in macrophages and other antigen-presenting cells	- Irreversible retinal damage - Cardiotoxicity - Blood dyscrasia	Fundus and visual field every 12 months
Sulfasalazine (csDMARD)	Anti-inflammatory salicylate and sulfa moieties	- Granulocytopenia - Hemolytic anemia (with G6PD deficiency)	CBC, chemistry, and LFTs every 4 weeks for the first 3 months, then every 12 weeks thereafter
Leflunomide (csDMARD)	Inhibits pyrimidine synthesis	- Hepatotoxicity - Myelosuppression - Infection - Pregnancy category X	CBC, chemistry, and LFTs every 4 weeks for the first 3 months, then every 12 weeks thereafter
Infliximab (bDMARD)	Chimeric anti–TNF-α antibody	- ↑ Risk bacterial and fungal infections - Reactivation of latent tuberculosis - ↑ Lymphoma risk - Drug-induced lupus - Neurologic deficits	LFTs periodically
Etanercept (bDMARD)	Anti-TNF-α–receptor protein	- As above	Monitor for injection site reactions
Adalimumab (bDMARD)	Human anti–TNF-α antibody	- As above	Monitor for injection site reactions
Golimumab (bDMARD)	Human antibody to TNF α	- As above	Monitor for injection site reactions
Certolizumab (bDMARD)	Fab portion of monoclonal antibody to TNF α	- As above	Monitor for injection site reactions
Abatacept (bDMARD)	Downregulation of T cells using recombinant CTLA4	- ↑ Risk bacterial, viral infections	Monitor for infusion reactions
Rituximab (bDMARD)	Monoclonal antibody against CD20. Targets B cells	- ↑ Risk bacterial and viral infections - Infusion reaction - Cytopenia - Hepatitis B reactivation	CBC at regular intervals
Tocilizumab (bDMARD)	Humanized monoclonal antibody to IL-6 receptor	- Infusion reaction - LFT elevation - Dyslipidemia - Cytopenias	CBC and LFTs at regular intervals
Tofacitinib (new agent-synthetic DMARD)	Inhibits Janus kinases (JAK)	- Risk of infection - LFT elevation - Dyslipidemia - Neutropenia	CBC, LFTs, and lipids at regular intervals

Abbreviations: LFTs, liver function tests; CBC, complete blood count; csDMARD, conventional synthetic disease-modifying antirheumatic drug; bDMARD, biological disease-modifying antirheumatic drug; TNF, tumor necrosis factor.
Adapted from Shilpa et al. Management of rheumatoid arthritis: Review of current guidelines. Journal of Arthroscopy and Joint Surgery. 2016; 3(2):45–50.

inflammation produces significant swelling, erythema, and immense pain in the affected joint(s). Joint aspiration is obtained to document negatively birefringent intracellular needle shaped monosodium urate (MSU) crystals. Although rare, concomitant septic arthritis and gout have been reported in a very small minority of cases.

Flares of gout may be precipitated by alcohol, changes in diet or medications, and acute illnesses. Tophaceous gout may develop over time with typical erosive changes marked by overhanging edges (Fig. 4), causing hand deformities. Gout, when polyarticular, may be confused with RA.

Medical management of gout is aimed at (a) control of acute inflammation, (b) prevention of flares, (c) urate lowering therapy, and (d) management of comorbidities. Patient education is pivotal in life style modifications, prevention of flares, compliance with medications, and treatment of comorbidities. For acute gout flares, NSAIDs, glucocorticoids (intra-articular or systemic), or colchicine are utilized based on patient preference, number of joints involved, and co-morbidities. There is no significant difference in efficacy between NSAIDs and oral prednisone in acute flares.[33] NSAIDs may be especially used within 48 h of symptoms onset in younger patients, in those without risk for gastrointestinal bleeding, in the absence of chronic kidney disease, or in those at low risk for cardiovascular disease. Intra-articular corticosteroids may be utilized for monoarticular gout after reasonable exclusion of septic arthritis. In fact, patients may be more receptive to intra-articular injections given concerns for potential side effects of systemic therapy (e.g. poor glycemic control, water retention, gastritis, or weight gain). In the case of polyarticular acute gout flare, oral corticosteroids (prednisone 30 mg daily) may be indicated and tapered off within 7–10 days. Colchicine when selected must be initiated within 24 h of gout flare onset. Low dose colchicine was found to be effective and shown to have a better safety profile compared to high dose colchicine in treatment of acute gout flare[34] and is thus preferred. Dose modifications are required with renal and hepatic impairment. In resistant acute flares, IL-1 inhibitors (anakinra and canakinumab) may be tried.

Reduction of acute gout flares during institution of urate lowering medications is accomplished by prophylaxis with low dose colchicine, NSAIDs, or low dose oral corticosteroids. Recurrent

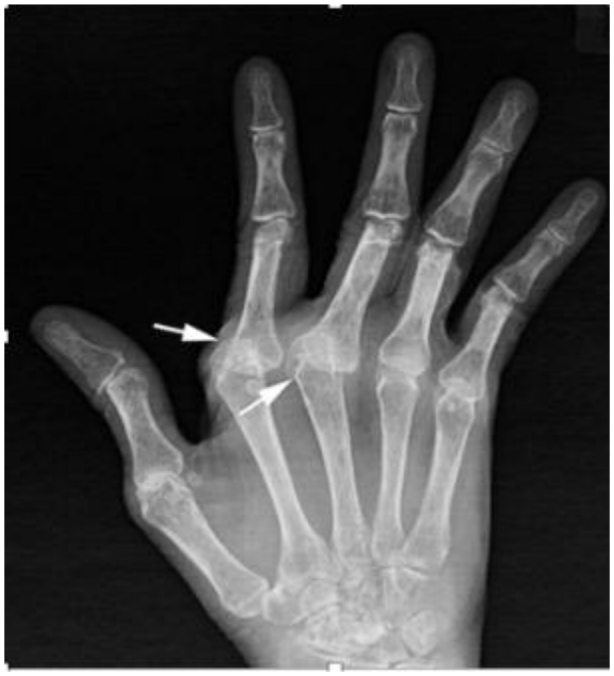

Fig. 2. Subluxations (MCP joints) in SLE.

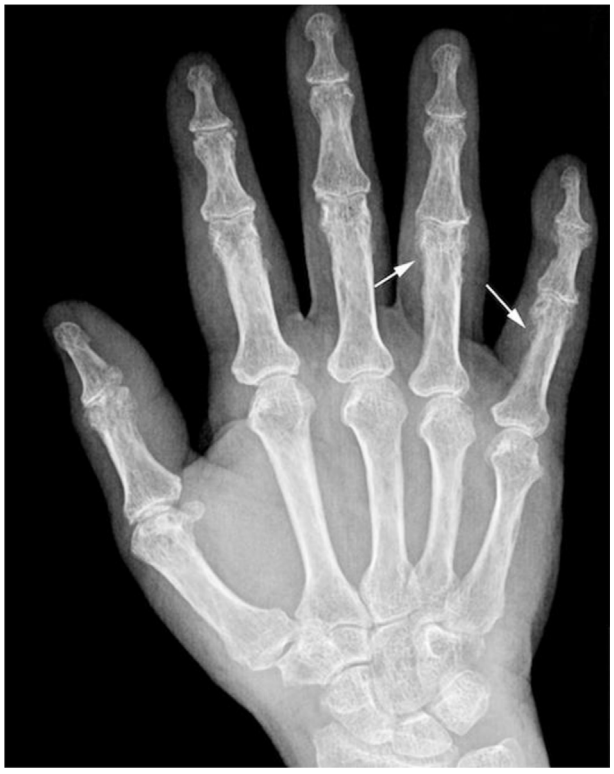

Fig. 3. Fluffy periostitis in psoriatic arthropathy.

acute gout, erosive and/or tophaceous arthritis, gout with renal insufficiency, and recurrent nephrolithiasis are some of the indications for institution of urate lowering therapy (ULT). The target serum urate goal for ULT is less than 6 mg/dl. Xanthine oxidase inhibitors (allopurinol or febuxostat) are the first line urate lowering drugs, followed by the addition of the uricosuric

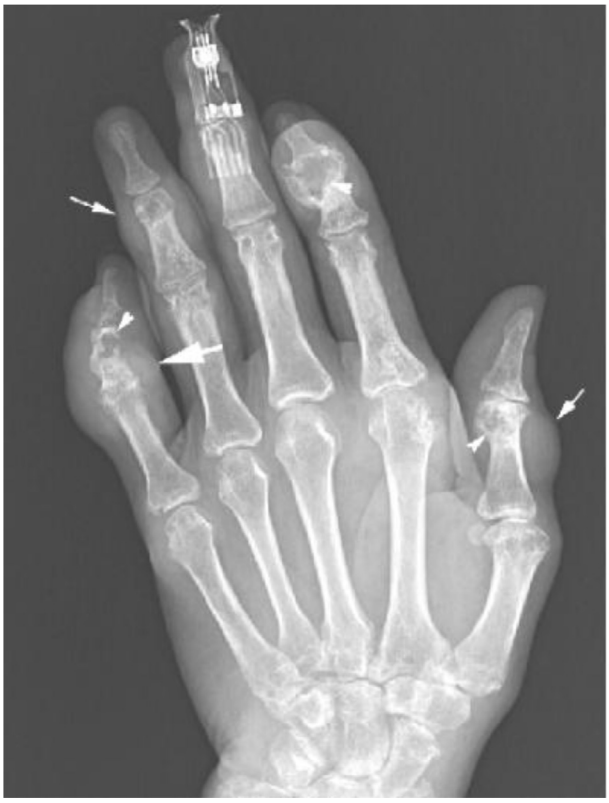

Fig. 4. Tophaceous gout.

(probenecid). Careful monitoring for development of rashes, hypersensitivity, and bone marrow suppression needs to be discussed with the patient when employing xanthine oxidase inhibitors. In poorly controlled gout patients, large depositions of extracellular MSU crystal may form visible nodules, referred to as tophi. Tophaceous gout can be managed with standard urate lowering drugs (allopurinol or febuxostat), but pegloticase may be the most effective drug in this situation. Pegloticase, a recombinant mammalian urate oxidase, is not commonly used though due to greater risk of gout flare and infusion reactions.

7. Pseudogout

CPPD crystals may also cause an inflammatory arthritis of the hand and wrist. Acute arthritis in this setting is referred to as pseudogout, as the clinical presentation may be similar to gout. Inflammatory and chronic degenerative joint disease may also occur with CPPD and may resemble RA in presentation. CPP deposition in articular cartilage is called chondrocalcinosis and is most often asymptomatic in the elderly. The prevalence of chondrocalcinosis increases with age. It may affect 4–5% of adult UK population.[35]

Patients may present with acute to subacute inflammation of the joints that may be self-limited and typically resolves over 2–3 weeks. In the hand, the wrist is the most common joint involved. When CPPD occurs in the wrist, plain radiographs may demonstrate calcifications within the triangular fibrocartilage complex (TFCC), radiocarpal narrowing, and scapholunate collapse in advanced cases. Patients undergoing certain stressors (trauma, surgery, or severe medical illness) or metabolic derangements are at higher risk for pseudogout flares. Pseudogout is on rare occasions associated with hemochromatosis, hypomagnesemia or hypo/

hyperphosphatemia, hypercalcemia, and hyperparathyroidism. In the right clinical setting, some of these conditions should be screened for with appropriate tests.

Diagnosis of pseudogout is made by imaging and documentation of weakly birefringent rhomboid or rod shaped CPPD crystals in synovial fluid. Acute flare is managed with NSAIDs or low to moderate dose corticosteroids (intra-articular or systemic) based on number of joints involved and co-morbidities. Corticosteroids may be tapered off within 2–3 weeks. Alternatively, low dose colchicine may be utilized if initiated within 24 h of symptoms onset. For prevention of recurrent flares, low dose colchicine may also be used. Patient education and appropriate monitoring for side effects of NSAIDs, corticosteroids, and colchicine are recommended. IL-1 inhibitors (anakinra and canakinumab) may also offer relief of acute pseudogout for those with resistant or recurrent pseudogout flares. In some patients with chronic pseudogout hand arthropathy, the clinical picture may mimic RA in a so called pseudorheumatoid presentation. These may be treated with NSAIDs, colchicine, hydroxychloroquine, or low dose corticosteroids.

8. Erosive osteoarthritis

Erosive osteoarthritis is an uncommon, aggressive variant inflammatory form of osteoarthritis that presents with subacute onset of bilateral, symmetric involvement of the interphalangeal joints of the hands. It may be mistaken for seronegative RA. Heberden and Bouchard nodes may be confused with rheumatoid nodules. Unlike RA, the DIP joints are affected in erosive hand OA. The classic radiographic changes of erosive OA are “gull wing” deformities, which help differentiate it from the marginal erosions of RA. The available treatments include NSAIDs and other analgesics.

9. Other autoimmune conditions

Systemic juvenile inflammatory arthritis frequently involves the wrists. Sarcoidosis may be associated with oligoarticular symmetrical joint disease, and hand involvement may mimic RA.[36] Chronic arthritis is rare in sarcoidosis, but dactylitis and Jaccoud's arthritis have been reported. In patients with mixed connective tissue disease, puffy hands are characteristically seen. Arthritis may be similar to RA (erosive) or SLE, and frequently rheumatoid factor and anti-CCP are present. Wrists, MCP, and PIP joints are the most frequently involved joints in patients with inflammatory muscle disease related arthritis.[37] Arthralgias and arthritis, especially in wrists, may be noted in serum sickness. Medical management of above conditions centers around control of acute inflammation and the underlying autoimmune condition.

10. Conclusions

Noninfectious conditions, in particular autoimmune diseases and crystalline arthritis, are commonly associated with inflammatory arthritis of the hands and pose diagnostic dilemmas. Appropriate diagnosis, patient education, timely institution of medical management of the underlying condition, and monitoring for potential medication side effects seems to improve patient outcomes.

Conflicts of interest

The authors declare that there is no conflict of interest.

Declarations of interest

None.

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Appendix A. Supplementary data

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