Changing Concept of Early Rheumatoid Arthritis

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Rheumatoid Arthritis (RA) is a chronic progressive inflammatory disease first described by Benjamin C. Brodie in 1819 and coined by AB Garrod in 1858. Rodolf Virchow was the first to point out in 1869 that it could eventually lead to joint deformities and long-term disability. Up to the early 1980’s, it was still generally thought that rheumatoid arthritis ran a benign course in most patients, spontaneous remission could be a possibility, disease-modifying drugs (DMARDs) were prohibitively toxic and symptom relief with nonsteroidal antiinflammatory drugs (NSAIDs) was sufficient in the first few years when the disease was still in its ‘early’ stage before deformities appeared.

This conservative approach has proven to be a total failure. Half of the patients became disabled within 5 years and half were severely disabled or dead after 20 years.

RA is not a benign disease. Early prospective studies has shown that 40% of patients with RA develop joint erosions on x-ray within the first year and 75% do so within 2 years after the onset of symptoms. Using more sensitive imaging technique such as magnetic resonance imaging (MRI), joint damage can occur as early as 4 weeks after onset of symptoms. In one study, 45% of patients with RA developed joint erosions within 4 months. These investigations present strong evidence that joint damage occurs very early in the course of disease.

Although joint pain and swelling contribute mostly to disability in the first 5 years of RA, joint damage progresses at a consistent rate over the course of the disease and it accounts for over 25% of the disability. The statistical association between radiographic damage and disability is strongest with disease duration of over 8 years; however, prevention of structural damage early in the disease is important and is likely to preserve joint function.

Several studies have shown that a delay of treatment with DMARDs by several months, not years, make a difference in long-term outcome of patients with RA. In an open randomised placebo controlled study on 119 patients with early RA, patients were randomised into 2 treatment groups. The early treatment group received hydroxychloroquine (HCQ) immediately after the diagnosis was made. In the late treatment group, HCQ was started 9 months after diagnosis. Both groups of patients were followed up prospectively for 3 more years. Compared with the early treatment groups, the late treatment group did much worse for both pain and physical disability outcomes over the 3 years follow up. A delay of 9 months in starting HCQ, a mild DMARD, has significant impact on long-term patient outcome.

In the past decade, early arthritis clinic has been set up in many European countries. A recent report from one of these clinics compared 2 cohorts of early rheumatoid patients who received different treatment strategies. Patients in the first cohort were initially treated with analgesics, and if they had persistent active disease, they were given either chloroquine or salazopyrine. The median lag time of starting DMARDs was 4 months. Patients in the second cohort were treated given similar DMARD within 2 weeks. After one year, there was no increase in joint damage in the early DMARD treatment group. At 2 years, the group that received early DMARD treatment also did better with less erosion on x-ray. A delay of less than 4 months in initiating DMARD makes a difference in long-term outcome in RA patients. A similar observation was made in the FIN-RAco (FINnish Rheumatoid Arthritis Combination therapy) trial; a delay of 4 months from the onset of symptoms to institution of therapy decreases the ability of single DMARD to induce remission in early RA with a median of 6 months’ duration.

Early treatment of RA is also important in terms of long-term mortality. A recent study examined the long-term mortality outcome of a cohort of 489 patients with RA. Early presenters (<5 years) treated early in the course of disease did better than late presenters (>5 years). In another European prospective study of a cohort treated aggressive with DMARD, there was no increase in mortality after 10 years. The use of methotrexate in the treatment of RA was also associated with 60% reduction in mortality and 70% reduction in cardiovascular mortality.

These observations argue strongly that we need to treat our patients with RA aggressively early in the first few months, not in the first few years, in the course of disease to achieve good results, to prevent long-term joint damage and to reduce premature mortality.
Methotrexate has revolutionised the treatment of RA since the mid 1980’s. Combination DMARDs using methotrexate as the backbone and the availability of leflunomide have improved the result further. Treatment of RA has entered a new era in the past few years with the arrival of anti-TNFα therapy. No joint damage has been reported in ongoing clinical trials after 1 year using each of the 3 anti-TNFα biological agents available.

As joint damage can be demonstrated as early as 4 weeks with MRI, it is tempting to initiate treatment within the few weeks in the early course of disease. Making an accurate and early diagnosis within the first few weeks in RA have been difficult for several reasons. Classical features of established disease such as symmetry, polyarthritis, morning stiffness, high ESR or C-reactive protein and rheumatoid nodules may be absent; IgM-rheumatoid factor is present only in two-thirds of patients while other viral arthritides may need to be excluded. The recent availability of a highly specific test for RA has made this task possible and easier. Anti-cyclic citrullinated polypeptide (anti-CCP) IgG antibody is 96% specific and 50-70% sensitive for RA, even in its early stage. Combining polypeptide (anti-CCP) IgG antibody is 96% specific and proven itself a disease that can be treated early within weeks and must be treated within months.

**References**


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**MCHK CME Programme Self-assessment Questions**

Please read the article entitled “Changing Concept of Early Rheumatoid Arthritis” by Dr. Ka-ho Chan and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 28 February 2005. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Please answer true or false for each multiple item of the following questions:

1. Which of the following statements regarding rheumatoid arthritis are true:

   (i) Viral related polyarthritis can be difficult to differentiate from early rheumatoid arthritis
   True  False

   (ii) Joint erosion occurs as early as 4 weeks after diagnosis of rheumatoid arthritis
   True  False

   (iii) Mortality may be increased if treatment for rheumatoid arthritis is delayed
   True  False

   (iv) Anti-cyclic citrullinated peptide antibodies are helpful in early diagnosis of rheumatoid arthritis
   True  False

   (v) The American Rheumatism Association criteria for rheumatoid arthritis apply well to early rheumatoid arthritis
   True  False

2. Which of the following statements regarding treatment of rheumatoid arthritis are true:

   (i) The old approach of management involving gradual stepping up of therapy results in significant joint damage
   True  False

   (ii) NSAIDs are the first line for management of rheumatoid arthritis
   True  False

   (iii) Seronegative rheumatoid arthritis can be managed with less aggressive treatment
   True  False
ANSWER SHEET FOR FEBRUARY 2005

Please return the completed answer sheet to the Federation Secretariat on or before 28 February 2005 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

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Signature: _____________________________  Contact Tel No.:_________________________

Answers to January 2005 issue

Surgical Treatment for Hepatocellular Carcinoma
1  e  2  e  3  d  4  d  5  e
6  T  7  F  8  F  9  T  10  T

(iv) Methotrexate is one of the most popular DMARD in use
True   False

(v) The use of mild DMARD such as hydroxychloroquine does not alter clinical outcome no matter treatment started early or not
True   False

3. Which of the following statements regarding anti-cyclic citrullinated peptide (CCP) antibodies are true:
(i) Anti-CCP antibodies have high sensitivity for diagnosis of rheumatoid arthritis True   False

(ii) Anti-CCP antibodies present in patients’ serum before the onset of rheumatoid arthritis True   False

(iii) Anti-CCP antibodies offer early and specific diagnosis of rheumatoid arthritis True   False

(iv) Anti-CCP antibodies can be detected in polymyalgia rheumatica True   False

(v) Anti-CCP antibodies are not present in seronegative rheumatoid arthritis True   False

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