Rheumatoid Arthritis: 
Soothing Steve’s Pain

Christopher Penney, MD, ABIM, FACR, FRCPC
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Steve’s Pain

- Steve, 38, presents complaining of:
  - Three months of hand and wrist pain
  - Forty-five minutes of joint stiffness in the morning
- Three months ago, he awoke with bilateral wrist pain. Within a week, the pain spread to his hands.
- Non-prescription ibuprofen has not helped.
- He has been off work for the past week.
- His complete blood cell count, erythrocyte sedimentation rate, urinalysis, creatinine, liver function tests, antinuclear antibody and thyroid-stimulating hormone are all normal.
- **Rheumatoid factor:** Positive (80)
- **X-rays of hands and wrists:** Normal

He is concerned he has rheumatoid arthritis since there is a family history of this condition.

For more on Steve, go to page 51.

What is RA?

Rheumatoid arthritis (RA) is a chronic inflammatory disease of the synovial tissue that leads to joint destruction and long-term disability. It affects 1% of the population and is the most common form of inflammatory arthritis.

Within 20 years of onset, 90% of RA patients have some form of disability. RA causes an economic burden comparable to that of coronary artery disease.

Seventy-five per cent of the time, the onset of polyarthritis in RA is insidious. Usually, the small joints of the hands and feet are involved before the larger joints. At the time of presentation, many patients with RA have normal inflammatory markers. Often they are seronegative for rheumatoid factor and most have normal X-rays.

Often, early on, RA is suspected only because of the symmetrical involvement of the small joints in the hands and feet and the absence of other conditions that imitate RA (Table 1).

The cause of RA is unknown. There is no cure for the condition. Modern treatments are nonspecific, but do target immune processes thought to be important in RA pathophysiology, such as tumour necrosis factor.

Is it important to treat RA early?

There is grade-A evidence that intervention with disease-modifying antirheumatic drugs (DMARDs) in early RA (disease duration less than one year) slows joint damage and improves the long-term outcome.

One recent study indicates that DMARDs introduced three months into the course of RA are more effective than treatment at 12 months, with regards to joint damage and disease activity.
What requires rapid referral to a rheumatologist?

Individuals with joint pain for longer than six weeks and any of the following:³

- three or more swollen joints;
- morning stiffness lasting longer than 30 minutes or
- pain upon squeezing the metacarpophalangeal or metatarsophalangeal joints.

What is the modern treatment paradigm for RA?

The patient is assessed by a rheumatologist within six to 12 weeks of arthritis onset. DMARD therapy is instituted as soon as possible, recognizing that not all patients fulfill the American College of Rheumatology criteria for RA early in the disease.

A tumour necrosis factor (TNF)-blocking drug is used if three to six months of treatment with methotrexate alone or in combination is not successful (Table 2).⁵

What do I need to know about TNF blockers?

- TNF blockers increase the risk of serious infection.
- Before starting, the patient must be screened for latent tuberculosis with a Mantoux test.
- Stop the TNF blocker if the patient develops a bacterial infection. Restart after the infection has resolved.
- Avoid TNF blockers in congestive heart failure.
- There may be an increased risk of lymphoma in individuals on TNF blockers.
- These agents should be stopped two to six weeks prior to surgery and restarted no sooner than two weeks after surgery in order to reduce the risk of infection.
- Rules for coverage vary depending on the insurer.
- These agents are quite expensive (approximately $18,000 per year) and can only be prescribed by a rheumatologist.

Table 1

<table>
<thead>
<tr>
<th>Differential diagnosis for RA</th>
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<tbody>
<tr>
<td><strong>Post-viral arthritis</strong></td>
</tr>
<tr>
<td>• Parvovirus</td>
</tr>
<tr>
<td>• Hepatitis B or C</td>
</tr>
<tr>
<td>• Rubella</td>
</tr>
<tr>
<td><strong>Seronegative spondyloarthritis</strong></td>
</tr>
<tr>
<td>• Psoriatic arthritis, etc.</td>
</tr>
<tr>
<td><strong>Crystal arthritis</strong></td>
</tr>
<tr>
<td>• Gout</td>
</tr>
<tr>
<td>• Chondrocalcinosis</td>
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<tr>
<td><strong>Collagen vascular disease</strong></td>
</tr>
<tr>
<td>• Lupus, etc.</td>
</tr>
<tr>
<td><strong>Other</strong></td>
</tr>
<tr>
<td>• Paraneoplastic syndrome</td>
</tr>
<tr>
<td>• Sarcoidosis</td>
</tr>
<tr>
<td>• Systemic vasculitis</td>
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</table>

RA: Rheumatoid arthritis

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More on Steve

On your five-minute screening musculoskeletal exam, you note the following:

- There is pain and swelling in both wrists and all metacarpophalangeal joints.
- He can only make a 70% fist bilaterally.
- There is pain and swelling in both knees.

What can you do for Steve? For the answer, go to page 52.
Managing Steve

- You phone a rheumatologist and have Steve seen within two weeks. You start him on hydroxychloroquine, 6.5 mg/kg/day, for presumed rheumatoid arthritis.

- The rheumatologist aspirates synovial fluid from Steve's right knee. The fluid is sterile, negative for crystals and inflammatory (8,000 neutrophils per cc).

- The rheumatologist agrees with your diagnosis and immediately starts him on subcutaneous methotrexate along with hydroxychloroquine, sulfasalazine and a non-steroidal anti-inflammatory drug. He is referred to a physiotherapist and an occupational therapist.

- After four months of combination treatment, his joint pain improves, but he still has obvious swelling in multiple joints.

- A tumour necrosis factor blocker is added to his drug treatment program (Table 2). Within three months, he has no detectable joint tenderness or swelling on examination.

- His hydroxychloroquine, sulfasalazine and anti-inflammatory drug are discontinued without an arthritis flare. He returns to work, but continues to be followed by the rheumatologist.

Table 2

<table>
<thead>
<tr>
<th>Current TNF blockers</th>
<th>Etanercept</th>
<th>Infliximab</th>
<th>Adalimumab</th>
</tr>
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<tbody>
<tr>
<td>Soluble TNF receptor</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>TNF antibody</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Binds to TNF</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Human origin</td>
<td>Entirely</td>
<td>Partially</td>
<td>Entirely</td>
</tr>
<tr>
<td>Half-life</td>
<td>4 days</td>
<td>9 days</td>
<td>13 days</td>
</tr>
<tr>
<td>Concomitant MTX</td>
<td>Optional</td>
<td>Required</td>
<td>Optional</td>
</tr>
<tr>
<td>Administration</td>
<td>Subcutaneously every 2 times/week</td>
<td>Intravenously every 8 weeks</td>
<td>Subcutaneously every 2 weeks</td>
</tr>
</tbody>
</table>

TNF: Tumour necrosis factor  
MTX: Methotrexate

References