Clinical problem solving

A patient with symmetrical polyarthritis affecting the hands

The value of hand x-rays

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Declaration:

I have no conflict of interest for this presentation.

Case presentation (I)

- A 60year old woman presented to a rheumatologist complaining for arthalgias and swelling affecting the small joints of the hands.
- She was well until 2 months earlier.
- Past medical and family history were unremarkable.
- She denies photosensitivity, skin rashes, Raynaud's phenomenon, psoriasis, mucosal ulcers, urethritis, gastrointestinal abnormalities.
- Physical examination revealed: swelling and tenderness affecting the MCPs and PIPs joints, as well as the wrists bilaterally.

Case presentation (II)

Laboratory evaluation showed:

- ESR: 68mm/h.
- CRP: 20mg/l (NV<6).
- IgMRF, ACPA and ANA were negative.
- The rest of laboratory tests including hepatitis B,C and CMV and EBV viruses were within normal limits, or negative.

Diagnosis of RA: ACR criteria

At least four of the following criteria

- ❑ Morning stiffness >1 hour
- ❑ Arthritis of ≥3 joint areas
- ❑ Arthritis of hand joints
- ❑ Symmetric arthritis
- ❑ Rheumatoid nodules
- ❑ Serum rheumatoid factor
- ❑ **Radiographic changes**

Must be present for at least 6 weeks

Arnett FC et al. Arthritis Rheum 1988;31:315–24

2010 ACR/EULAR Classification Criteria for RA

JOINTS (0-5)	
1 large joint	0
2-10 large joints	1
1-3 small joints (large joints not counted)	2
4-10 small joints (large joints not counted)	3
>10 joints (at least one small joint)	5
SEROLOGY (0-3)	
Negative RF AND negative ACPA	0
Low positive RF OR low positive ACPA	2
High positive RF OR high positive ACPA	3
SYMPTOM DURATION (0-1)	
<6 weeks	0
>=6 weeks	1
ACUTE PHASE REACTANTS (0-1)	
Normal CRP AND normal ESR	0
Abnormal CRP OR abnormal ESR	1

Definite RA: score of ≥ 6/10

Case presentation (III)

- According to the EULAR/ACR classification criteria, the patient was diagnosed as seronegative RA.
- She started on MTX: 15mg/w, plus prednisone 10mg/day.
- Two months later she felt very well, without pain and swelling. The ESR and CRP were normalized.
- The dose of prednisone was tapered until complete discontinuation.
- She continued receiving MTX 15mg/w.

Case presentation (IV)

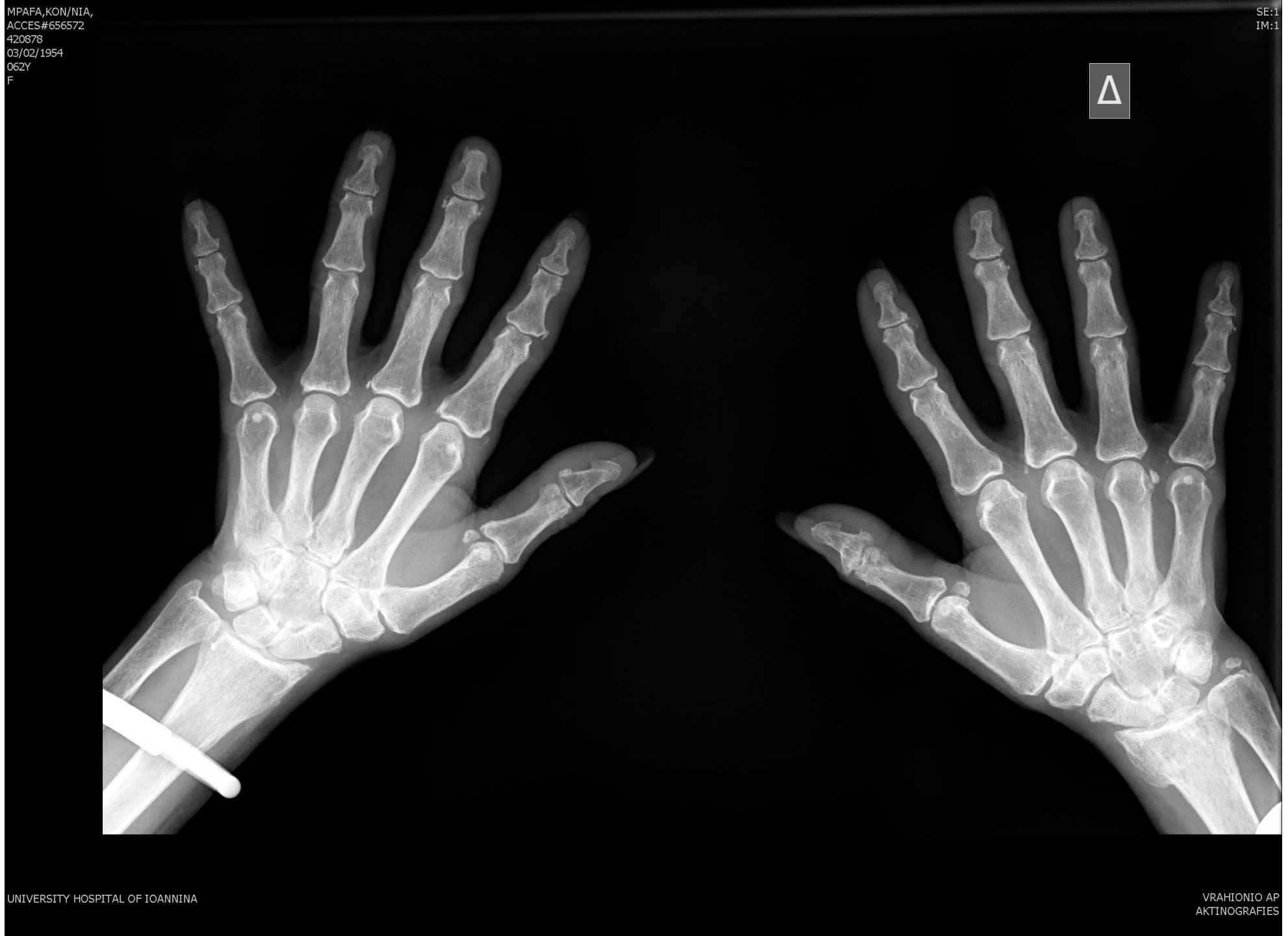
- One year later the patient was in complete clinical and laboratory remission.
- Since the patient felt well, she asked the doctor to discontinue MTX.
- The answer was negative, because according to the EULAR/ACR guidelines for RA treatment, MTX should be continued for many years.

Case presentation (V)

- The patient visited another rheumatologist who after a careful clinical and laboratory evaluation found out that the patient was on clinical remission.
- He ordered a hands and wrists x-rays where the diagnosis was evident.
- MTX was discontinued.
- After 6 and 12 months, the patient continued feeling well, and the laboratory tests were within normal limits.

Questions to be answered

- What the hands and wrists radiographs showed.
- What is the diagnosis of our patient.
- How to evaluate hands and wrists radiographs.
- What is the usefulness of conventional radiographs.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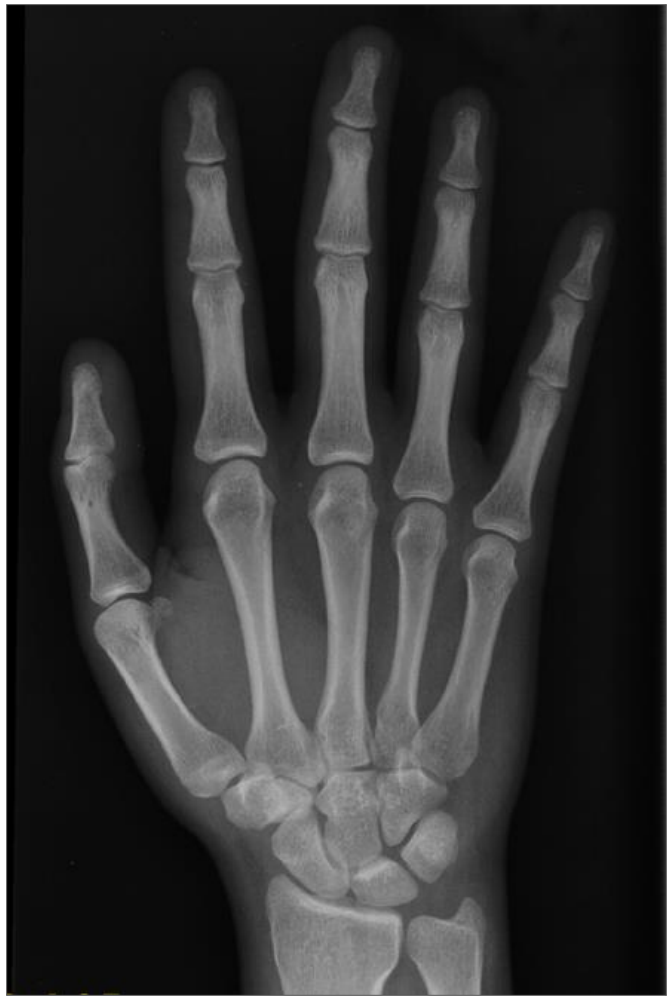
Conventional radiography

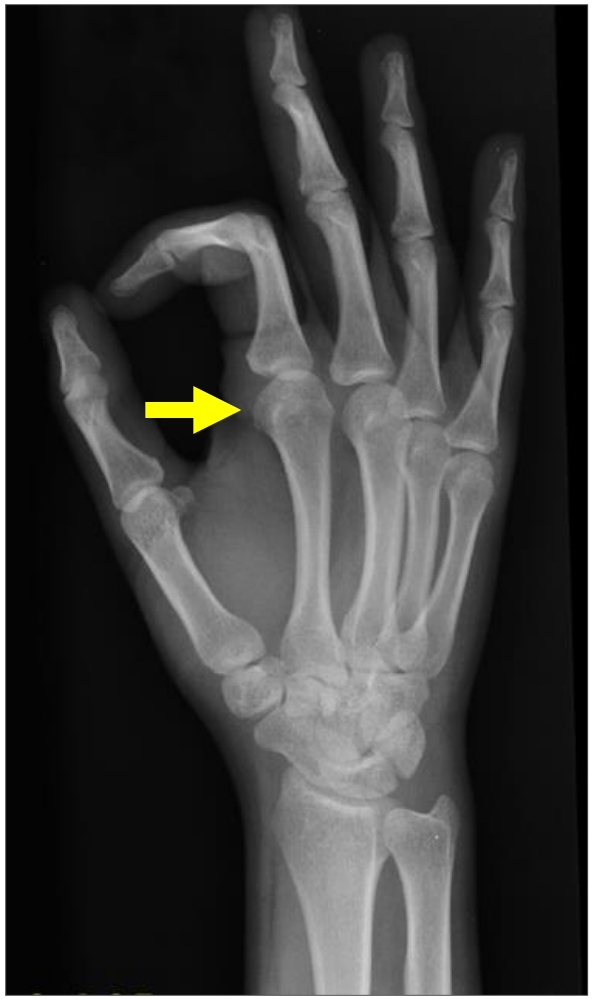
- Evaluation of articular disease should begin with the conventional radiograph, which is the best modality to evaluate accurately and subtle change occurring in the bone
- If high-quality radiographs are obtained in properly positioned patients, accurate evaluation can often be made without further studies

Brower AC. Arthritis in Black and White. Saunders (2nd Ed), 1988

Normal hands



posteroanterior



oblique

Evaluation of the hand film

One must observe

- the radiographic changes occurring in a specific joint and
- the distribution of these changes within the hand and wrist in order to make an accurate diagnosis

Brower AC. Arthritis in Black and White. Saunders (2nd Ed), 1988

Radiographic changes

The radiographic changes occurring around a specific joint to be evaluated are:

- ❑ Soft tissue swelling
- ❑ Subluxation/dislocation
- ❑ Mineralization
- ❑ Calcification
- ❑ Bone production
- ❑ Joint space narrowing
- ❑ Erosions

Brower AC. Arthritis in Black and White. Saunders (2nd Ed), 1988

Erosions (I)

- Are seen in the inflammatory, metabolic and septic arthritis as well as in OA
- The type and the distribution (location) of erosions within a specific joint is important in distinguishing one arthropathy from another
- The erosions of an inflammatory arthropathy occur at the margins of the joints

Erosions (II)

- The erosions of erosive OA tend to occur in the central portion of the joint
- The marginal erosion of PsA have been compared to mouse ear
- While the centre erosion of erosive OA has been compared to a seagull

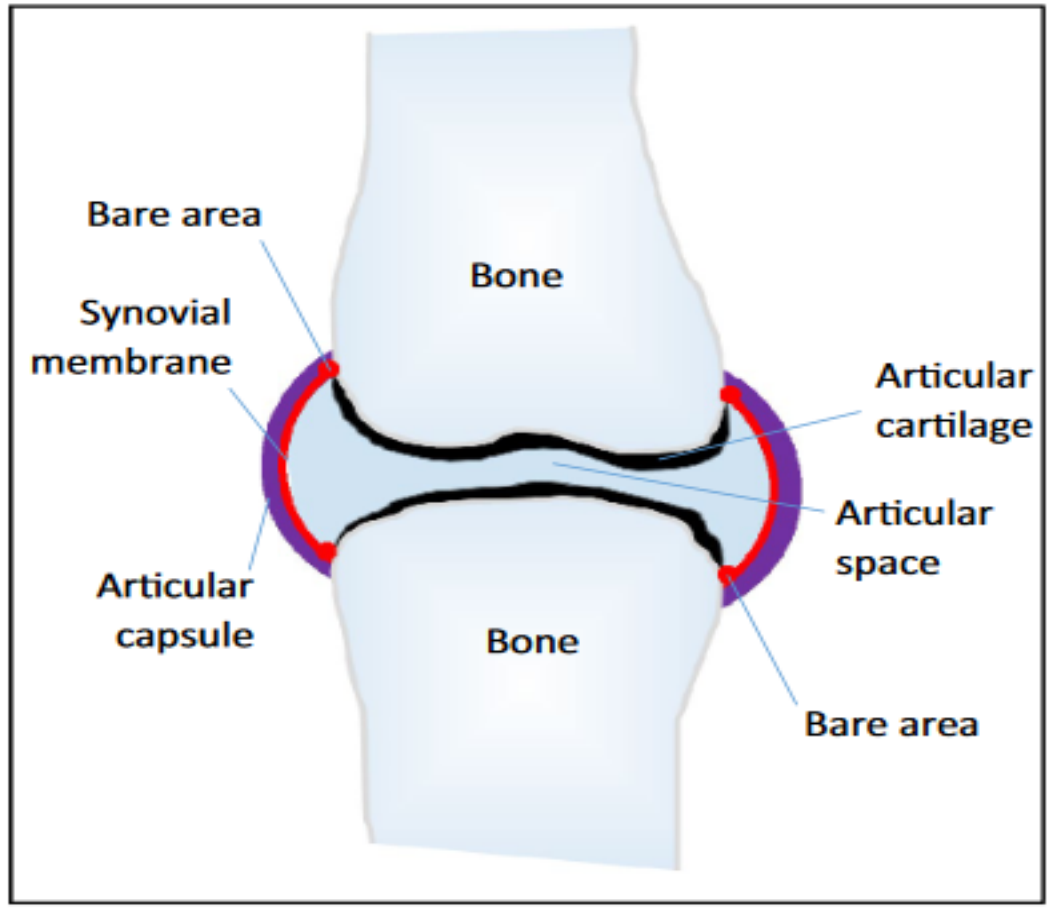


Fig. 6 Schematic representation of a diarthrodial joint in which the bare areas of the joint are shown. These areas are located between the edge of the articular cartilage and the attachment of the synovial membrane. Owing to the direct contact with the synovium, without any protecting layer of the cartilage these areas are very susceptible to inflammation, which leads to erosions and bone destruction

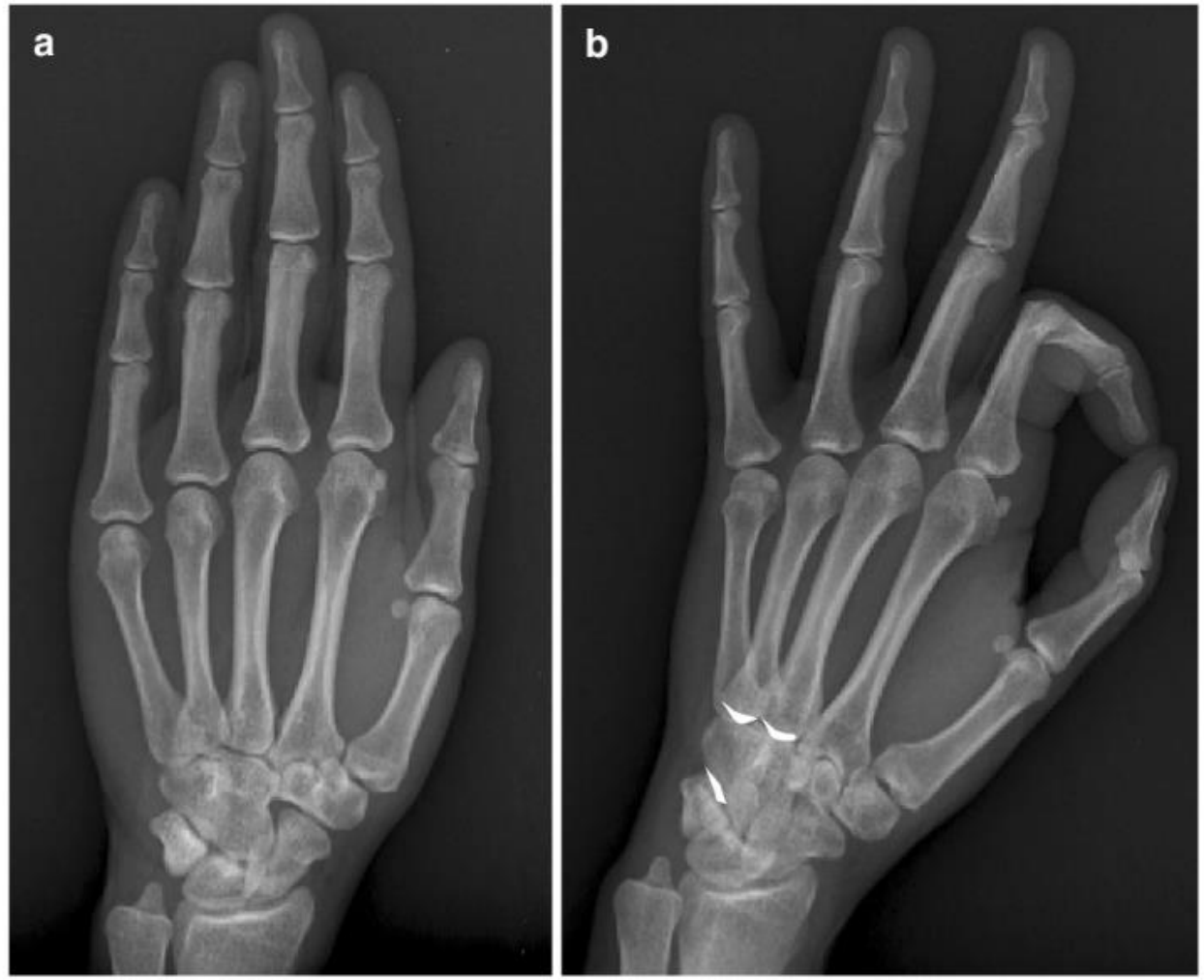


Fig. 1 **a** Posteroanterior and **b** Nørgaard view of a healthy individual. In the latter, the anatomic regions of early erosive changes of an inflammatory arthropathy are marked in white

Distribution of digits involvement

I. **DIP and PIP involvement**

A. Osteoarthritis – osteophytes without erosions

B. Erosive osteoarthritis – osteophytes and erosion

C. Psoriatic arthritis – erosion without osteophytes

II. **MCP and PIP involvement**

A. Rheumatoid arthritis – erosions without new bone formation; spares the DIPs

B. Psoriatic arthritis, Reiter's disease, ankylosing spondylitis - erosions and new bone formation; will involve DIPs

III. **MCP involvement**

A. Inflammatory arthropathies

B. CPPD - osteophytes

IV. **Random involvement**

A. Gout

Brower AC. Arthritis in Black and White. Saunders (2nd Ed), 1988

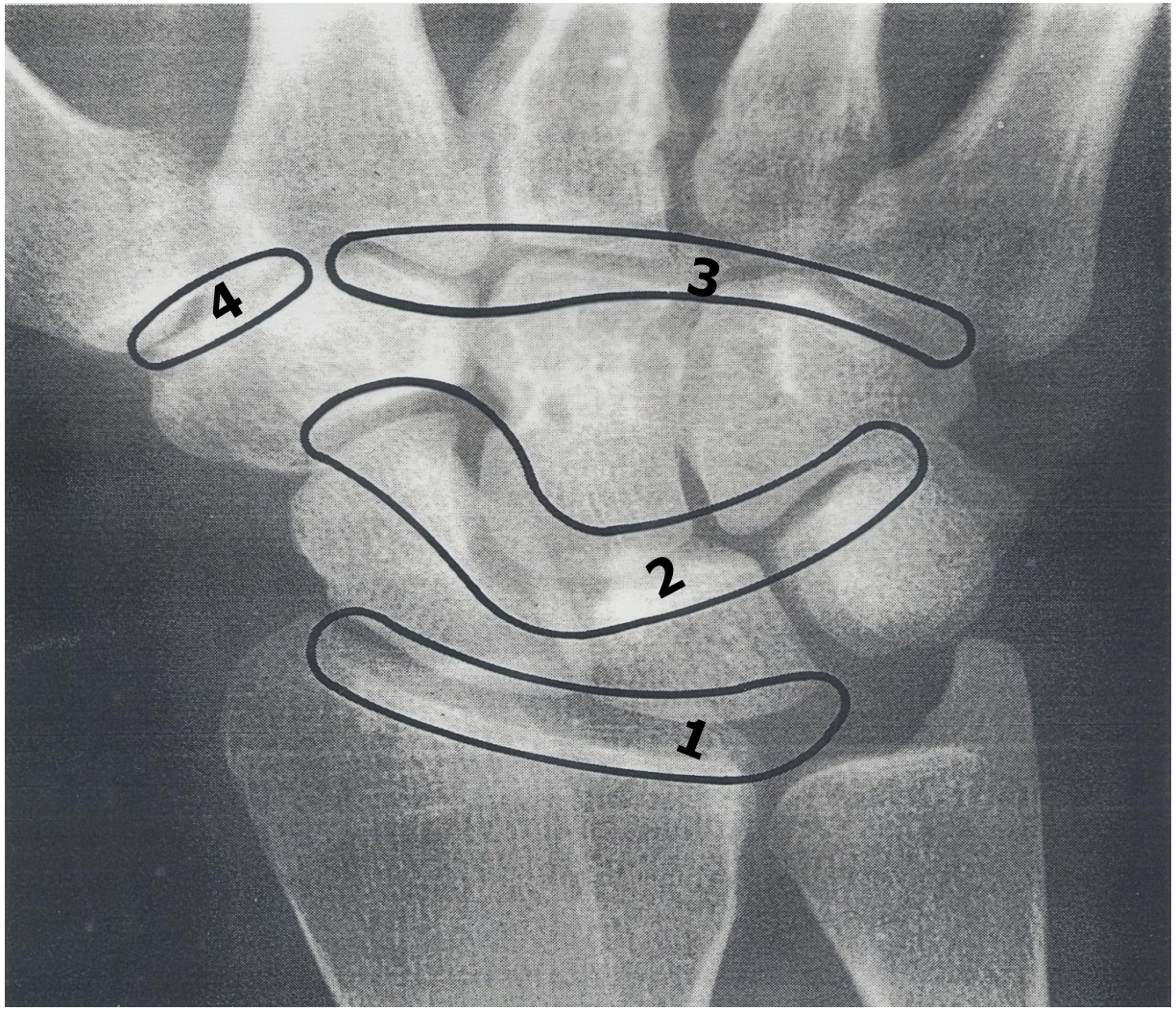
Carpal bones

(1) the radiocarpal compartment,

(2) the midcarplal compartment,

(3) the common carpometacarpal compartment, and

(4) the 1st carpometacarpal compartment



Distribution of carpal erosions

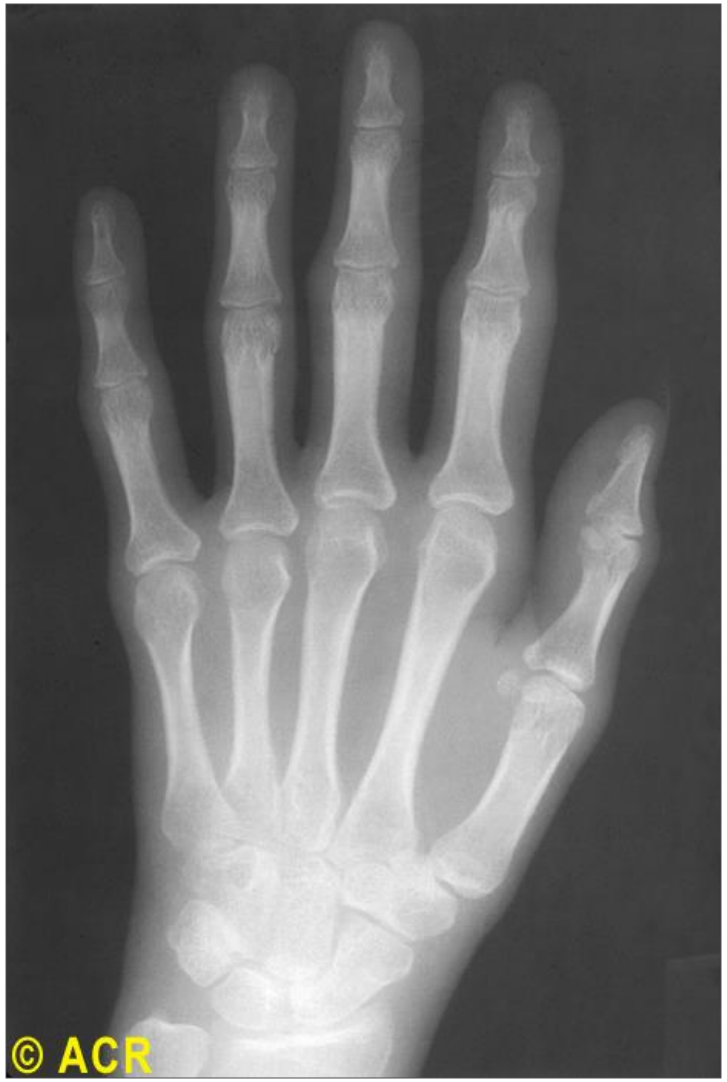
- The inflammatory arthropathies affect all the carpal bones causing erosions and joint space narrowing
- OA affects the 1st carpometacarpal joint
- If OA like erosions are present in other carpal compartments then other conditions must be excluded e.g. traumatic or metabolic conditions

Table 1 Imaging changes occurring in hands and wrists in RA patients using conventional radiography

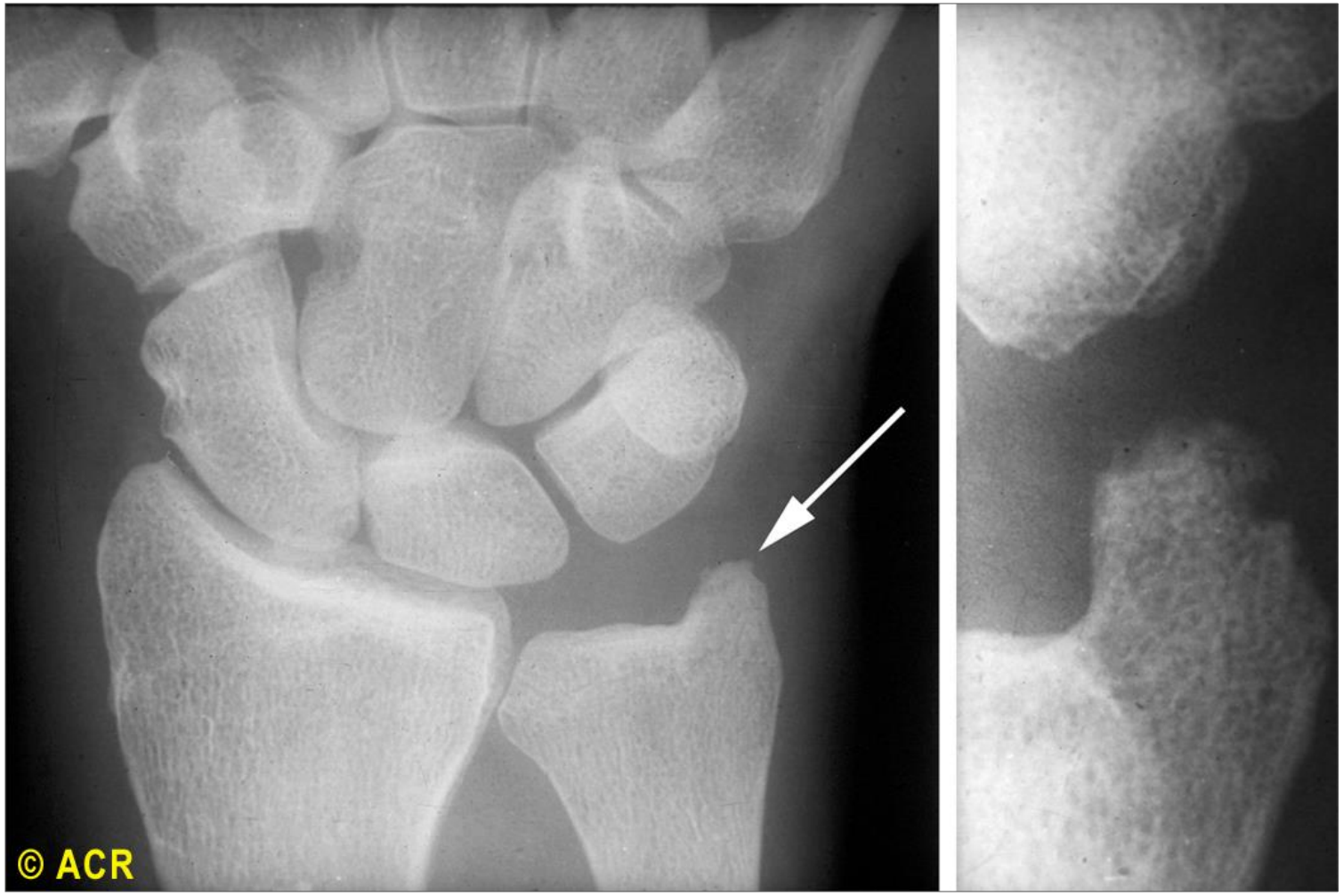
Imaging changes	Early RA	Advanced RA
Soft tissue changes	Symmetrical swelling around the PIPs and wrists	Atrophy
Mineralization	Juxta-articular osteoporosis	Diffuse osteoporosis
Subluxation	None	MCPs (proximal phalanges subluxed ulnarly and palmarly)
Joint space narrowing	Maintained	Uniform loss in PIPs, MCPs and carpal bones
Erosions	Mild, sometimes aggressive	Large, aggressive
Joint distribution	PIPs, MCPs, and pancarpal	PIPs, MCPs, and pancarpal

RA rheumatoid arthritis, *MCPs* metacarpophalangeals, *PIPs* proximal interphalangeals

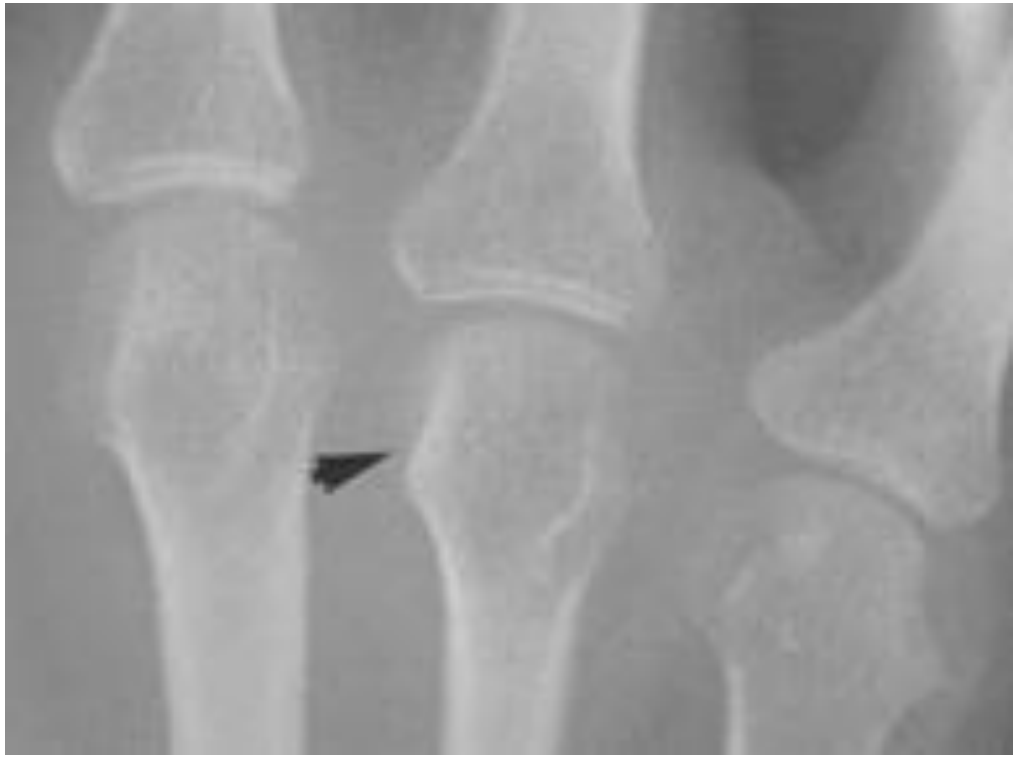
Early RA

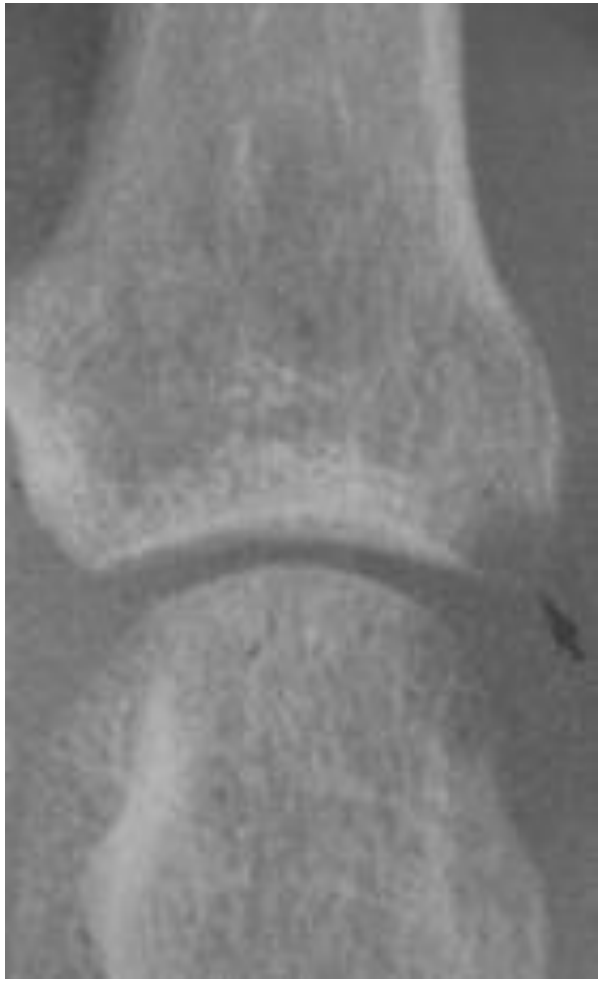


RA: early erosions

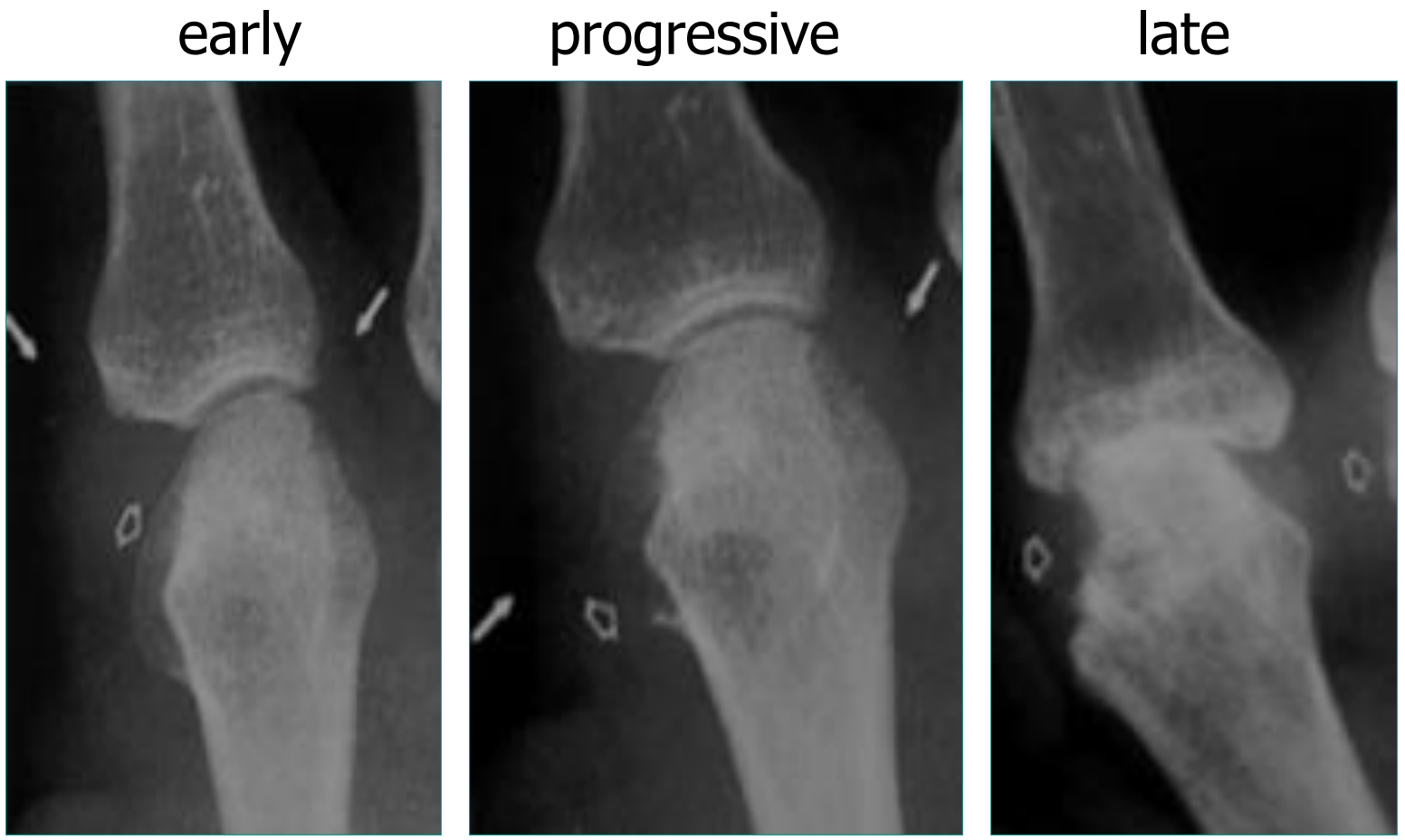


RA: early aggressive erosions

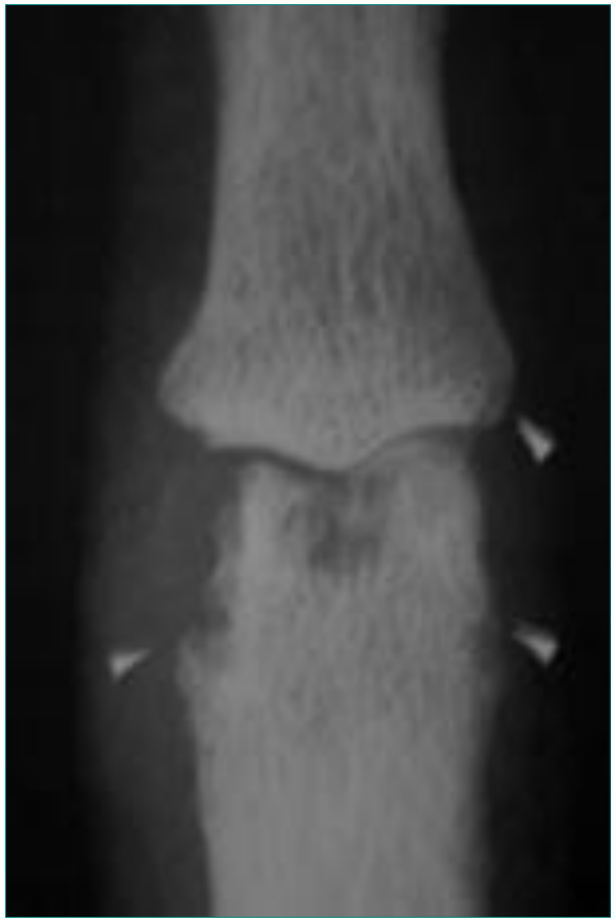




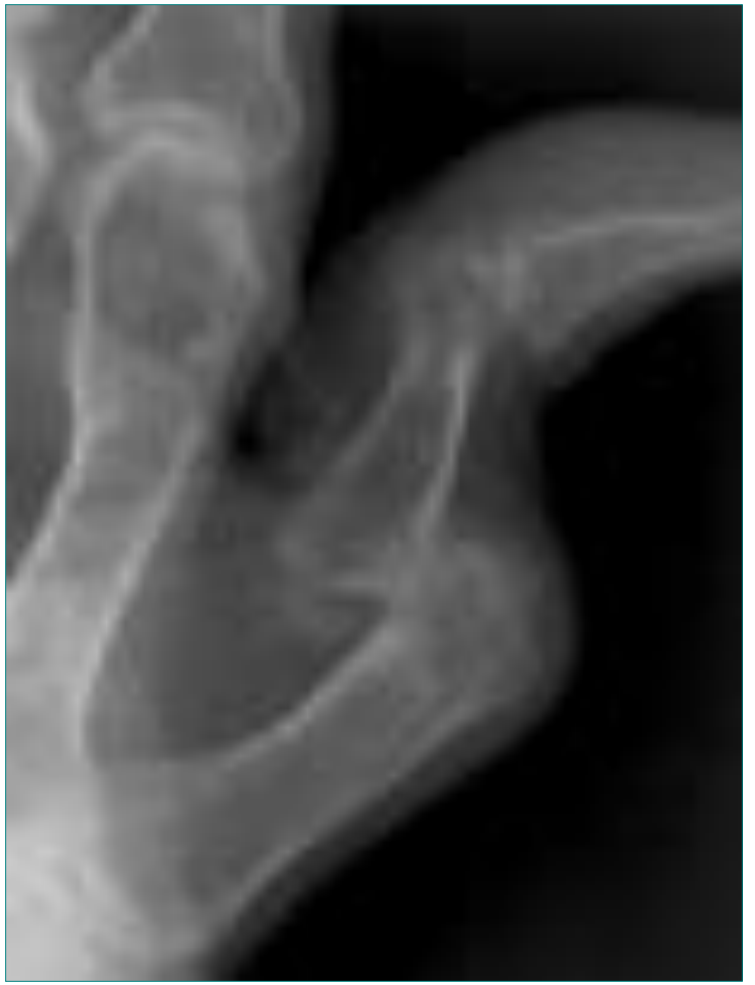
RA- MCP joints



RA - PIP



RA - MCP



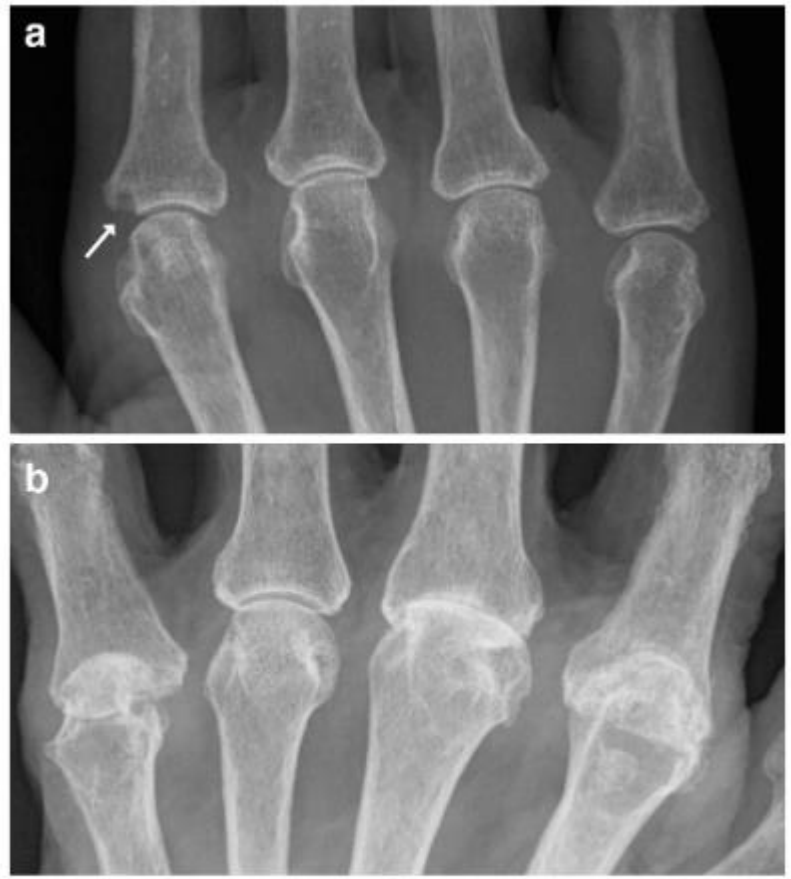
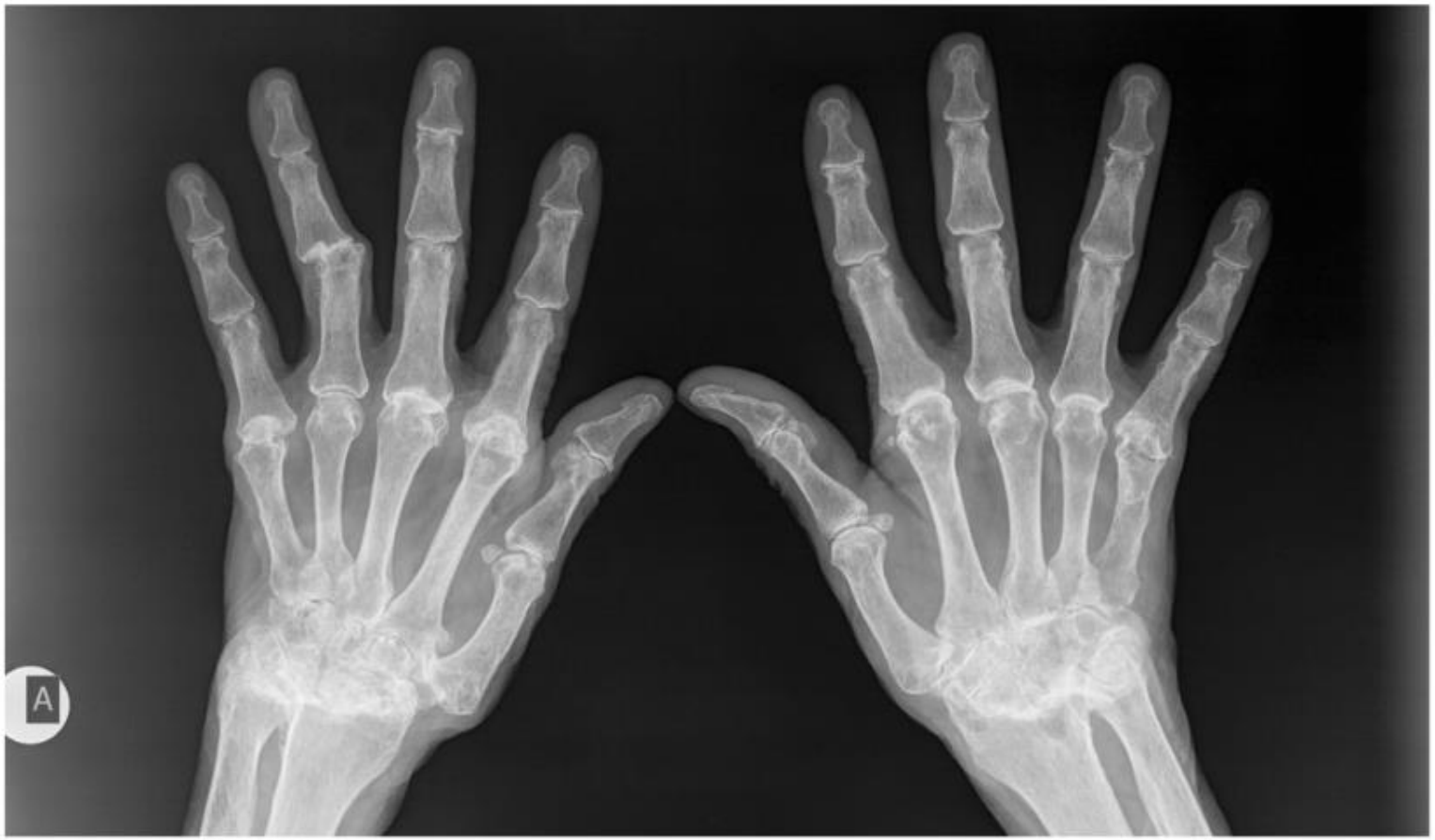


Fig. 7 **a** RA patient. Large erosive changes of the second MCP joint (arrow) are depicted (corresponding to the bare area of the second MCP joint). **b** Extensive erosive changes affecting the second, third, and fifth MCP joints in an RA patient with advanced disease



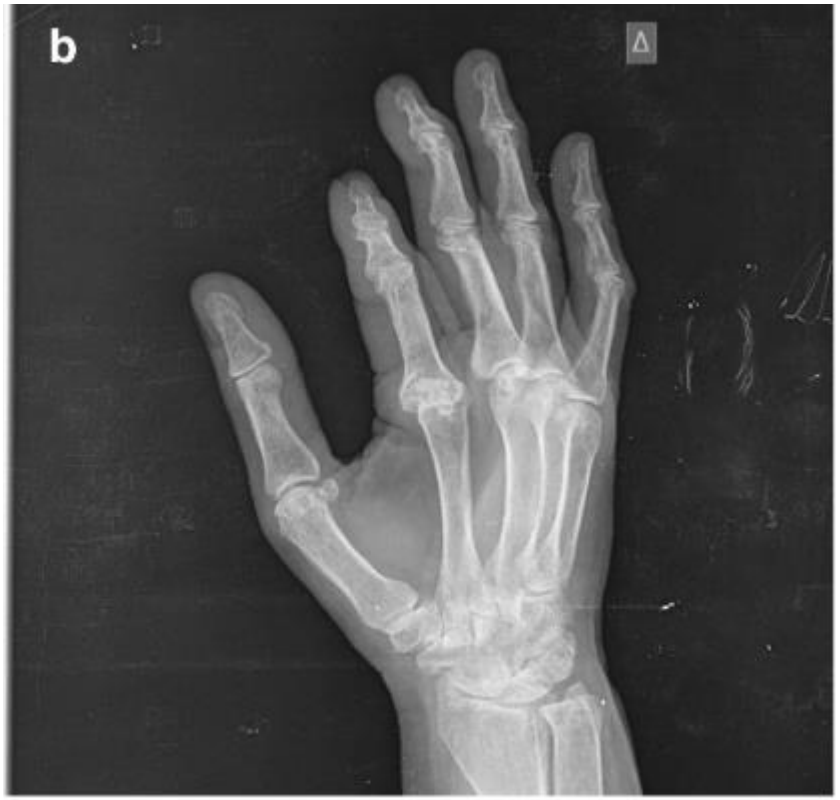
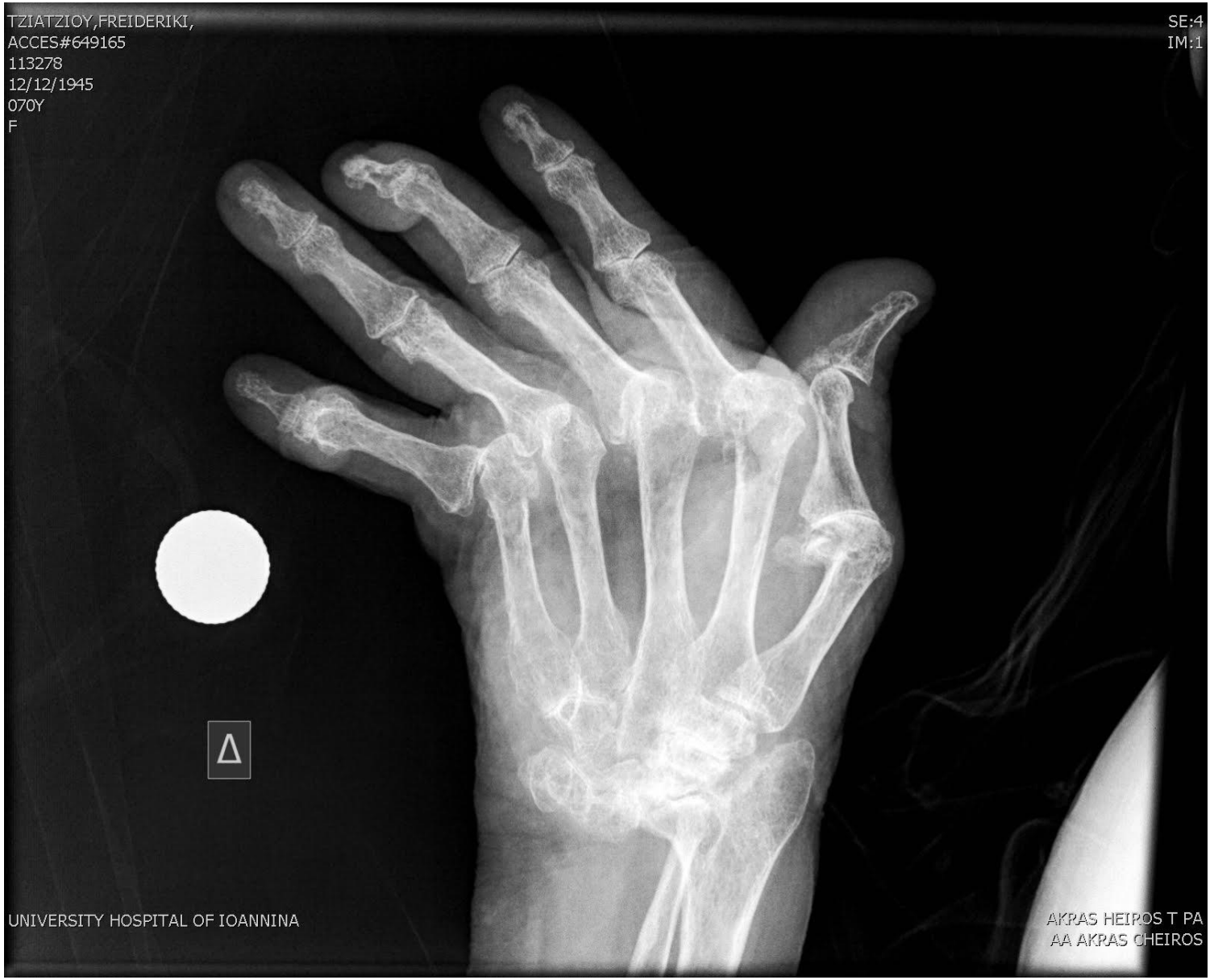


Fig. 9 Established RA. Joint space narrowing of the second–fifth PIPs bilaterally is shown. Note also severe erosive changes of the MCPs in various degrees bilaterally. In addition, extensive erosions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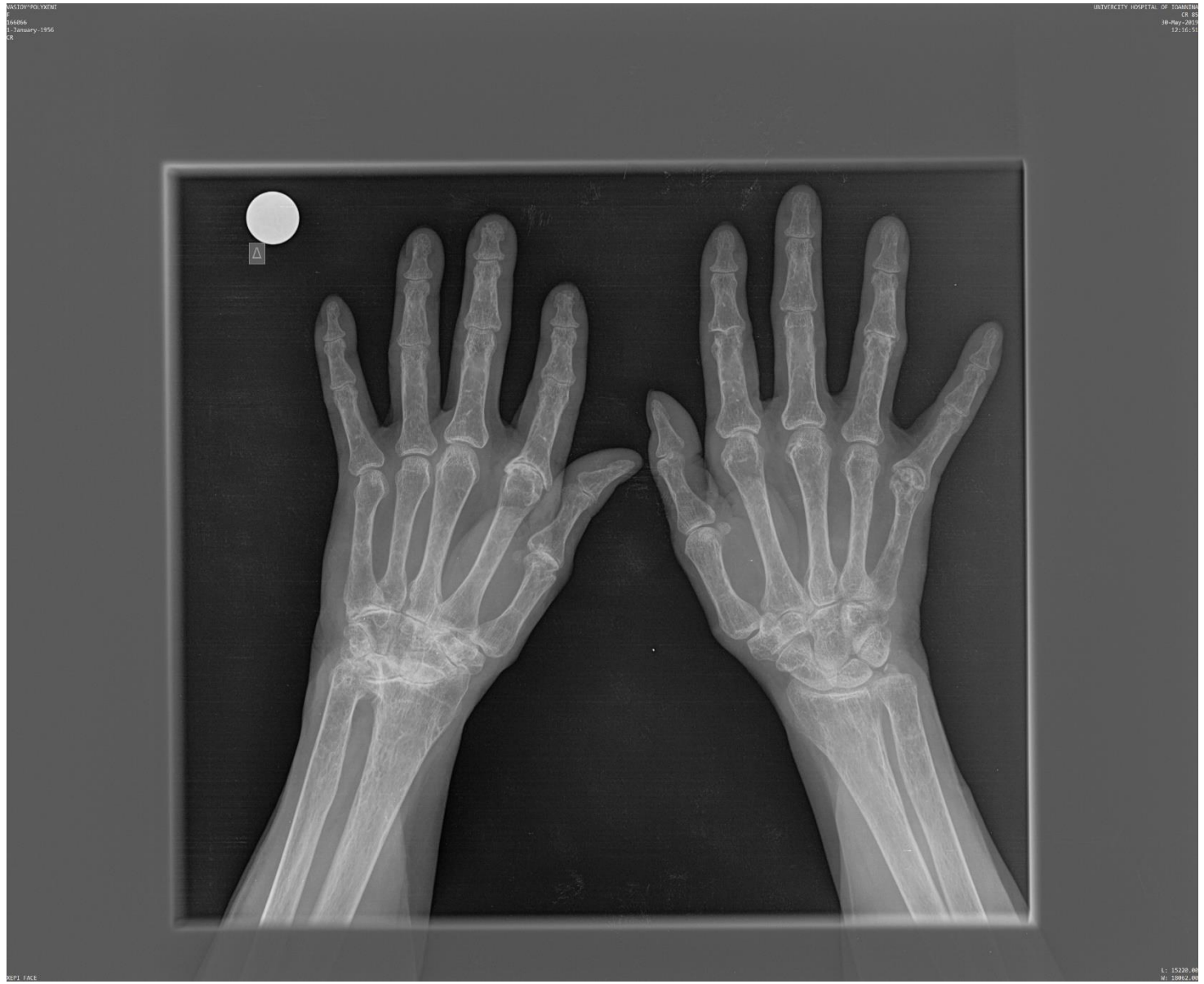
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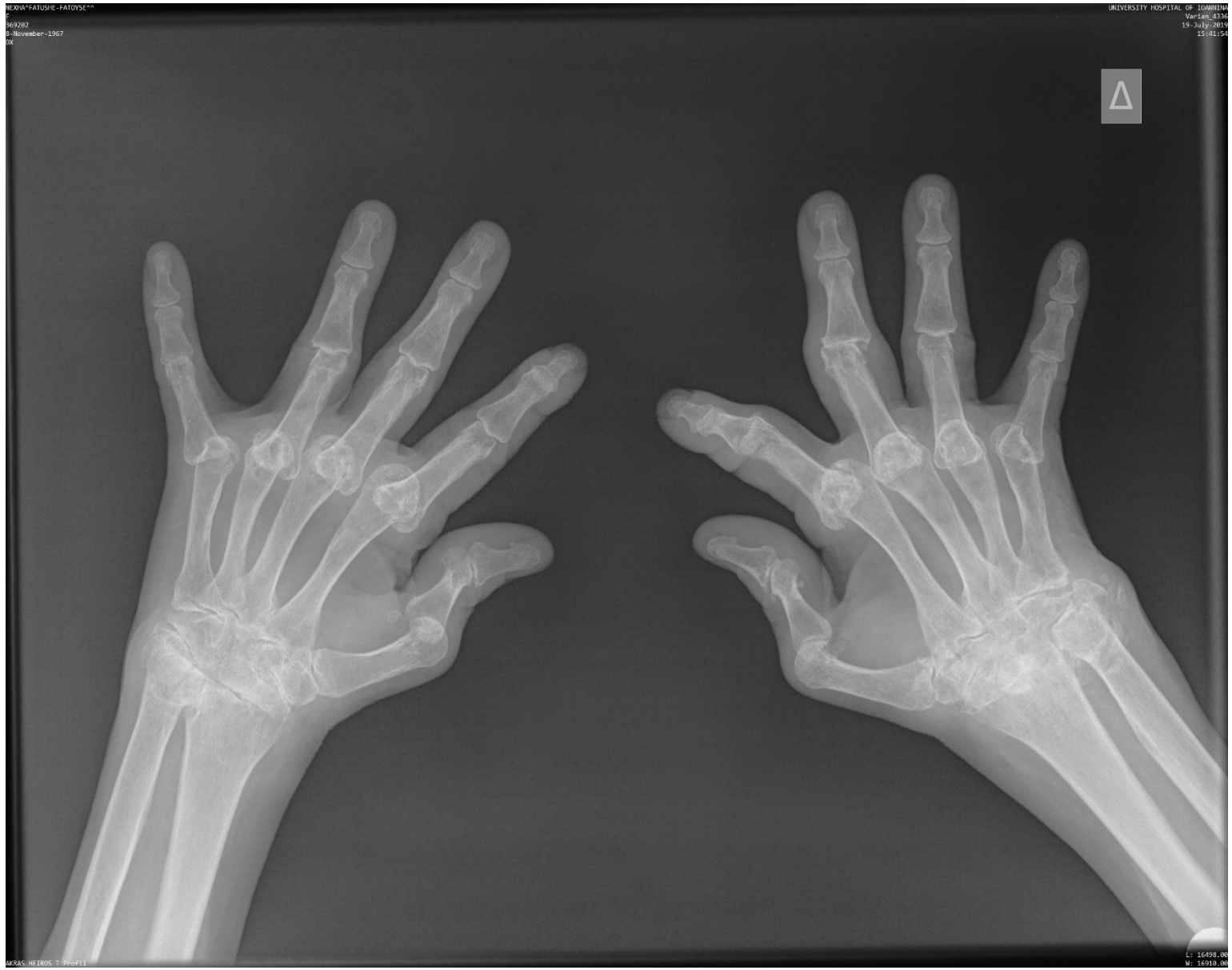
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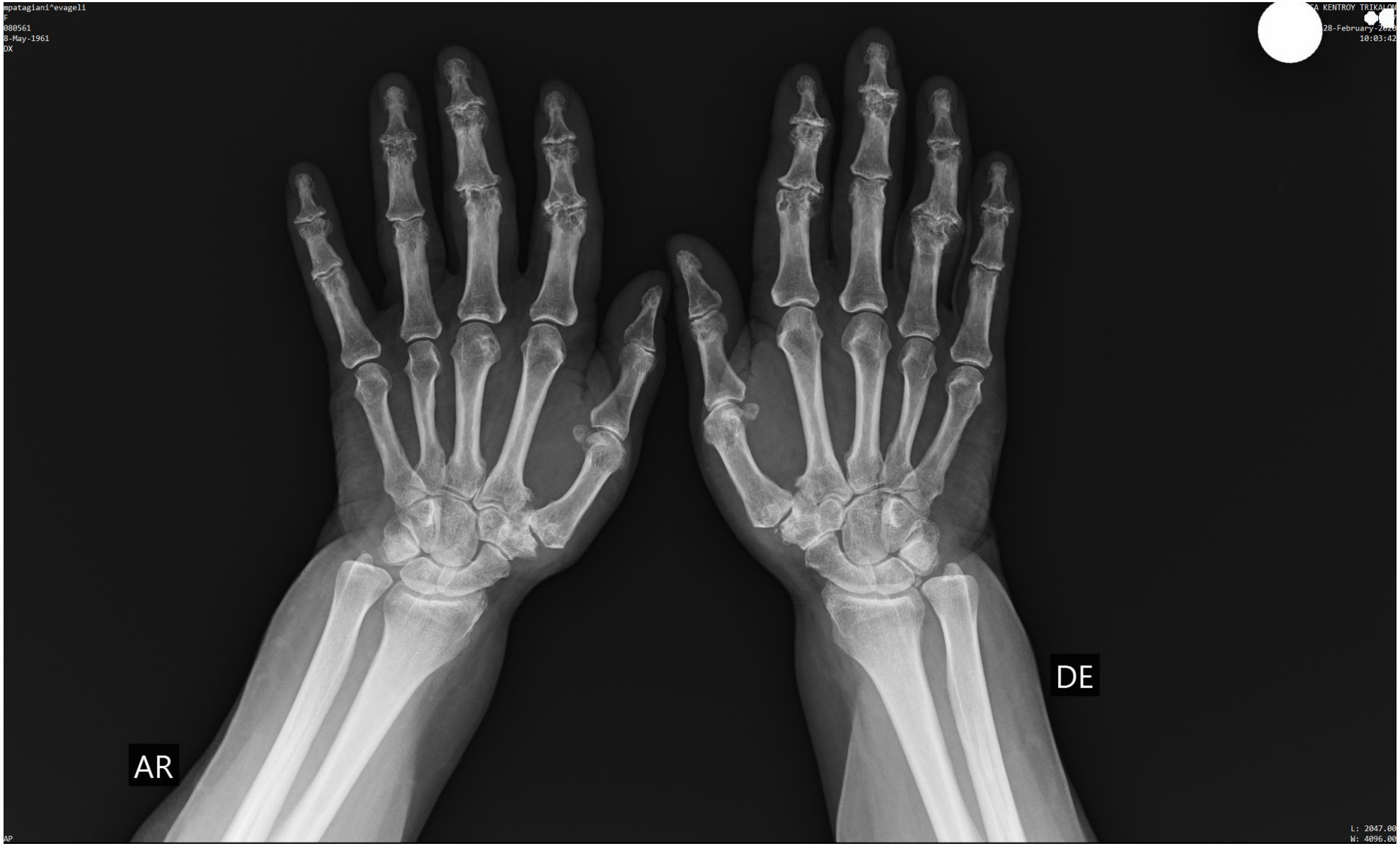
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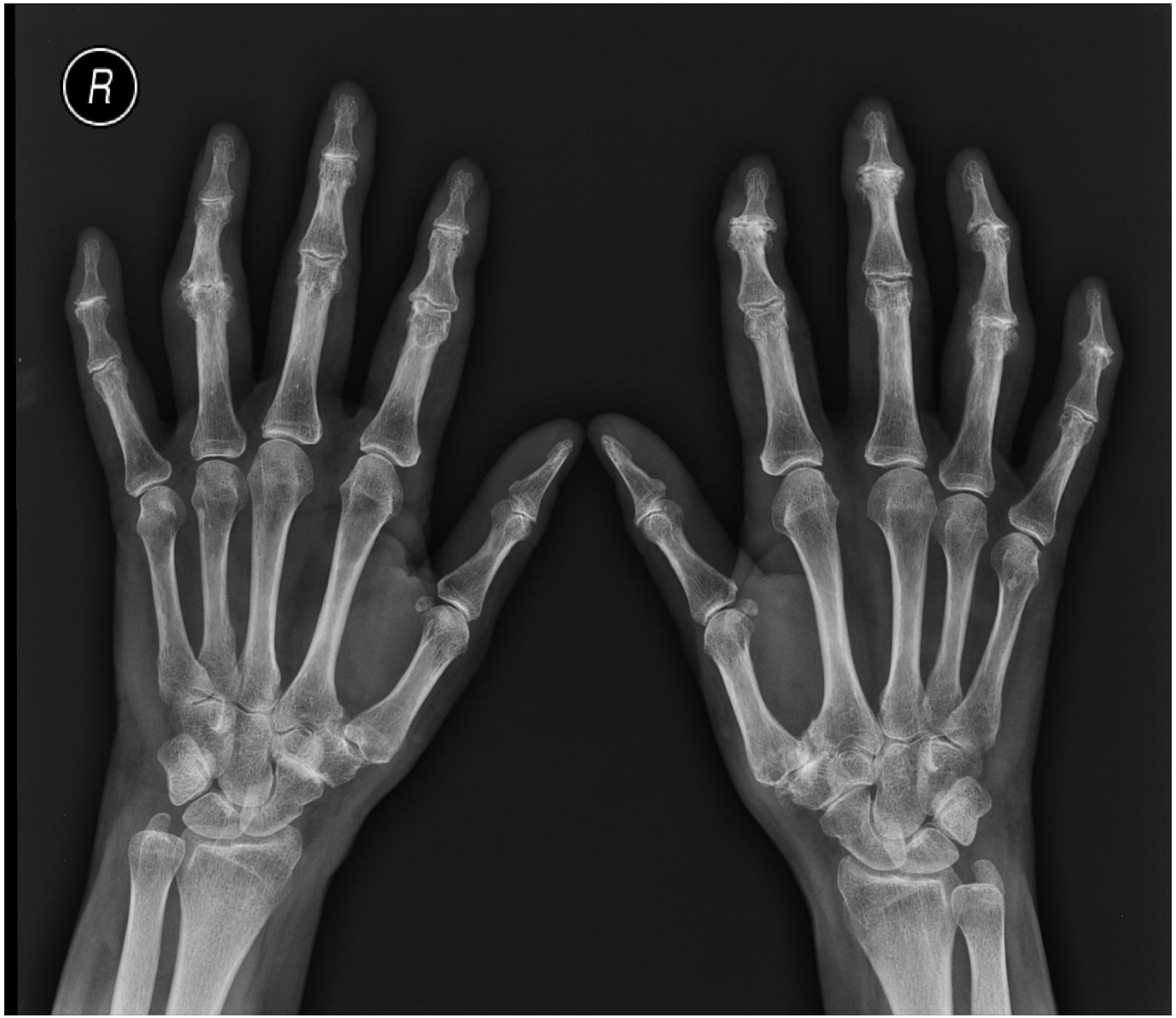
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Case presentation continued

- Our patient had a chronic, symmetrical polyarticular CPPD, affecting the small joints of the hands with presence of high acute phase reactants, mimicking RA.
- Indeed, this patient satisfied the ACR/EULAR classification criteria for RA, but if hand and wrist x-rays were performed at the first visit, the diagnosis of a chronic form of CPPD would be obvious to the examiner.
- In this case, the treatment is different, as well as the disease severity and prognosis.

Does early seronegative arthritis develop into rheumatoid arthritis? A 10-year observational study

K. Paalanen[1], K. Rannio[2], T. Rannio[1], J. Asikainen[1], P. Hannonen[1], T. Sokka[1]

[1]Department of Rheumatology, [2]Department of Radiology, Central Hospital of Central Finland, Jyväskylä, Finland.

Abstract

Objective

To investigate the 10-year clinical course of patients with seronegative arthritis with the emphasis of reclassification of diagnoses when applicable.

Methods

A total of 1030 patients including 435 seronegative cases were classified as early RA in 1997-2005 at Jyväskylä Rheumatology Centre and prospectively scheduled for a ten-year follow-up. Clinical data from the follow-up visits and the case-reports until and including the 10-year visit or death, whichever happened earlier, were retrospectively collected and reviewed with re-classification of the cases when applicable. Descriptive statistics were used.

Results

Among the 435 seronegative cases (69 % women, baseline mean age was 59 years), 13 (13/435 [3%]) could be reclassified as seropositive or erosive RA: 4 turned seropositive (2 for ACPA and 2 for RF [> 2x reference level]) and 9 developed erosions typical for RA. Reclassification revealed 68 (16%) cases of polymyalgia rheumatica, 46 (11%) psoriatic arthritis, 45 (10%) osteoarthritis, 38 (8.7%) spondyloarthritis, 15 (3.4%) plausible reactive arthritis, 10 (2.3%) gout, 17 (3.9%) pseudogout, 6 (1.4%) paraneoplastic arthritis, 6 (1.4%) juvenile arthritis, 2 (0.5%) haemochromatosis, 3 (0.7%) ankylosing spondylitis, 2 (0.5%) giant cell arteritis, and 8 miscellaneous diagnoses. The other 140 patients (32%) could not be reclassified in any clear-cut diagnosis and had features of transient arthritis (n=41), seronegative spondyloarthritis (n=47), while 49 remained unspecified.

Conclusion

Over a 10-year follow-up period, reclassification revealed significant heterogeneity in the diagnosis of seronegative RA. Therefore, seronegative arthritis should not be studied as a homogenous entity.

Clinical and Experimental Rheumatology 2019; **37**: 37-43.

Prevalence of calcium pyrophosphate deposition disease in a cohort of patients diagnosed with seronegative rheumatoid arthritis

K. Paalanen[1], K. Rannio[2], T. Rannio[1], J. Asikainen[1], P. Hannonen[1], T. Sokka[1]

[1]Department of Rheumatology, [2]Department of Radiology, Central Hospital of Central Finland, Jyväskylä, Finland.

Abstract

Objective

We aimed to characterise the clinical and radiographical phenotype of calcium pyrophosphate dihydrate deposition (CPPD) disease in patients initially diagnosed with seronegative RA, and to increase the awareness that CPPD disease can be falsely diagnosed as seronegative rheumatoid arthritis (RA).

Methods

Altogether 435 early seronegative RA patients were clinically diagnosed in a single rheumatology centre and scheduled for a 10-year follow-up. All clinical data were collected and reviewed. CPPD-related arthritis was suspected if a patient had typical radiographical findings and suitable clinical pattern of CPPD or calcium pyrophosphate crystals were found in the synovial fluid. These patients are the subjects of this study.

Results

Among 435 seronegative RA patients, 17 patients (3.9%) (baseline mean age 71.2 years, 82% women) with CPPD disease were identified. CPPD resembling clinical patterns in these patients were: chronic CPP crystal inflammatory arthritis (9 patients), acute CPP crystal arthritis (6 patients) and OA with CPPD (2 patients). All had typical radiographical findings of CPPD: Chondrocalcinosis (CC) of triangular fibrocartilage (17 patients [100%]), CC of knee (9 patients [53%]), CC or narrowing of metacarpophalangeal joints (7 patients [41.2%]), CC of metatarsophalangeal joints (4 patients [23.5%]), CC of symphysis pubis (1 patient [5.8%]), CC of glenohumeral joint (1 patient [5.8%]) and scapholunate advanced collapse (5 patients [29.4%]). None of these patients developed typical RA-like erosions.

Conclusion

CPPD disease can mimic seronegative RA at baseline and is important in the differential diagnosis of seronegative arthritis at baseline and during follow-up. The prevalence of CPPD patients in our early seronegative RA patients was 3.9%, the percentage was 7.0% among patients ≥60 years at baseline.

Clinical and Experimental Rheumatology 2020; **38**: 99-106.

Calcium pyrophosphate dehydrate crystals

Calcium pyrophosphate dehydrate (CPP) crystals and CPP deposition disease (CPPD) are associated with a variety of clinical pictures, especially in the elderly, which are frequently asymptomatic.

CPPD (I)

- Is a term which comprises many clinical features.
- CPP crystal arthritis, which is an acute arthritis that has been called “pseudo gout”, resembling acute gout arthritis.
- It is manifested as mono, or oligo arthritis and some times as polyarticular disease.

CPPD (II)

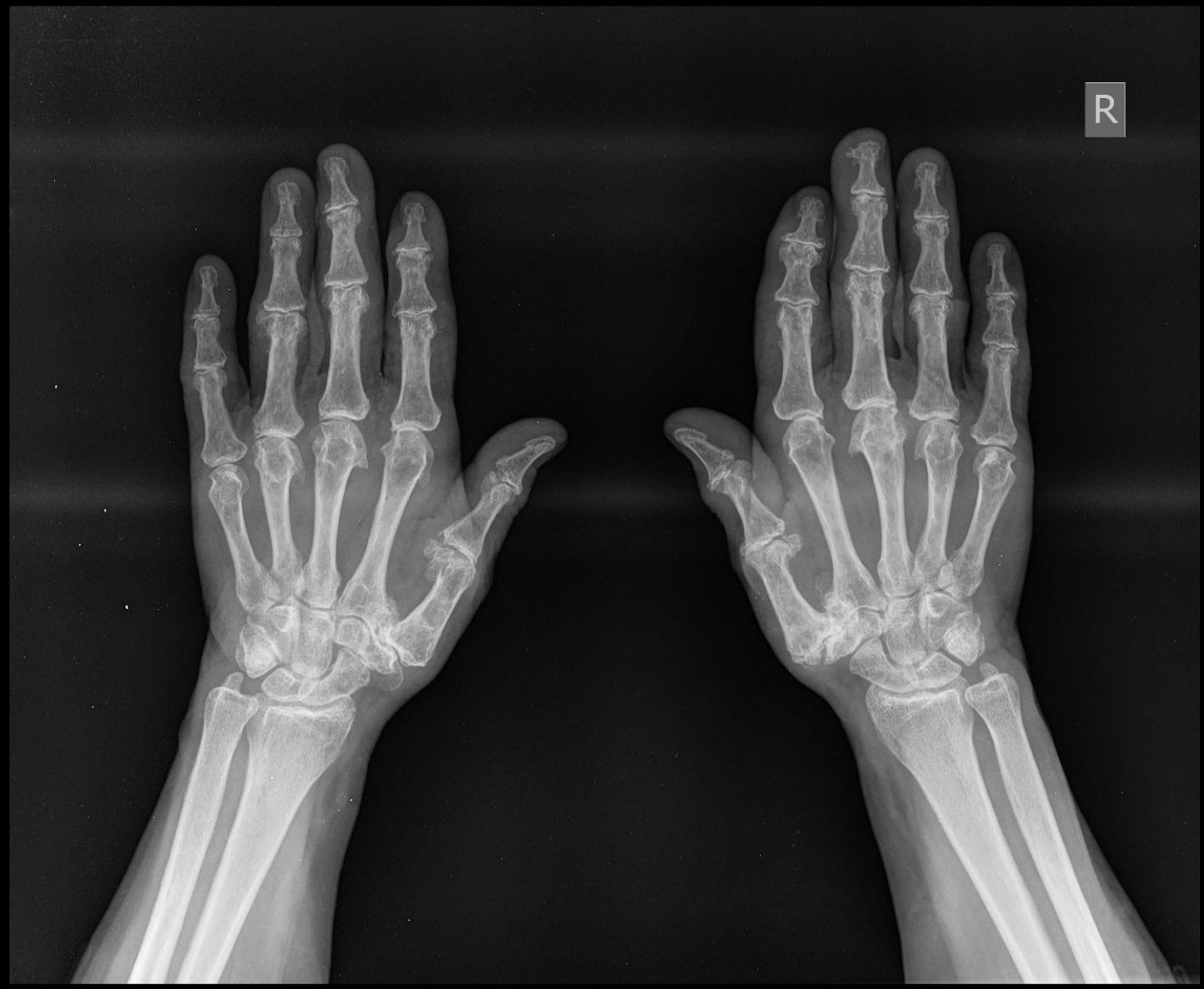
- Another form of CPPD is the chronic CPP crystal inflammatory arthritis, which may mimic RA with long standing polyarticular disease called “pseudo-RA”.
- Chondrocalcinosis (CC) is a CPPD disorder characterized by CPP crystals deposition in the cartilage.
- OA with CPPD is the most common form of CPPD disorder.

Diagnosis of CPPD

- Requires the identification of CPP crystals in the synovial fluid with the characteristic finding of rod-shaped crystals with weakly positive birefringence by compensated polarized light microscopy.
- Conventional radiography (CR) of the affected joints is a useful screening tool for CPPD diagnosis.
- Musculoskeletal ultrasonography (MSUS) and dual energy CT scan are more appropriate and sensitive techniques.
- The laboratory tests are usually normal but, in cases of acute arthritis, or chronic inflammatory arthritis the acute phase reactants are elevated.

Radiographic finding of CPPD

- Comprise the deposition of CPP crystals into fibrous and/or hyaline cartilage, in synovial capsules, tendons and ligaments, which visualized very well with CR.
- The most common sites of CPPD deposition include: the knees, pubic symphysis and hands.
- As regards to the hands, in these locations one must observe CPP crystals deposition in the joint capsule and as a consequence of the chronic inflammation there is a squaring of the bone ends, joint space narrowing and hook like osteophytes formation.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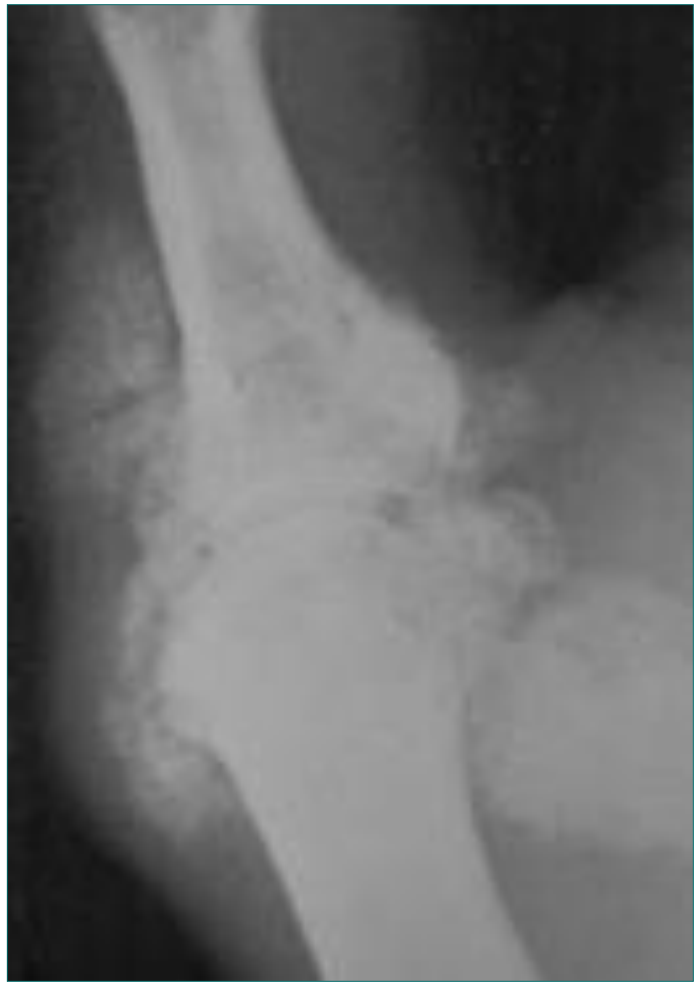
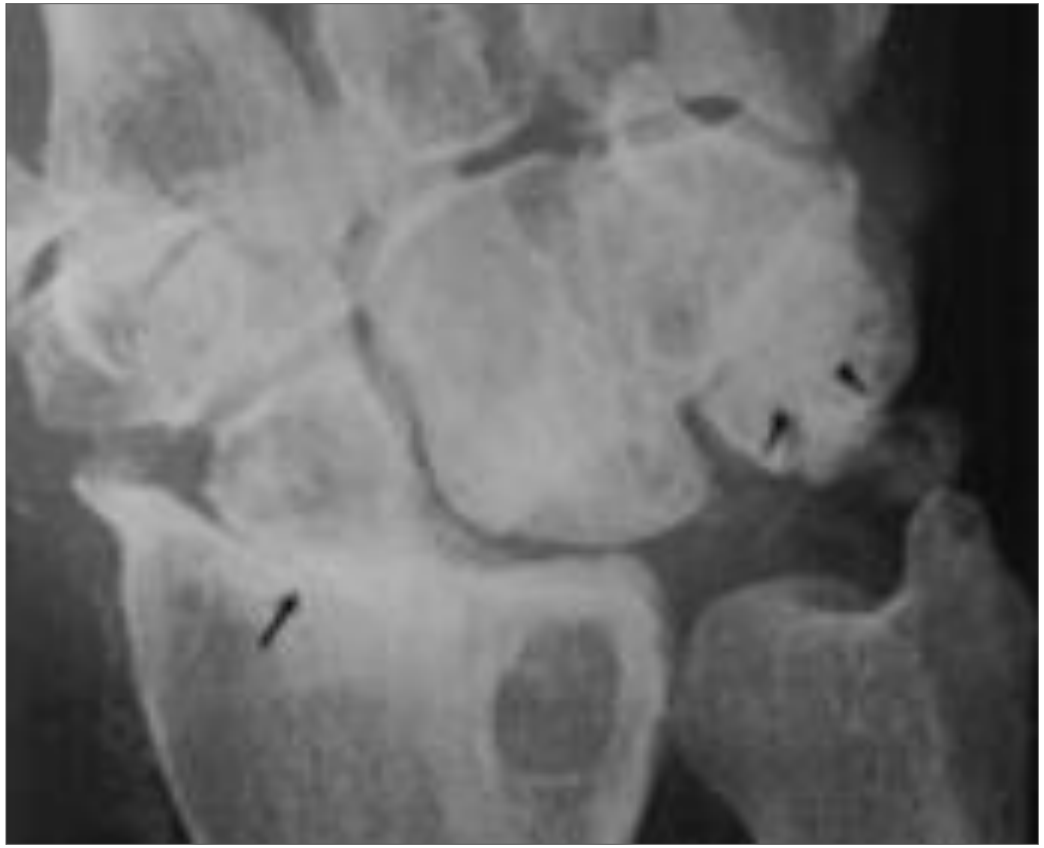


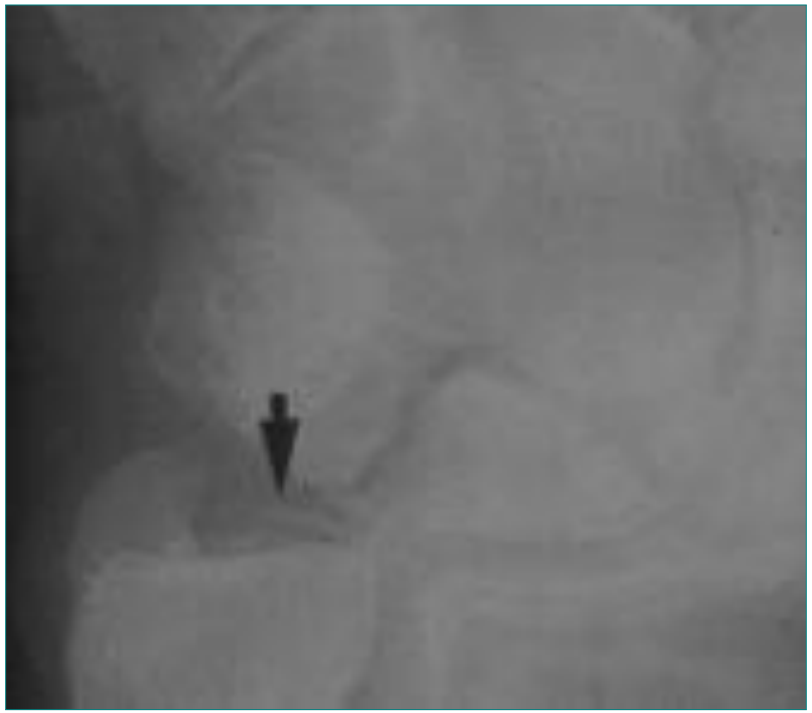


CPPD treatment

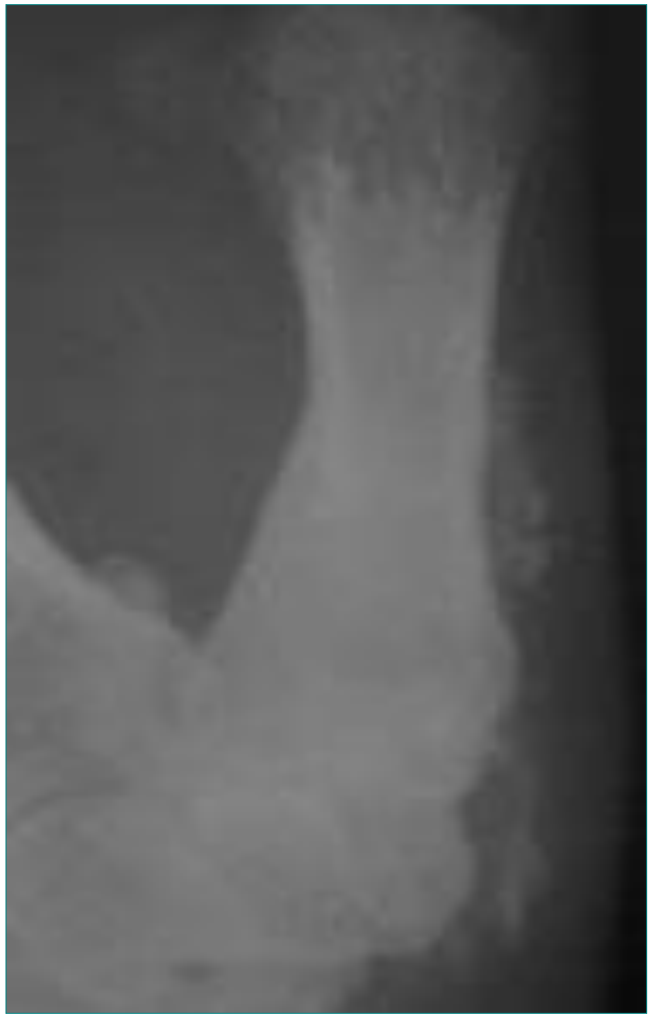
- In the acute form of the disease: intraarticular steroids injection, NSAIDs and colchicine.
- In the chronic forms: oral steroids (10-15mg/day of prednisone) for short period of time, NSAIDs, or/and colchicine. HCQ, or MTX have been used in some studies with controversial results. Anakinra is used in severe cases.

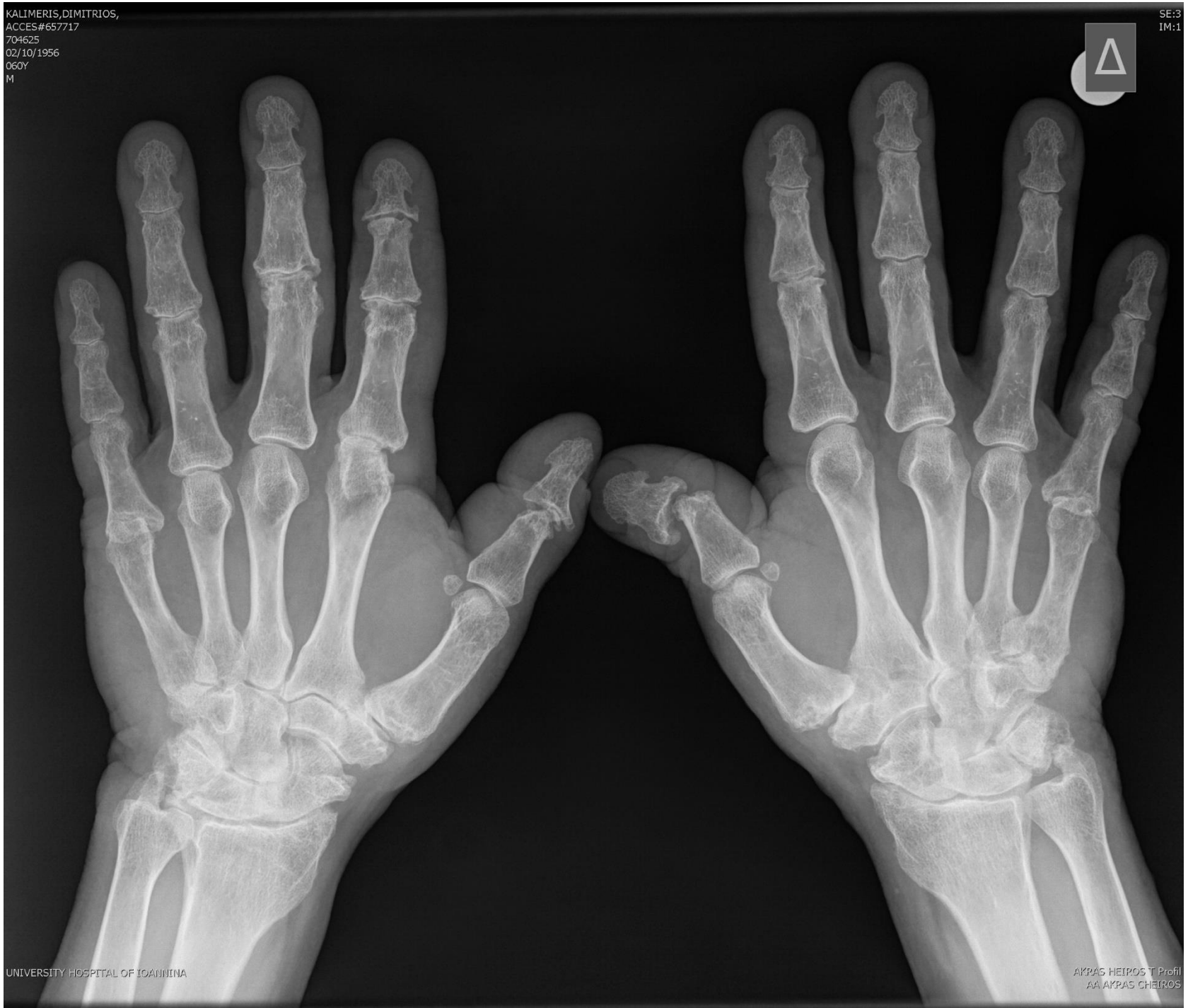
Clinical usefulness of conventional radiography

Cartilage calcification (Chondrocalcinosis)



Tendinous and soft tissue calcifications

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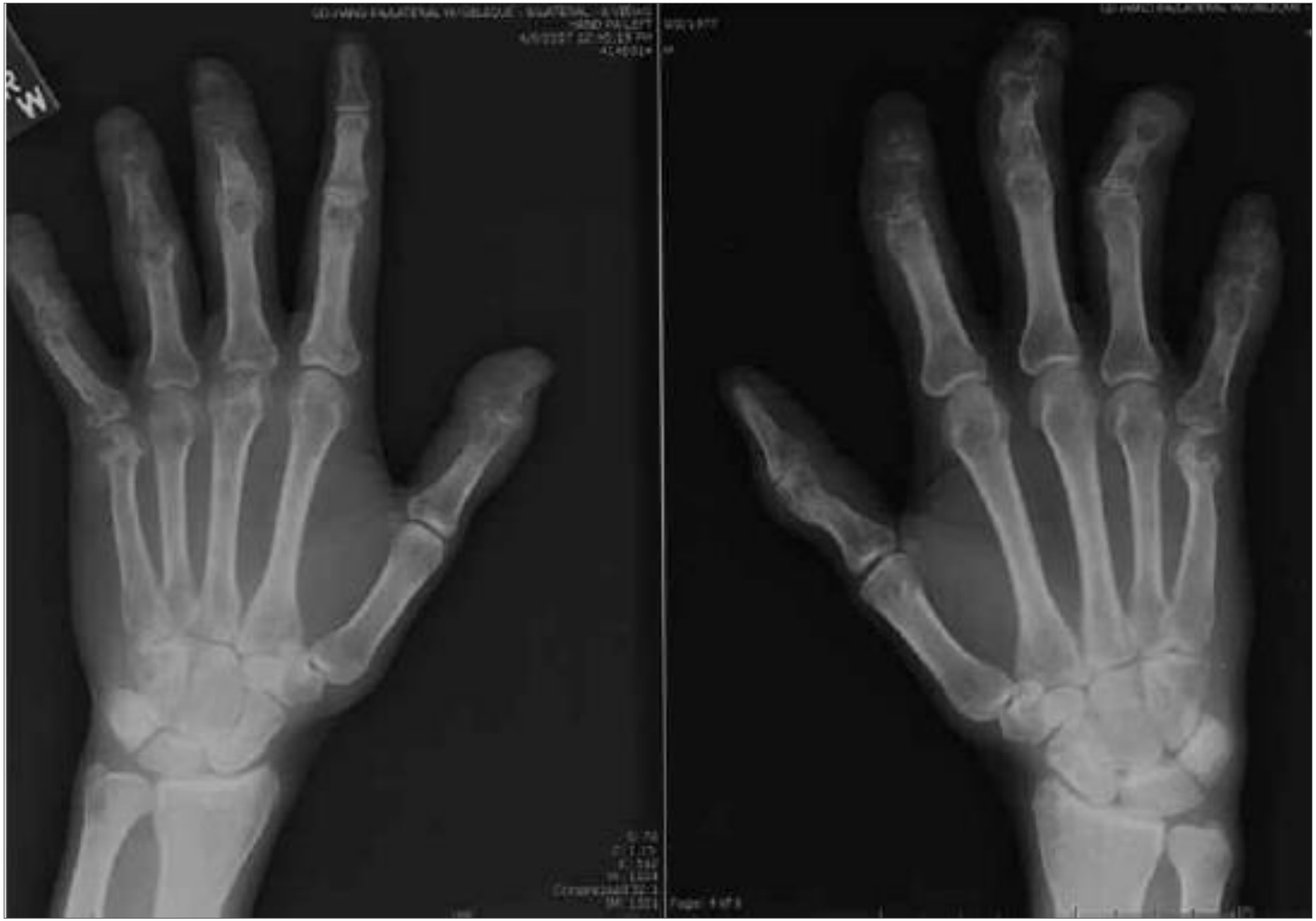
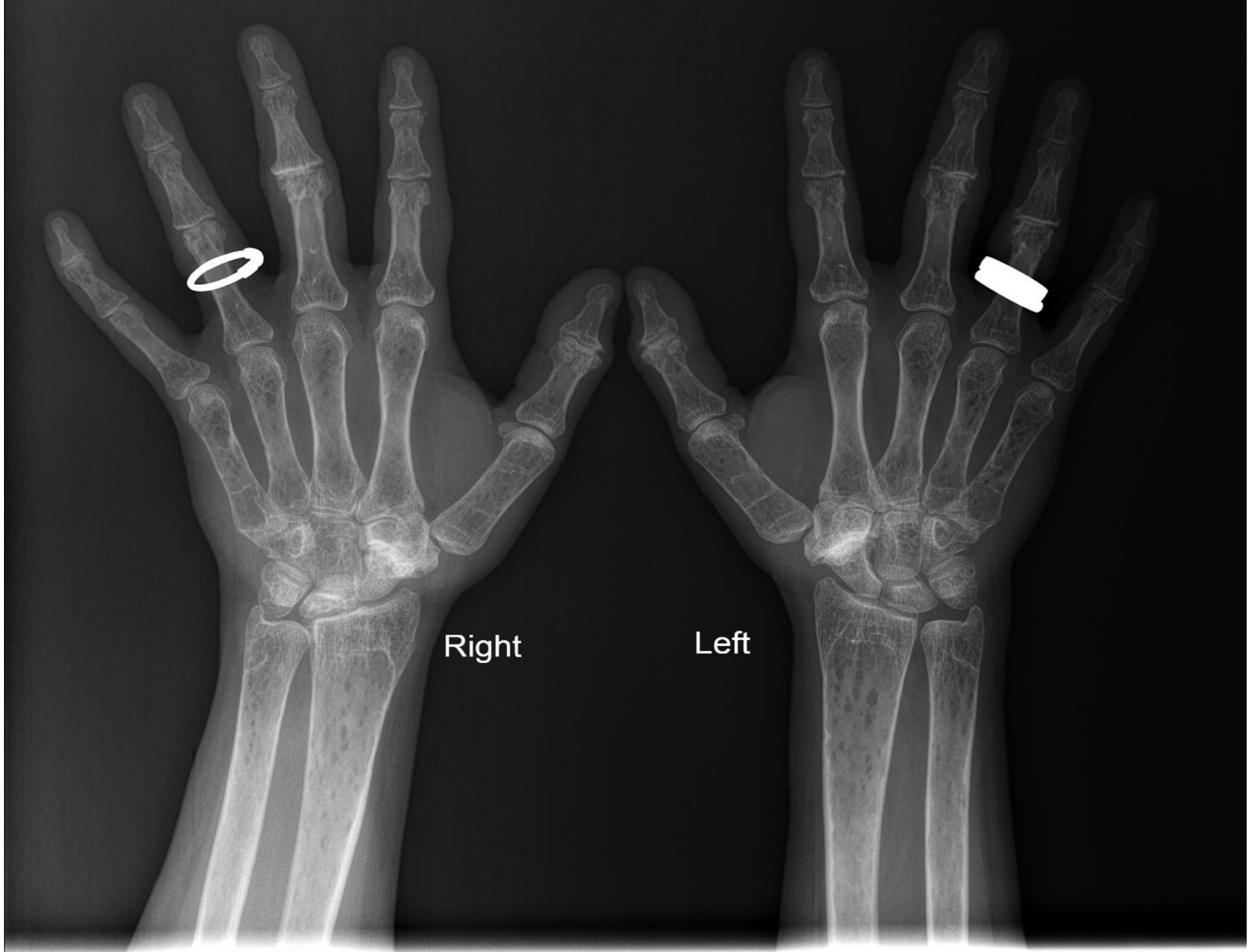
Sarcoidosis



Shanmugam s, Brent LH. J Rheumatol 2008;35:1892


Right
Left

Recommendations:
When to Take Films?

- At the first visit, time of diagnosis
- In patients with persistently active disease, repeat after 6 or 12 months
- Radiographs in the event of a change of therapy
- In clinical trials to determine the clinical efficacy of the investigated drug.

EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT)

B Combe, R Landewe, C Lukas, H D Bolosiu, F Breedveld, M Dougados, P Emery, G Ferraccioli, J M W Hazes, L Klareskog, K Machold, E Martin-Mola, H Nielsen, A Silman, J Smolen and H Yazici

Ann Rheum Dis 2007;66;34-45; originally published online 5 Jan 2006;
doi:10.1136/ard.2005.044354

Table 4 Final set of 12 recommendations on the management of early arthritis based on both evidence and expert opinion

- Arthritis is characterised by the presence of joint swelling, associated with pain or stiffness. Patients presenting with arthritis of more than one joint should be referred to, and seen by, a rheumatologist, ideally within six weeks after the onset of symptoms.
- Clinical examination is the method of choice for detecting synovitis. In doubtful cases, ultrasound, power Doppler, and MRI might be helpful to detect synovitis.
- Exclusion of diseases other than rheumatoid arthritis requires careful history taking and clinical examination, and ought to include at least the following laboratory tests: complete blood cell count, urinary analysis, transaminases, antinuclear antibodies.
- In every patient presenting with early arthritis to the rheumatologist, the following factors predicting persistent and erosive disease should be measured: number of swollen and tender joints, ESR or CRP, levels of rheumatoid factor and anti-CCP antibodies, and radiographic erosions.
- Patients at risk of developing persistent or erosive arthritis should be started with DMARDs as early as possible, even if they do not yet fulfil established classification criteria for inflammatory rheumatological diseases.
- Patient information concerning the disease and its treatment and outcome is important. Education programmes aimed at coping with pain, disability, and maintenance of work ability may be employed as adjunct interventions.
- NSAIDs have to be considered in symptomatic patients after evaluation of gastrointestinal, renal, and cardiovascular status.
- Systemic glucocorticoids reduce pain and swelling and should be considered as adjunctive treatment (mainly temporary), as part of the DMARD strategy. Intra-articular glucocorticoid injections should be considered for the relief of local symptoms of inflammation.
- Among the DMARDS, methotrexate is considered to be the anchor drug, and should be used first in patients at risk of developing persistent disease.
- The main goal of DMARD treatment is to achieve remission. Regular monitoring of disease activity and adverse events should guide decisions on choice and changes in treatment strategies (DMARDs including biological agents).
- Non-pharmaceutical interventions such as dynamic exercises, occupational therapy, and hydrotherapy can be applied as adjuncts to pharmaceutical interventions in patients with early arthritis.
- Monitoring of disease activity should include tender and swollen joint count, patient's and physician's global assessments, ESR, and CRP. Arthritis activity should be assessed at one to three month intervals, for as long as remission is not achieved. Structural damage should be assessed by radiographs of hands and feet every 6 to 12 months during the first few years. Functional assessment (for example, HAQ) can be used to complement the disease activity and structural damage monitoring.

Conclusions

- The assessment of joint pathology in patients with clinical manifestations of peripheral arthropathy should begin with CR.
- CR is the best imaging, as an initial screening test to evaluate any changes occurring in the joints and bones.
- It is an easy and available technique, it is inexpensive, relatively safe and provides immediate information in the established disease and helps physicians to differentiate one disease from another.

Conclusions

- Hand and wrist plain radiographs are simple and valuable imaging tools for the diagnosis of an established arthropathy
- Their diagnostic value are high when associated with the clinical picture of the patient
- Hand and wrist radiographs are the “disease mirror” for arthropathies

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REVIEW

Conventional radiography of the hands and wrists in rheumatoid arthritis. What a rheumatologist should know and how to interpret the radiological findings

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