REPORTS ON THE RHEUMATIC DISEASES SERIES 5

Hands On

Practical advice on management of rheumatic disease

DIAGNOSING INFLAMMATORY ARTHRITIS

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Introduction

The early recognition of chronic inflammatory arthritis is crucially important as there is increasing evidence of the benefits of early intervention. The concept of a 'window of opportunity'[1] implies that the benefits of early intervention may be disproportionately large and last a long time. The problem in primary care is to recognise an inflammatory arthritis early and refer to secondary care.

The problems faced by a secondary care physician in recognising inflammatory arthritis are similar to those of a primary care physician; I therefore write this manuscript with the benefit of my experience in secondary care, but secure in the knowledge that this is perfectly applicable to primary care.

Assessment

History

The assessment of a patient starts with the history. The points we are particularly interested in are:

- the pattern of joint involvement (does it fit with rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis or reactive arthritis?)
- the pattern of stiffness (more than 30 minutes in the morning for inflammation, stiffening on rest in osteoarthritis)
- the presence of swelling is a cardinal sign of inflammation (but beware 'swollen ankles')
- the relationship of symptoms to use (the stronger the relationship the more mechanical/degenerative the problem).

A good history will not be complete without answers to other questions, although these are not as good at discriminating inflammatory from degenerative disease. The impact of the illness will be crucial in justifying interventions and may contribute to referral. Fatigue may be a prominent symptom in inflammatory conditions, but if associated with poor sleep and pain all over then think of fibromyalgia. The presence of associations of seronegative arthritis (psoriasis, inflammatory bowel disease, uveitis) or multi-system involvement will help complete the picture.

Examination

Examination will confirm any persisting joint involvement (due to the day-to-day variation, some joints, previously involved, may be normal when you see them). It is useful to confirm the presence of synovitis (a soft boggy feel along the joint line), and to give some idea of the severity of the condition (degree of tenderness). Hard, knobbly, crepitating degenerate joints may be recognised.

Recognising a pattern that looks like RA, symmetrical involvement of say the metacarpophalangeal and metatarsophalangeal joints (MCPs and MTPs) especially with swelling, prolonged morning stiffness and 'flares' is more than suggestive of onset of RA. A combination of synovitis and enthesitis (inflammation of tendons where they attach to bones) is suggestive either of a seronegative or a reactive arthritis. Prolonged morning stiffness of the spine helped by movement is typical of ankylosing spondylitis provided it is in a young person. Inflammatory arthritis may even start with synovitis around the tendons, rather than in the joints.

Recognising inflammatory arthritis is however rarely that straightforward. It can start anyhow it likes and at the time you first see the patients it may be atypical. Patients should be referred on suspicion in order that time is not lost. Most of us in secondary care would be happy with two to three

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referrals for each genuine inflammatory arthritis. It may be much clearer a few weeks later when we see them but we promise not to think worse of you for that!

> **RED FLAG**
> **If there is a monoarthritis, especially if there is a lot of inflammation (red, hot, swollen, tender) think 'Could this be septic?' and follow the appropriate guideline.**[2]

Investigations

The role of investigations is subject to a variety of views. No investigation will exclude an inflammatory arthritis in someone with an appropriate history and therefore if you are convinced of inflammation and the need for referral then do not delay the referral waiting for the investigations.

Conversely all investigations are subject to false positives. In particular rheumatoid factor is not a screening test for RA. There are too many non-RA conditions such as infections that can cause it to be elevated, so it should only be done in those patients who give a probably inflammatory history, otherwise if positive it will be regarded as false positive. The main use is in classification and slightly in prognosis. It is quite possible to manage a patient with RA without ever knowing their rheumatoid factor status. If positive with an inflammatory history then RA is more likely and referral is encouraged. Measures of acute phase response are similarly non-specific, but if high would suggest that there is inflammation and encourage referral.

X-rays in early disease will usually be normal or only show equivocal changes such as peri-articular osteopenia and are therefore usually unhelpful. If you do see erosions on x-ray then the patient should be referred urgently. My preference is to have the bloods (full blood count (FBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and rheumatoid factor) with the referral but not the x-rays. This allows me to have two points on the graph with the bloods I take and allows me to introduce the idea of RA as a diagnosis, giving the patient time to absorb the information in the **arc** booklets 'Rheumatoid Arthritis' and 'Introducing Arthritis' prior to our subsequent discussions. I will order x-rays of hands and feet at the first appointment as a baseline.

When to refer

The difficulty is to decide what threshold of suspicion should result in referral. What follows is my personal view and there will be variations in views on this. To a certain extent the threshold will depend on the proximity and set-up of your local rheumatology service. Attempts have been made to use screening tools for inflammatory arthritis[3] (see Table 1) and this does give good guidance on the features to look for, but I think that the whole area is much more complicated and that experienced clinicians function on a lot of other features as yet not studied.

TABLE 1. Screening tool for inflammatory arthritis.
(Reproduced from Ann Rheum Dis 2003;62(2):187 with permission from the BMJ Publishing Group.)

The presence or absence of the following items was recorded:

- Early morning stiffness >1 hour
- Characteristic distribution for IJD
- First degree relative with IJD
- Clinical evidence of synovitis
- ESR ≥20 mm/1st h (men), ≥30 mm/1st h (women)
- Positive rheumatoid factor (≥1/80)
- Erosions on hands or feet x-ray
- Benefit from NSAID or steroids

ESR erythrocyte sedimentation rate; IJD inflammatory joint disease; NSAID non-steroidal anti-inflammatory drug

Patients should be referred:

- If **you** are sufficiently suspicious that they have an inflammatory arthritis. You might think this simply from the history even if the examination was normal when you saw them. The presence of swelling of several joints lasting more than a couple of weeks would be very suggestive of inflammation on its own and should probably be referred. If it is coupled with the finding of synovitis on examination then the case for inflammation is made.
- **Recognising synovitis is not always easy and there is no substitute for experience.** Attending your local rheumatology service for a morning as part of your Continuing Professional Development may be time well spent. At this stage it will not be possible to separate say RA from a reactive arthritis which will be self-limiting. Whether you should refer reactive arthritis will depend on a variety of factors. If it is sufficiently transient then there will be no need or indeed time for referral. If it persists too long then referral will be appropriate (too long is when either you or the patient are not content to wait). This is a situation where investigations will affect your expectations and may be helpful. For example a positive rheumatoid factor may indicate persistence (the anti-cyclic citrullinated peptide (anti-CCP) antibody may be more promising in this regard – see below).
- The absence of abnormal investigations should not stop a referral. Indeed most rheumatologists would not want the wait for investigations to delay the referral. If you can decide clinically that you are going to refer then don't wait for the investigations.
- Investigations such as ESR and CRP may be helpful to you where your index of suspicion of inflammatory arthritis is not sufficient for referral by itself and where a high result might persuade you to refer or a low one not to. Similarly, if a positive or negative rheumatoid factor would alter your decision then it is worth doing. In probable reactive arthritis, it might be used as an indicator of persistence and therefore referral although it will still be subject to false positives.

In a study of referrals (from many years ago) we defined various other reasons to refer to your rheumatology service[4]

and any of these might apply to your patient with inflammatory arthritis:

- where there is diagnostic uncertainty and you or the patient are not happy to live with this. This might include a differential diagnosis of fibromyalgia.
- where your explanation has failed to satisfy the patient that there isn't someone, somewhere, who could do more for them. (A rule of three can be helpful here, i.e. if they have been back three times with the same problem you should think whether your management is working.)
- if you or they think a second opinion would be helpful.
- if the impact on the patient's quality of life is large.

In primary care one of the best diagnostic tools you have is 'the passage of time'. Wait and see but **don't wait too long**.

Patients with inflammatory arthritis will usually need treatment before referral. Most will need an anti-inflammatory which they can tolerate and which helps their pain and stiffness. It is very much the role of primary care to start this process. Analgesia using the analgesic ladder is also appropriate.

Most patients with persistent inflammatory arthritis will be offered disease-modifying drugs. I believe that even such relatively non-toxic drugs as sulfasalazine should be started in secondary care. The reason is that it is necessary to have a confident diagnosis and the personal observation of the condition and its evolution over time can be very helpful in future discussions over the risks and benefits of treatment if the first choice is not satisfactory.

The future

As mentioned above, one interesting development is the advent of anti-CCP antibodies, which show better sensitivity and specificity than rheumatoid factor.[5] Anti-CCP testing can be useful in diagnosing early RA. An elevated anti-CCP can be found in a significant number of patients who have a negative rheumatoid factor, the classic test for RA, and therefore can help to make a diagnosis. According to Wiik and van Venrooij,[6] anti-CCP antibodies may be detected in about 50–60% of patients with early RA (as early as 3–6 months after the beginning of symptoms). Early detection and diagnosis of RA allows doctors to begin aggressive treatment of the condition, minimising the associated complications and tissue damage. Anti-CCP may also be ordered to help evaluate the likely development of RA in patients with undifferentiated arthritis (those whose symptoms suggest but do not yet meet the criteria of RA). Again according to Wiik and van Venrooij, approximately 95% of patients with a positive anti-CCP will develop RA in the future. The usefulness of these tests in the primary care setting needs to be evaluated.

The way we manage RA has also changed dramatically with a range of biological drugs which have dragged research outcome tools such as the DAS 28 (a disease activity score that includes a 28-joint count, patient and physician opinion, questionnaires and ESR)[7] and inviolable protocols into the outpatient clinic. The use of several drugs at the same time and the early suppression of inflammation are more common. We are moving to a situation where a swollen joint will be unacceptable. This is of course delivering much better care for patients.

The observation that patients with inflammatory arthritis are at greater risk of cardiovascular disease has also changed practice and it is likely that GPs will have a greater role in prevention of this. This will be discussed in the next set of guidelines on the management of RA (after the first 2 years) due to be released by the British Society for Rheumatology and British Health Professionals in Rheumatology later in 2007.

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continued/

COMMENT

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Rheumatologists aim to see patients with inflammatory joint disease early in the course of the disease and it is reassuring to hear that they too may have difficulties in definitively diagnosing these conditions early on. Inevitably, therefore, in order to catch all those people with inflammatory arthritis during this 'window of opportunity' GPs will refer some patients who turn out to have reactive or degenerative conditions.

Early arthritis clinics have conveyed this message of early referral very well where they exist. In other areas there are still worrying lengths of wait to see a rheumatologist. Erosions on ultrasound can be seen by 3 months from symptom onset, underlining the aggressive nature of the disease in some patients.

If rheumatoid factor is not sensitive or specific we probably do not need it for diagnosis. The message that comes across is look at pattern of joint involvement, for morning stiffness of more than 30 minutes, and for tender boggy swelling with warmth along the joint line – if you see that you are duty bound to refer immediately; blood results can be sent on later. Lesser degrees of inflammation do occur and it is then that the GP may wish to wait for the inflammatory markers, blood count etc before referring. The place of anti-CCP antibody testing in primary care has yet to be established. It could be argued that people with not much evidence of synovitis but positive anti-CCP antibodies should be referred and, if negative, the patient observed. We await the research.

Finally, will 'Choose and Book' and patient choice help or hinder appropriate timely referral? When early arthritis clinics are available on 'Choose and Book' with links to referral criteria I would be hopeful that patients will be diagnosed earlier. The caveat with this is that we should continue to positively diagnose and treat degenerative conditions and fibromyalgia within primary care so as not to swamp early arthritis clinics.

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