RHEUMATOLOGY POTPOURRI
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COLORADO CENTER FOR ARTHRITIS AND OSTEOPOROSIS
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DISCLOSURES
• I HAVE NO DISCLOSURES

OBJECTIVES
AT THE CONCLUSION OF THE PRESENTATION, LEARNERS WILL BE ABLE TO:
1. IDENTIFY CLINICAL PEARLS WHICH MAY BE BENEFICIAL IN THE DIAGNOSIS AND MANAGEMENT OF RHEUMATIC DISEASES
2. UNDERSTAND THE IMPACT RHEUMATIC DISEASES HAVE AND TREATMENTS HAVE ON PRIMARY CARE PRACTICE
3. RECOGNIZE NEW TREATMENTS AND MANAGEMENT FOR RHEUMATIC DISEASES
TOPICS

- SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
- LABORATORY TESTING: THE ANA
- PSORIATIC ARTHRITIS (PSA)
- SCLERODERMA
- GIANT CELL ARTERITIS
- OSTROPOROSIS
- GOVT
- TNF INHIBITORS
- MAUGNANCY RISK
- PERIOPERATIVE MANAGEMENT
- HAND OSTEOARTHRITIS
- PSOROMYALGIA

What's the differential diagnosis?

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)
SLE DIAGNOSIS – SLICC CRITERIA


Minimum of 4 criteria with at least one from each category

OR

Lupus nephritis in the presence of ANA or dsDNA antibodies

SLE TREATMENT: HYDROXYCHLOROQUINE – THE WONDER DRUG?


Benefits of HCQ in SLE

HCQ DOSING

THE GREAT DEBATE AT ACR 2018:

HYDROXYCHLOROQUINE DOSING FOR SLE
If an ANA is indicated, the initial screening test should be an ANA using immunofluorescence (ANA by IFA).

A positive ANA can be found in normal individuals and in patients with other autoimmune diseases.
CAUSES OF A + ANA

- Rheumatic / Connective Tissue Diseases
- Thyroid Disorders
  - Hashimoto’s, Graves’s Disease
- Autoimmune Disorders of the Liver
  - Autoimmune Hepatitis, Primary Biliary Cirrhosis
- Multiple Sclerosis
- Infection Diseases
  - Hepatitis C, HIV, Parvovirus, Bacterial Endocarditis, Syphilis
- Malignancy
  - Lymphoma, Paraneoplastic Syndromes
- Inflammatory Bowel Disease
- Lung Disorders
  - Idiopathic Pulmonary Fibrosis

5 CLINICAL PEARLS ON ANA TESTING

3. A + ANA in a 1:40 or 1:80 titer is seldom pathogenic.

4. A + ANA in a high titer may precede the development of a connective tissue disease by years.
5 CLINICAL PEARLS ON ANA TESTING

Don’t repeat the ANA once it has been checked.

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Spondyloarthropathies (SpAs)

Psoriatic Arthritis (PsA)

Ankylosing Spondylitis (AS)

Undifferentiated SpA (USpA)

Reactive Arthritis (ReA)

Spondyloarthropathies (SpAs)

Inflammatory Bowel Disease-Associated SpA (IBD-SpA)

Juvenile-Onset SpA
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SCLERODERMA

https://health.clevelandclinic.org

Scleroderma Renal Crisis (SRC)
1st Line: ACEI
2nd Line: ACE + CCB
3rd Line: ACE+ CCB+ ARB

Pulmonary Arterial Hypertension (PAH)
1st Line: PDE5 inhibitors
2nd Line: PDE4 inhibitors + endothelial receptor antagonists
3rd Line: Prostanoids

Interstitial Lung Disease (ILD)
Induction: Mycophenolate, IV Cytoxan, Rituximab
Maintenance: Mycophenolate

Raynaud’s
1st Line: CCB
2nd Line: CCB + PDE5I
3rd Line: ARB or new CCB

Skin Involvement (MRSS)
MRSS 24 – MTX, MMF
MRSS 32 – MMF, MTX, IV CYC, and HSCT

Fernandez-Codina et al. A&R, 2018

Diffuse, Scleroderma

Scleroderma Renal Crisis (SRC)
1st Line: ACEI
2nd Line: ACE + CCB
3rd Line: ACE+ CCB+ ARB

Raynaud’s
1st Line: CCB
2nd Line: CCB + PDE5I
3rd Line: ARB or new CCB

Skin Involvement (MRSS)
MRSS 24 – MTX, MMF
MRSS 32 – MMF, MTX, IV CYC, and HSCT

Fernandez-Codina et al. A&R, 2018
75 patients in 26 centers randomized to either monthly cyclophosphamide vs. myeloablative autologous stem cell transplant

Patients followed for 4.5 years, aged 18-69 years, 80% white and 64% female

Patients had scleroderma for at least 5 years and either pulmonary or renal disease

End points at 54 months included:

- Global rank composite score
- Death
- Event free survival
- Forced vital capacity
- HAQ disability index
- Modified Rodnan score

At baseline, mean Rodnan skin score of 30, DC1O 53% and 97% had lung involvement

Event free survival

- 79% HSCT
- 50% CYC
- p=0.02*

Initiation of disease modifying drugs

- 9% HSCT
- 54% in CYC
- p=0.001*

Sullivan et al. NEJM, 2018
At 72 months - event free survival
74% HSCT
47% CYC
p=0.03*

Overall survival
85% HSCT
51% CYC
p=0.02*

Treatment related mortality
6% HSCT
0% CYC

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- GIANT CELL ARTERITIS

GIAN T CELL ARTERITIS - DIAGNOSIS

Thorsten et al. Dtsch Internat, 2013
GIANT CELL ARTERITIS DIAGNOSIS

Giant Cell Arteritis: Diagnostic Accuracy of MR Imaging of Superficial Cranial Arteries in Initial Diagnosis—Results from a Multicenter Trial

Kliè et al. Radiology, 2014

GIANT CELL ARTERITIS TREATMENT

Finally, an alternative to prednisone monotherapy!

• 251 PATIENTS FROM 14 COUNTRIES
• DEMOGRAPHICS: LATE 60S>75% FEMALE, >95% WHITE
• PRIMARY OUTCOME: SUSTAINED STEROID FREE REMISSION FROM WEEKS 12-52
• SECONDARY OUTCOME: RATE OF REMISSION IN EACH TZD GROUP VS PLACEBO/PREDNISONE GROUP

TZD 162 mg once weekly + 26 week prednisone taper (N=100)
TZD 162 mg every other week + 26 week prednisone taper (N=50)
Placebo + 26 week taper (N=50)
Placebo + 52 week taper (N=50)
Sustained remission at 52 week

Treatment groups

Significantly more patients in sustained remission at 52 weeks in the TZD group Compared to prednisone, p=0.001*

Time to first flare significantly later in TZD group vs. prednisone; p=0.001*

Significantly less prednisone use in the tocilizumab groups vs prednisone; p=0.01*

Serious adverse events
14-15% in TCZ
22-25% in placebo
TOPICS

- Systemic Lupus Erythematosus (SLE)
- Laboratory Testing: The ANA
- Psoriatic Arthritis (PSA)
- Scleroderma
- Giant Cell Arteritis
- Osteoporosis
- Gout
- TNF Inhibitors
  - Risk of Malignancy
  - Perioperative Management
- Hand Osteoarthritis
- Fibromyalgia

OSTEOPOROSIS – TREATMENT OPTIONS

Antiresorptive agents

- Oral Bisphosphonates
  - Alendronate (Fosamax®) – Most Affordable
  - Benefit Beyond 3-4 Years, BMD Plateaus at 3-4 Years
  - Risk of Atypical Fractures with Prolonged Use
- Zolendronic Acid (Reclast®)
  - IV Option for Patients with GI Issues
  - Very Long ½ Life

- Denosumab (Prolia®)
  - Strong BMD Gains Over 10 Years (22% Spine, 9% Hip)
  - Shouldn’t Be Stopped Without a Plan

Anabolic agents
ANABOLIC AGENTS

- TERIPARATIDE (Forteo®)
  - COSTLY
  - OVER 19 MONTHS, REDUCED VERTEBRAL FRACTURES BY 65%, NONVERTEBRAL FRACTURES BY 53%
- ABACLOPARATIDE (Tymlos®) – APPROVED IN 2017
  - COSTLY
  - OVER 18 MONTHS REDUCED VERTEBRAL FRACTURES BY 86% AND NON-VERTEBRAL FRACTURES BY 43%

VERO STUDY: TERIPARATIDE VS RISENDRONATE

- 680 POSTMENOPAUSAL WOMEN WITH SEVERE OR TWO MODERATE VERTEBRAL COMPRESSION FRACTURES AND A T SCORE < -1.5

VERO STUDY: TERIPARATIDE VS RISENDRONATE

- AFTER 12 AND 24 MONTHS, FEWER NEW VERTEBRAL FRACTURES SEEN IN THE TERIPARATIDE ARM VS. THE RISENDRONATE ARM (5.4 VS 12%, P=0.0001)
VERO STUDY: TERIPARATIDE VS RISENDRONATE

Teriparatide also bested Risedronate for non-vertebral fractures

DENOSUMAB FREEDOM & EXTENSION TRIAL

- LONG-TERM BENEFITS AND SAFETY OF DEOSUMAB IN POSTMENOPAUSAL WOMEN
- LARGE TRIAL: 4550 WOMEN
- PATIENTS FOLLOWED FOR 8 YEARS

DENOSUMAB group:
8 year gain of 18.4% at lumbar spine and 8.3% at the hip

Crossover group:
5 year gain of 13.1% at lumbar spine and 6.4% at the hip
HOW LONG DOES IT TAKE ANTIRESORTIVES TO WORK?

Antiresortive agents usually only reduce the fracture risk 20-25% and it may take up to 3 years to get a significant benefit.

OSTEOPOROSIS CLINICAL PEARLS

Mild to moderate risk of fracture

Who: Osteopenia with high FRAX T-score between -2.5 and -3.0

Consider Antiresorptive

High risk of fracture

Who: 2+ fractures, recent fracture; T score <-3.0; chronic steroid use

Consider anabolic agent

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  - FIBROMYALGIA

- GIANT CELL ARTHRITIS
- FIBROMYALGIA
2015 ACR/EULAR Gout Classification Criteria
Fields, T. Rheum Dis Clinics, 2019

**8 points required for classification of gout**

**5 GOUT CLINICAL PEARLS**

1. Target uric acid: <= 6 mg/dL in most patients
   <= 5 mg/dL in tophaceous gout or difficult to control gout

   When initiating uric acid lowering therapy, always start prophylaxis against a gout flare and continue it for 2-3 months or until the target uric acid is achieved.

   *combination therapy needed in some patients*

**GOUT PROPHYLAXIS**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dose</th>
<th>Side effects/precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colchicine</td>
<td>0.6 mg BID or QD (oral)</td>
<td>Dose adjustment is CKD</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>75 mg QD (oral)</td>
<td>CAD, PUD, CKD</td>
</tr>
<tr>
<td>Prednisone</td>
<td>5 mg daily (oral)</td>
<td>Weight gain, hyperglycemia</td>
</tr>
<tr>
<td>Anakinra (IL-1 inhibitor)</td>
<td>200 mg daily (sul)</td>
<td>Infection</td>
</tr>
</tbody>
</table>

*combination therapy needed in some patients*
URIC ACID LOWERING THERAPY

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism</th>
<th>Starting Dose/Max Dose</th>
<th>Most common side effects</th>
<th>Precautions/Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allopurinol</td>
<td>XO1</td>
<td>100 mg (50 mg in CKD)/800 mg (oral)</td>
<td>Rash, nausea, LFT elevations</td>
<td>Specific Asian ethnicities, CKD</td>
</tr>
<tr>
<td>Febuxostat</td>
<td>XO1</td>
<td>40 mg /80 mg (oral)</td>
<td>Rash, nausea, LFT elevations</td>
<td>Consider in CKD, caution in CAD</td>
</tr>
<tr>
<td>Probenecid</td>
<td>Uricosuric</td>
<td>250 mg BID x 1 week/500 mg BID (oral)</td>
<td>Nausea, light-headedness</td>
<td>Prescribe with a XO1</td>
</tr>
<tr>
<td>Lesinurad</td>
<td>URA T1 inhibitor</td>
<td>200 mg daily (oral)</td>
<td>Renal Cl abnormalities, headaches</td>
<td>Prescribe with a XO1</td>
</tr>
<tr>
<td>Pegloticase</td>
<td>Urate oxidase enzyme</td>
<td>8 mg/kg q 2 weeks (IV)</td>
<td>Infusion reactions</td>
<td>Discontinue XOI, check G6PD</td>
</tr>
</tbody>
</table>

Check uric acid q 2-3 weeks until target achieved

CARES TRIAL – CV SAFETY IN FEBUXOSTAT?

- QUESTIONABLE CONCLUSIONS
- IN SECONDARY ANALYSIS CV DEATH HIGHER IN FEBUXOSTAT GROUP
- LARGE # OF DROP OUTS IN TRIAL AND MOST PATIENTS STOPPED ULT PRIOR TO DEATH

ALLOPURINOL IN CKD

- INITIATE AT A LOW DOSE OF 50 mg/DAY AND TITRATE UPWARDS AS TOLERATED
- INCREASE BY 50 mg q 2-3 WEEKS UNTIL TARGET ACHIEVED
- PRESENCE OF HLA*B5801 INCREASES THE RISK OF ALLOPURINOL HYPERSENSITIVITY
- CONSIDER CHECKING IN HANS CHINESE, KOREAN OR THAI ETHNICITIES
2. Never stop ULT in the midst of a gout flare or initiate ULT during a gout flare.

3. Uric acid levels may be artificially low during a gout flare.

4. Dietary changes alone usually only have a mild impact on uric acid levels.
GOUT CLINICAL PEARLS

If it doesn’t fit pursue an alternative diagnosis
Dx of podagra: TB, PsA, RA, Lyme

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RISK OF RECURRENT MALIGNANCY WITH TNF-INHIBITOR TREATMENT
Results of interest:

Tumor Necrosis Factor Inhibitors and Cancer Recurrence in Swedish Patients With Rheumatoid Arthritis:
A Nationwide Population-Based Cohort Study

7.3 years after initial cancer dx

<table>
<thead>
<tr>
<th>Group</th>
<th>TNF inhibitor (467)</th>
<th>Matched control (2164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% cancer recurrence</td>
<td>42 (9%)</td>
<td>155 (7.2%)</td>
</tr>
<tr>
<td>Mean follow-up (years)</td>
<td>5.3</td>
<td>4.3</td>
</tr>
</tbody>
</table>

HR = 1.06, 95% CI 0.73-1.54

Despite channelling bias, TNFi use
Not associated with increase in cancer

PERIOPERATIVE MANAGEMENT OF DMARDS AND BIOLOGICS

2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty

Goodman et al, ACR 2017
PERIOPERATIVE MANAGEMENT OF DMARDS AND BIOLOGICS

DO NOT HOLD
• DMARDS
  • METHOTREXATE
  • SULFASALAZINE
  • LEFLUNOMIDE
  • HYDROXYCHLOROQUINE
  • AZATHIOPRINE
  • AYCPHENOBALATE

HOLD – WHEN TO SCHEDULE SURGERY
• INFliximab (every 6 weeks) – 7 weeks after last infusion
• ETANERCEPT (weekly injection) – 2 weeks after last injection
• RITUXIMAB (Q6 month infusion) – 7 months after last infusion
• TOFACITINIB (daily oral) – one week after last dose

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HAND OA MANAGEMENT

1. EDUCATION AND TRAINING IN ERGONOMIC PRINCIPLES, PACING OF ACTIVITY AND USE OF ASSISTIVE DEVICES SHOULD BE OFFERED TO EVERY PATIENT.

2. EXERCISES TO IMPROVE FUNCTION AND MUSCLE STRENGTH, AS WELL AS TO REDUCE PAIN, SHOULD BE CONSIDERED FOR EVERY PATIENT.

3. ORTHOSES SHOULD BE CONSIDERED FOR SYMPTOM RELIEF IN PATIENTS WITH THUMB BASE OA. LONG-TERM USE IS ADVOCATED.

4. TOPICAL TREATMENTS ARE PREFERRED OVER SYSTEMIC TREATMENTS BECAUSE OF SAFETY REASONS. TOPICAL NSAIDS ARE THE FIRST PHARMACOLOGICAL TOPICAL TREATMENT OF CHOICE.

5. ORAL ANALGESICS, PARTICULARLY NSAIDS, SHOULD BE CONSIDERED FOR A LIMITED DURATION FOR RELIEF OF SYMPTOMS.

6. CHONDROITIN SULFATE MAY BE USED IN PATIENTS WITH HAND OA FOR PAIN RELIEF AND IMPROVEMENT IN FUNCTIONING.

7. INTRA-ARTICULAR INJECTIONS OF GLUCOCORTICOIDS SHOULD NOT GENERALLY BE USED IN PATIENTS WITH HAND OA, BUT MAY BE CONSIDERED IN PATIENTS WITH PAINFUL INTERPHALANGEAL JOINTS.

8. PATIENTS WITH HAND OA SHOULD NOT BE TREATED WITH CONVENTIONAL OR BIOLOGICAL DISEASE-MODIFYING ANTIRHEUMATIC DRUGS.

9. SURGERY SHOULD BE CONSIDERED FOR PATIENTS WITH STRUCTURAL ABNORMALITIES WHEN OTHER TREATMENT MODALITIES HAVE NOT BEEN SUFFICIENTLY EFFECTIVE IN RELIEVING PAIN. TRAPEZIUCTOMY SHOULD BE CONSIDERED IN PATIENTS WITH THUMB BASE OA AND ARTHRODESIS OR ARTHROPLASTY IN PATIENTS WITH INTERPHALANGEAL OA.

10. LONG-TERM FOLLOW-UP OF PATIENTS WITH HAND OA SHOULD BE ADAPTED TO THE PATIENT’S INDIVIDUAL NEEDS.

Kloopenberg et al. BMJ, 2018

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FIBROMYALGIA - DIAGNOSIS

- Fibromyalgia triad
  - Widespread pain
  - Tender trigger points
  - Sleep disturbance
- Hurt all over, impressive ROS history of dysfunction, but normal joint exam
- Aches and pains
- "Total body toothache"

FIBROMYALGIA – CLINICAL PEARLS

- Do not check an ANA unless clinically indicated
- Rule out thyroid disorders and sleep apnea
- Validate symptoms
- Avoid narcotics
  - Tramadol
- Rx options:
  - Duloxetine
  - Lyrica/gabapentin
  - Savella/Elavil
  - Cyclobenzaprine
- Emphasize exercise and non-pharmacological therapy
- Address mood disorders
- Frequent, shorter visits
- Avoid disability, work restrictions okay
- Rheumatologic DDx:
  - Vasculitis (PAN)
  - Raynaud’s
  - Antiphosholipid syndrome
  - Cryptococcosis
  - Buerger’s Disease