

# Erosive osteoarthritis: a current review of a clinical challenge

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**Abstract** Erosive osteoarthritis, a less common subtype of osteoarthritis, is often described as a more severe form. This combination of cartilage degeneration with pathologic features suggestive of inflammatory synovial changes generally manifests in women around the time of menopause and hormonal levels as well as genetics are thought to play a role in its onset. The hands are most often involved with the sudden onset of palpable pain and swelling of the distal interphalangeal joints and proximal interphalangeal joints most frequently, but other joints have been reported. Phalangeal deformities appearing as wavy or subluxed as well as Heberden and Bouchard nodes can be seen clinically. Laboratory tests for systemic inflammation are usually normal but small studies looking at markers of bone resorption have shown increased levels in these patients. Radiographs reveal central joint erosions implying an inflammatory process which has been described in synovial specimens. Treatment options that have been tried include those utilized for general osteoarthritis as well as those for rheumatoid arthritis. Since prolonged disability in hand function can occur, further studies looking at its pathogenesis and targeted treatment options are needed.

**Keywords** Erosive osteoarthritis · Inflammatory osteoarthritis · Nodal osteoarthritis · Osteoarthritis

## Introduction

Despite being the most common form of arthritis encountered in clinical practice, osteoarthritis (OA) continues to be poorly

understood. Research focused on its etiology; pathophysiology and treatment has failed to produce consistent results making long-term management difficult. Erosive osteoarthritis (EOA), a less common subtype of osteoarthritis is often described as being a more severe form. This unique combination of cartilage degeneration with pathologic features suggestive of inflammatory synovial changes continues to frustrate those managing it. This paper provides an updated review of the history, etiology, clinical findings, radiographic changes and current management approaches to EOA in order to summarize the limited understanding and clinical challenge still felt since its initial description in the 1960s.

## Background history

The earliest descriptions of OA date back to 1802 when William Heberden described in his memoirs “hard knobs” upon the distal interphalangeal joints (DIP) of the hands known to be “nonpainful and inconvenient” [1]. In 1884 and 1887, Bouchard described similar findings occurring in the proximal interphalangeal joints (PIP) [2]. These commonly described “Heberden and Bouchard nodes” were added to the findings by Kellgren and Moore in 1952 who reported a “generalized osteoarthritis” of the hands after detailing clinical cases of a painful inflammatory arthritis followed by a chronic period of bone growth with less pain but deformity of the digits after several months [3]. This unique subset with an inflammatory phase was the earliest description of EOA. It is to be contrasted with limited OA of the hands without clinical inflammation commonly seen by many practicing physicians and known as nodal degenerative arthritis or nodal OA.

In 1961, Crain published a paper of similar clinical findings he called “interphalangeal osteoarthritis”. In it, he describes multiple cases over a 5-year period of a chronic inflammatory form of OA involving the DIP and PIP joints like those described by Kellgren and Moore [2]. The

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characteristics of the 23 cases he reviewed describe involvement of women more than men, ages 40–50 years with a familial hereditary tendency to have painful prominent, tender, swollen interphalangeal joints. The DIP joints were involved first in 61% of cases followed by the PIP joints resembling symmetrical synovitis like that seen in rheumatoid arthritis. Later on, this inflammatory phase evolved into nodular enlargement and lateral deformities or subluxations of the digits physically limiting the use of the hands. [2].

In 1966, Peter again expanded on this concept in a review of six similar cases [4]. This paper set out to further understand the histopathology of synovial samples obtained from these patients. Their clinical description most closely resembled that of Crain's paper with PIP and DIP involvement and an initial inflammatory onset evolving into a more chronic course. In this publication, the name EOA was given due to the central erosions seen on X-ray as well as the inflammatory findings that were found on pathology of the synovial tissue samples taken from the involved joints.

The differences between generalized OA, nodal OA, and EOA are apparent by their distribution of involvement and clinical characteristics (Table 1). The classic asymmetrical diffuse generalized degenerative OA affecting the weight-bearing joints, spine, and distal interphalangeal joints of the hands without swelling or am stiffness is to be compared to nodal noninflammatory OA affecting the DIP, PIP, and first carpo-metacarpal joints primarily of the hands in a more symmetrical fashion. These two are to be compared to EOA affecting primarily the hands, but with an early inflammatory component, younger age, and resultant medial or lateral joint instability [5].

#### Epidemiology and genetics

The clinical onset of EOA is generally in women 40–50 years, around the time of menopause [2]. This is contrasted with the

younger age of those affected by rheumatoid arthritis (20–40 years) and those of generalized OA (50–60 years) [4]. Men can also be affected by EOA, but generally in much smaller numbers [4]. No other medical conditions have been reported in conjunction with EOA; however, obesity has been connected with generalized OA involving the back, knees, and hips [3]. Caucasians are most commonly affected by EOA.

Previous studies have linked OA to inherited chromosomal abnormalities on chromosomes 2, 4, and 16 [6]. Stern et al. studied the serum of 68 patients with hand OA, of which 26 had EOA and compared these patients to a control group ( $N=51$ ) without hand OA [6]. DNA was extracted for sampling of the study subjects for evaluation of abnormalities in the interleukin (IL)-1 region on chromosome 2q suggested to be linked to knee and hand osteoarthritis [7, 8]. Prior work in vitro has shown IL-1 plays a role in facilitating cartilage degradation [9]. The results showed a significant association ( $p=0.007$ ) between the presence of the IL1B5810 AA genotype in those with EOA vs. controls, and those with EOA vs. non erosive hand OA ( $p=0.008$ ). This data supports the theory that there may be a genetic abnormality in the IL-1 region for the development of EOA. This may help to explain the destructive nature of EOA since IL-1 has previously been shown to also be involved in the erosive pathogenesis of rheumatoid arthritis.

In a related study, patients with hand OA of which 90 were nodal and ten EOA were studied by Patrick et al. to determine if a genetic difference in those with nodal OA vs. EOA exists [10]. An increased frequency of the HLA-A1B8 phenotype was present in the group with nodal OA. The erosive group demonstrated an increase in the MS alpha 1 antitrypsin phenotype (30% vs. 9%) with an overall increase in both groups of the MZ alpha 1 antitrypsin phenotype compared to the reference population (12% vs.

**Table 1** Clinical differences between types of osteoarthritis

|  | Generalized OA                  | Nodal OA  | EOA   |
|--|---------------------------------|---|---|
| Joints involved                              | Hips, knees, spine, hands (DIP) | Hands (DIP, PIP, first CMC),<br>MTP, knees, spine, hips | Hands (DIP, PIP, first CMC, MCP)<br>feet (rare)             |
| Inflammatory component                       | No                              | No  | Yes   |
| Age of onset                                 | >55                             | >52   | 40–50   |
| Symmetry                                     | Asymmetrical                    | Asymmetrical>symmetrical                                | Symmetrical>asymmetrical                                    |
| Male/female ratio                            | 1:1                             | 1:10  | 0:10; rare male   |
| Progression                                  | Slowly progressive              | Slowly progressive                                      | Early aggressive highly inflammatory<br>with chronic course |
| Interphalangeal instability<br>and ankylosis | Rare                            | Rare  | May be seen   |

OA osteoarthritis, EOA erosive osteoarthritis, DIP distal interphalangeal, PIP proximal interphalangeal, CMC carpometacarpal, MTP metatarsalphalangeal, MCP metacarpalphalangeal

3.6%). There were no significant differences in the ages or sex of the subjects in the nodal OA and EOA groups. The alpha 1 antitrypsin phenotype presence has been studied in other inflammatory diseases such as RA, and with the increased expression in the EOA group, the clinical question remains whether this leads to the inflammatory component of EOA [10].

### Clinical findings

As mentioned, EOA is unique in that it shares features typical of OA as well as inflammatory arthritis. Typically, the onset is sudden and earlier than OA beginning around menopause. The joints affected are generally those of the small joints of the hands typically the DIP and PIP joints as well as the first carpometacarpal (CMC) joint but less frequently [2]. Rare involvement of the metacarpophalangeal (MCP) joints as well as the trapezioscapoid area of the midcarpal joints have been reported [11]. Clinical studies of patients with EOA, such as the 15 studied by Utsinger et al, reported morning stiffness generally less than 1 hour despite clinical inflammation, a symmetrical distribution to the hand involvement with swollen painful PIP and DIP joints and reports of knee involvement [12].

Nodal OA of the hands can be physically deforming due to the presence of bulky Heberden and Bouchard nodes. However, the erosive variant may tend to be more deforming due to the added subluxation of the interphalangeal joints creating a “Z-shaped” or “wavy” appearance to the fingers along with the presence of existing Heberdens and Bouchards nodes (Fig. 1). The hand joints can also be red, tender, edematous, and warm with palpable synovitis

implying inflammation and restricted range of motion often confused with rheumatoid arthritis except for the joint distribution (Table 2). Eventually, joint fusion can occur and arthritis mutilans or resorptive osteopathy has also been reported [13]. The symptoms can wax and wane and the inflammatory signs can be involved in different joints at different times. Ehrlich in 1975 published a review of the clinical characteristics of 170 patients seen with EOA with a mean onset of 50 years. He reported that 68% related a family history of this condition and 76% had a mean of 30 min of morning stiffness. On exam, 9% developed mucoid cysts, and documented right greater than left hand involvement. In some, swelling of the finger pads created a nighttime tingling and fullness of the fingers causing the sensation of having to shake the hands for relief. The joint distribution was that of the DIP's in 70%, the PIPs in 50% and the MCP's (particularly the second and third) in approximately 25% [14].

In their study, Fioravanti et al. observed 56 patients with EOA and 46 with nodal OA nailfold capillaries to see if there were any further physical distinguishing characteristics between the two groups. Prior studies have shown a reduction in capillary density and evidence of microhemorrhages in nodal OA patients compared to controls [15]. Their results found shorter and tortuous capillary loops in the EOA population (61%) resembling those with psoriatic arthritis compared to the control (26%) and nodal OA (50%) groups. They hypothesize these microvascular changes in the nailbed could lead to the inflammatory DIP involvement seen in these two diagnoses [15]

Although EOA generally affects the hands, occasional descriptions of similar symptoms of the feet have been

**Fig. 1** Erosive osteoarthritis on exam. Notice the wavy Z-shaped fingers, and distal subluxations of the DIP joints. Heberden and Bouchard nodes are seen clinically on exam



**Table 2** Differences between rheumatoid arthritis and erosive osteoarthritis

|                             | Rheumatoid Arthritis     | EOA                                 |
|-----------------------------|--------------------------|-------------------------------------|
| Morning stiffness           | >1 h                     | <1 h                                |
| DIP involvement             | No                       | Yes                                 |
| PIP involvement             | Yes                      | Yes                                 |
| MCP involvement             | Yes                      | Rare                                |
| Symmetry?                   | Yes                      | Yes or No                           |
| Deformity                   | Swan neck or boutonniere | Z-shaped deformity; DIP subluxation |
| Palpable Swelling/synovitis | Yes                      | Yes                                 |
| Erosions on X-ray           | Yes, marginal            | Yes, central                        |

*DIP* distal interphalangeal, *PIP* proximal interphalangeal, *MCP* metacarpalphalangeal, *EOA* erosive osteoarthritis

published. Foot involvement has been reported to manifest as complaints of foot pain and reduction of motion of the IP joints of the toes. Bone ankylosis on radiographs and pain with palpation of the IP joints of the toes in those also diagnosed with EOA of the hands has been reported [16].

The clinical course of EOA is generally one that waxes and wanes and can last from several months up to 5 years before the cycling acute inflammation and pain symptoms finally subside leaving behind joint deformities resulting in hand disability which may be worse than nodal OA [17].

#### Lab investigation

Laboratory tests are usually negative despite the clinical findings of inflammation. At this time, there are no lab tests that have been consistently shown to diagnose or follow the progression of a patient with EOA. Cyclic citrullinated peptide (CCP) antibody whose presence has been diagnostic of rheumatoid arthritis was studied by Morozzi et al. They evaluated 32 EOA patients for the presence of anti-CCP antibodies and the presence of rheumatoid factor (RF). None of their EOA patients exhibited CCP antibodies and only two controls were positive for RF, confirming EOA is likely not an immunologically similar subset of RA [18]. The serum RF and anti nuclear antibody (ANA) are usually negative.

As EOA patients exhibit central erosions on standard radiographs, it can be postulated that there is accelerated bone turnover that could be measured in the serum to determine diagnosis and rate of progression. Type 1 collagen C-telopeptide found in the bone matrix and released into the bloodstream during bone remodeling is considered to be a measurable marker of bone resorption. To investigate its role in EOA, Rovetta and colleagues in a cross-sectional study sampled 21 women with EOA and compared them with 21 women with nodal OA of the hands for levels of type 1 collagen C-telopeptide. They discovered a statistically significant release of type 1 collagen C-telopeptide in the EOA patients implying a more rapid, aggressive bone turnover process that can be likened to rheumatoid arthritis [19]. In a similar study, Silvestri et al [20] studied cartilage degradation in 30 subjects with EOA

and 29 with nodal OA. They were then compared with 21 healthy controls. Levels of collagenase cleavage neoepitopes (Col2-3/4, C2C) and CS846, a marker of proteoglycan turnover, were measured in serum. A significant difference was measured in the serum between those with OA and the controls, again demonstrating an accelerated cartilage destructive process.

As OA has not been generally thought of as a systemic process, one expects the two popular serum markers used to detect inflammation, the sedimentation rate (ESR) and C-reactive protein (CRP), to be normal. However, if EOA is thought to be a more “inflammatory” destructive form of OA, it would be worthwhile to study whether these markers of inflammation are elevated. Punzi and colleagues [21] looked at the value of serum high resolution CRP as a marker of erosive osteoarthritis. The average CRP measurement was 4.7 in the EOA subjects and 2.1 in the non-EOA subjects ( $p=0.0001$ ). The CRP measurement was the most significant in those with more tender, clinically active joints (10.7 vs. 8.2) and correlated with those who had active joint counts ( $r=0.72$ ). In Ehrlich's group of 173 EOA patients, the ESR was within normal range ( $\leq 20$  mm/h) in 43% of patients, 36% had modest values (20–40 mm/h) and 20% were higher than 40 mm/h in the subset who later went on to be diagnosed with rheumatoid disease [17].

#### Pathophysiology

Although the physical changes have been well described in the literature, what has led to them has been far less investigated. The earliest pathologic report was published 1966 [4]. Synovial samples from six women with EOA were studied after exclusion of rheumatoid disease. The six women varied in their presentations of arthritis such that some had chronic OA with minimal erosive changes without active inflammation to those whose exam consisted of active inflammation with pain, swelling, and prominent erosive and osteophyte changes on X-ray. Synovial biopsy samples were obtained from six DIP, 14 PIP, and four interphalangeal thumb joints of the study subjects. The histopathology was variable within the same joint and

corresponded in many ways with the inflammatory activity of the joint. What was discovered was a proliferative synovial change in acute EOA similar to that of RA with lymphocytic and neutrophilic infiltration, synovial hypertrophy and pannus formation. Changes in bone and cartilage in the acute and chronic stages of EOA most closely mimicked chronic OA with cartilage ossification, marginal osteophyte formation, and clustering of chondrocytes. These findings may implicate an early inflammatory response leading to the advanced cartilage destruction and erosions seen on radiographs.

The centrally located erosions within the joint space would imply that the synovium which lines the lateral joint margin is not the only potential source of bone destruction. The centrally located cartilage must therefore be damaged through enzyme and chemical messengers from the synovium such as IL-1 [11]. However, the cartilage can also signal the synovium via large molecular weight polysaccharides which have been shown experimentally to induce a secondary synovitis when injected into joints for about 4 weeks through mediators such as IL-1 and tumor necrosis factor- $\alpha$  (TNF $\alpha$ ) [11]. In OA, TNF $\alpha$  contributes to cartilage instability by inhibiting proteoglycan matrix synthesis through upregulation of destructive enzymes such as matrix metalloproteinases. TNF $\alpha$  exerts its effect by binding to articular chondrocytes through its receptors p55 and p75. Although OA has been traditionally thought not to be an inflammatory disease, the role of TNF $\alpha$  has been limited in its relationship to secondary articular cartilage destruction rather than taking on a primary pathologic role. However, its potential role in cartilage destruction and inflammation in the early inflammatory stages of EOA makes it an attractive potential target for symptom modifying therapy. In their study utilizing dogs with surgically induced OA, Kammerman and colleagues demonstrated TNF $\alpha$  staining throughout the cartilage early on in the OA process after 12 weeks. Also observed was TNF receptor staining within the smooth muscle cell nuclei of the blood vessels within the synovial membrane of the OA joints [22]

Since EOA involves the DIP joints, the pathologic role of crystals (both hydroxyapatite and CPPD) released from cartilage into the joint space has been proposed as a cause to explain the inflammatory and erosive process [11]. Gerster reported on two cases from which apatite crystals were isolated from EOA joints. Follow up X-rays done approximately 2-5 years later in each case showed evidence of erosions only in the joints involved which directly related to those with prior inflammation and crystal detection [23]. The development of destructive EOA in two men on chronic hemodialysis for more than 3 years was described by Duncan et al. [24]. Although one man had a successful transplant, they both were in their 30s when

they developed symptoms and X-ray changes of EOA involving the PIP, DIP, and thumbs. Proposed etiologies have included hyperparathyroidism, iron overload, and perhaps collapse of osteopenic bone from osteodystrophy.

As females tend to be affected around menopause, a link to the absence of estrogen has been postulated. In a review by Rosner et al. [25] focusing on animal-induced OA after meniscectomy with concomitantly given intramuscular administration of estradiol-demonstrated depressed proteoglycan synthesis indicating a hormonal effect on cartilage. Another animal model study in ovariectomized rats done by Oestergaard et al. showed that with estrogen replacement, serum levels measuring the degradation products of type II collagen significantly decreased at weeks 3-5 while serum estradiol increased [26]. Clinical thinking suggests that replacement of estrogen would improve symptoms, however there is mixed literature. Some studies indicate a positive role in prevention of moderate to severe hip OA in those taking long-term hormonal replacement for 10 years or longer. Other studies looking at the prevention of knee OA found some preventative benefit in those taking estrogen replacement for longer than 4 years but the study failed to achieve significance [27]

Drug-induced arthritis has been widely recognized and a report of the onset of EOA after therapy for ovarian cancer was described by Jaishuen et al. They report a 59-year-old female with a 20-year history of OA who developed profound severe and explosive DIP and PIP arthropathy with normal serologies with erosions noted on radiograph consistent with EOA after starting bevacizumab, a fully humanized monoclonal antibody to vascular endothelial growth factor, and paclitaxel for ovarian cancer. She received 1 month of treatment. After discontinuation of treatment, her symptoms improved. There are no other such reports related to medications, but the inflammatory response with documentation of erosions may have indicated prior EOA with flare. It is unknown if this is related to a direct drug effect but may indicate the true inflammatory nature of EOA [28].

## Radiology

When confronted with a patient complaining of joint pain, physicians may order a series of standard radiographs looking for specific signs to aid them in making a diagnosis. This is especially true of EOA. In comparison to nodal OA, EOA generally presents with similarities and differences. Characteristically, erosions seen in those with EOA are generally centrally located “gull-wing” (Fig. 2) and found in the DIP and PIP joints, in contrast with marginal erosions found in those with psoriatic arthritis and rheumatoid arthritis (Table 3). More general findings such as joint space narrowing, cystic formation, and bone

**Fig. 2** Radiographic findings in EOA: Note classic “gull-wing” erosion of right fourth PIP, and early central erosions and subluxations of left second PIP and right third PIP joints. This patient has had joint arthroplasty of the left third, fourth PIP joints due to cosmetic deformity. The MCP joints and wrists are spared without erosive changes



ankylosis are also seen. In an attempt to further define these differences, Smith et al. [29] studied hand radiographs of 33 EOA patients and compared them with 33 nodal OA patients. They found that patients with EOA had more statistically significant involvement of the DIP and PIP joints in respect to severity of erosive changes, joint space narrowing, osteophytes, and subchondral sclerosis. Joint space narrowing seemed to be more severe even in the EOA group whose joints did not show erosive change.

In a similar study, Cobby [30] studied 500 patients and found 24 of them to have EOA by clinical criteria. The patients with EOA had nearly double the amount of involved joints compared to those of nodal OA. Abnormalities were seen mainly in the DIP and PIP joints compared to the standard control OA group. Seventy-one percent of joints in the erosive group had radiographically identified erosions. Other joints were evaluated and found no difference between the groups other than erosive elbow involvement seen in the EOA group. The erosive changes

seen on radiograph were described in an earlier published paper by Utsinger [12] who described the radiographic changes seen in 15 patients (12 females and three males). Each of the patients had both productive and destructive changes seen on radiograph. Joint space narrowing and osteophytes were present as well as erosions in the central and peripheral zones of the joint space along with cystic degeneration. All of the patients as well had involvement with erosions seen of the first carpometacarpal joint. All of these patients as well had inflammatory involvement in the affected joints at the start of their illness.

In an attempt to further detect characteristic erosions for earlier diagnosis, ultrasound has gained recent popularity in the rheumatology literature. Iagnocco et al [31]. Studied this technology in EOA looking at 22 patients with EOA and 88 patients with classical OA by two independent rheumatologists blinded to the clinical status of the patients and prior radiographs showing central erosions. Ultrasound detected 73% of central erosions in patients with EOA and

**Table 3** Radiographic differences between EOA, non-EOA, and psoriatic arthritis

|  | Erosive OA    | Non-erosive OA | Psoriatic arthritis         |
|--|---------------|----------------|-----------------------------|
| Osteophytes                            | Yes           | Yes            | Yes—part of “cup” formation |
| Joint Space narrowing                  | Yes           | Yes            | Yes—late                    |
| DIP involvement                        | Yes           | Yes            | Yes                         |
| Central erosions “gull wing deformity” | Yes           | No             | No                          |
| Marginal erosions                      | No            | No             | Yes                         |
| Ankylosis/fusion                       | Yes           | Not usually    | Yes                         |
| Wrist involvement                      | No except CMC | No             | Yes                         |

EOA erosive osteoarthritis, DIP distal interphalangeal joint

in no patients with classical hand OA. Osteophytes interfering with the detection of erosions by the ultrasound probe they felt may have accounted for the missed 27% of erosions. In similar fashion, erosions were able to be detected in 35% of hand joints compared to 17.4% in radiographs in 22 patients in a recent study [32] and interestingly, thickened synovium by increased power Doppler signal (22% of joints studied) found primarily in the DIP joints confirming the “inflammatory” nature of EOA. This would imply that ultrasound use may help differentiate those with EOA from nodal OA.

### Symptom management

Although first attracting attention in 1952, EOA itself does not have a management strategy specific for its unique pathophysiology. Therefore, the approach often involves the accepted treatment for nodal OA. However, due to the inflammatory features of EOA, a more aggressive approach is sometimes necessary. This decision is based upon the severity of patient symptoms such as pain, swelling and poor functional capacity. The European League against Rheumatism published their guidelines for management of hand OA in 2007 based upon the strength of published literature [33]. These recommendations include combinations of hand physical and occupational therapy for strengthening of the intrinsic muscles, use of finger splints in those with subluxation/angulation, moist heat and paraffin wax baths to help pain and stiffness, oral acetaminophen up to 4 g/day in those without hepatic or renal insufficiency, oral non-steroidal anti-inflammatory drugs (NSAIDs) at the lowest effective dose necessary, topical NSAIDs or capsaicin cream, and low-dose opioid analgesic agents if pain is the primary complaint. Surgical joint fusion or replacement is to be considered in extreme cases with prevalent pain unresponsive to other means.

The role of joint injection therapy with corticosteroids in EOA was examined by Utsinger [12] in 15 patients (12 females and three males) each having two joints injected with 10 mg of triamcinolone hexacetonide into the most painful joints. The patients were re-examined 7 days later with efficacy determined by reduction in the size of the joint >1 mm and reduction in pain. Following injection, all but seven injected joints showed decreased swelling [12] indicating a therapeutic role for injectible corticosteroids.

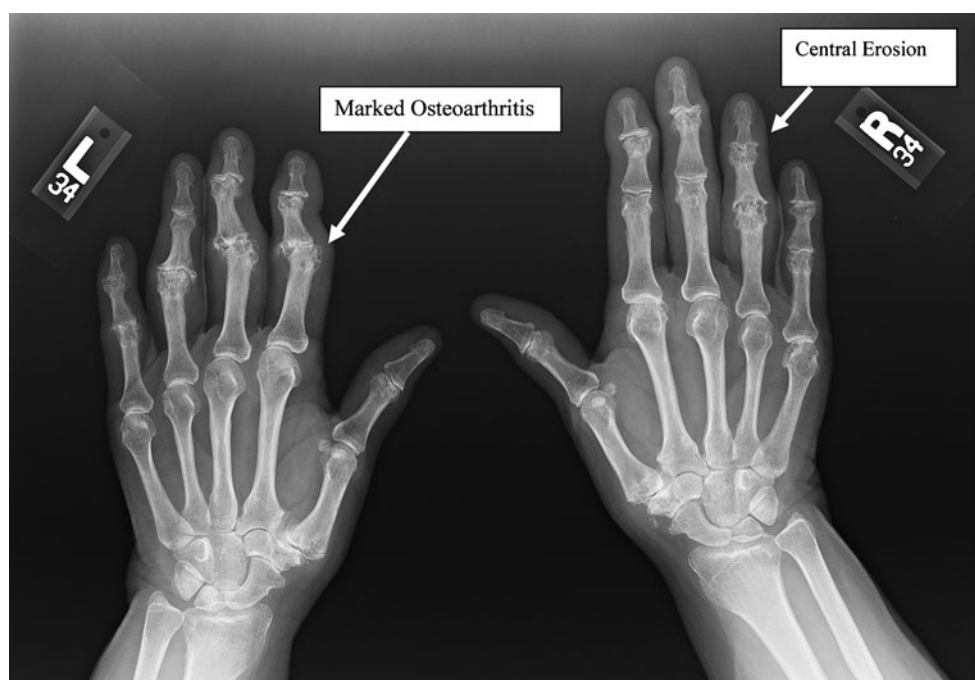
Some studies in EOA have been done looking at the role of DMARD therapy typically used for those with rheumatoid arthritis in order to control the inflammation and secondarily help with pain. Hydroxychloroquine (Plaquenil) is often utilized in those with mild inflammatory arthritis unresponsive to oral NSAIDs. A retrospective study of eight patients with EOA of the DIP and PIP joints published in 1995 examined the use of hydroxychloroquine 200 mg BID for

symptom improvement. An improvement in synovitis in six of eight patients between 7 weeks and 7 months was seen. The two non-responders did exhibit some response in patient global assessment [34] suggesting a recommendation for its use. Anecdotal responses to oral prednisone have been reported to result in significant improvement in pain and synovitis [35]. Clinical studies utilizing colchicine although theoretically useful due to the potential for crystalline involvement have not been published. Although there are no published clinical studies specifically looking solely at the symptomatic improvement seen with oral methotrexate in EOA, this author has used weekly oral methotrexate in a few EOA patients who have failed other medication options. One case is described below:

A now 61-year-old female with radiographically documented central erosions consistent with EOA has been followed in our clinic since 2002. In 2003, she was taking daily NSAIDs and hydroxychloroquine 200 mg/day after having failed NSAIDs alone for DIP and PIP dysfunction. She noted it was hard to grip and use her hands for daily tasks such as peeling potatoes and cleaning her house due to weakness and pain. On exam, she had mild synovitis noted to a few PIP joints and DIP subluxations indicative of the clinical deformities of EOA. Hand therapy was added for strengthening, and her Plaquenil dose was increased to 400 mg/day. Updated X-rays showed some interval progression of the central erosions of the PIP and DIP joints that were present previously on earlier radiographs in 2002 (Fig. 3). In 2004, she complained of increasing stiffness of her hands and noted on clinical exam was synovitis of the second and third MCPs on the right hand and minimal but continued PIP synovitis; low-dose prednisone at 5 mg daily was added to her regimen. In 2004 and 2005, she stabilized on this regimen combined with hand therapy and glucosamine orally. In 2006, she presented to the clinic with significant disability of her hands due to a marked increase in daily pain and palpable swelling in her second, third, and fourth right PIPs, third, fifth left PIPs and tenderness of her MCPs and pain in her right wrist without synovitis. Multiple DIP joints were tender with worsening deformity from lateral subluxations. She was started on methotrexate 5 mg orally once a week in addition to her Plaquenil and low-dose prednisone at 5 mg/day. At her next appointment 6 weeks later, she noted marked improvement in her amount of pain and swelling in her PIP joints. Her exam did not reveal synovitis but continued subluxations in her DIP and PIP joints consistent with Z shaped deformities of her fingers. Her ESR, RF, CCP, and ANA remained normal. She has continued methotrexate at low doses and continues to do well without flares. Her pain and disability have improved, and her steroids have been withdrawn.

The popularity of over-the-counter supplements or nutraceuticals aimed at slowing the progression of EOA

**Fig. 3** 2004 hand X-rays of EOA patient on methotrexate. Multiple areas of central erosions in DIP and PIP joints along with wavy Z shaped deformities. Wrists spared of erosive changes. OA changes noted at CMC joints. Periarticular osteopenia usually associated with rheumatoid arthritis is absent



was studied in 24 patients by Rovetta [36]. Patients were divided into two groups; one treated with naproxen 500 once daily, the other with chondroitin sulfate 800 mg/day plus naproxen 500 mg/day and followed for a period of 24 months. New erosions of two or more were seen on radiograph of the hands at the end of 24 months in three patients in the naproxen-treated group, whereas the chondroitin group had no subjects with progression at year 2 of two or more erosions. Thus, it is postulated that the chondroitin group had a reduction in the total number of new erosions and symptoms during the second year. Similarly, an observational one year study of 104 patients with a mean age of 61 of which 30 patients had EOA were treated with combinations of glucosamine 1,000 mg and chondroitin 1,000 mg vs. glucosamine 1,000 and chondroitin 1,000 mg plus native type II collagen 2 mg. Differences in pain and radiographic changes were compared between the EOA and OA groups. After 6 months and 1 year, visual pain scores were reduced in both treatment arms in both groups compared to baseline. Radiological scores showed decreased progression after 1 year compared to baseline in both groups especially in the GCC group. No real significant differences were seen in the two groups in these areas, but it suggests a difference utilizing nutraceuticals in the symptoms management of EOA and OA patients [37].

Due to the effect of  $\text{TNF}\alpha$  in cartilage destruction and inflammation previously mentioned,  $\text{TNF}\alpha$  inhibitors have been studied in an open label pilot study involving 12 patients with EOA [38]. Patients were given six subcutaneous injections of adalimumab (Humira) 40 mg bi-weekly for 12 weeks. Outcomes of safety and efficacy in reducing

the amount of swollen joints, pain, and disability were measured. At the end of 12 weeks, there was a modest trend toward improvement in all measures although only statistically significant improvement was found in the number of swollen joints. No statistically significant change in pain assessment or disability was seen and no serious adverse events were noted. Further studies are needed to determine long-term outcome effect. Intra-articular injectable infliximab was studied in ten patients with bilateral symptomatic EOA for a mean of 7.5 years of the hands and its effects on pain and radiographic progression were studied over a period of 12 months. Fifty-six joints in total in all patients were treated monthly in the EOA patients in painful joints compared to 34 injected with saline in less painful joints. At 12 months, there was a significant reduction in pain in the infliximab-treated hand, but no change in morning stiffness. A trend was seen toward slowing of radiographic progression in the infliximab group although not significant [39]. As IL-1 has been postulated to play a role in cartilage destruction in OA, anakinra, and IL-1 receptor antagonist was studied in three postmenopausal women with severe EOA who had failed conventional treatment. All were treated with 100 mg/day subcutaneously of anakinra (Kineret) for 3 months. Outcomes included improvement in pain and amount of handicap and use of daily NSAIDs for symptoms. At the end of the 3 months, there was improvement in all parameters with an average 70% reduction in pain, 47% reduction in handicap and NSAID withdrawal in all patients [40]. Further studies on larger groups of patients are needed to confirm these findings but the results suggest a role of inflammatory cytokines in clinical inflammatory phase of EOA.



## Summary

Since its name was coined in 1966, little has been added to the overall understanding of the pathogenesis of EOA. The clinical and radiographic features have been well described separating EOA into its own unique clinical entity. The prognosis is generally good however limitation of hand function and pain can occur resulting in significant disability as well as disfiguring cosmetic changes of the hands [33]. Due to its distinctive clinical characteristics including younger age, abrupt onset, palpable synovial inflammation, gross deformities, and central radiographic erosive features, EOA deserves further exploration in order to uncover more targeted treatment options.

**Disclosures** None.

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