Review Article

Atypical Presentations of Rheumatoid Arthritis

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Abstract

Rheumatoid Arthritis is a common rheumatological problem. It may involve many extra articular organic systems along with joints. Disability resulting from progressive Rheumatoid Arthritis has an enormous effect on our society and it is a drain for human as well as monetary resources. About half of all patients with Rheumatoid Arthritis stop working by 10 years, 90% by 30 years. Disability may be due to both to obvious limitation of joint destruction and pain to complication of therapy and to extra articular problems of Rheumatoid Arthritis, it also shortens life significantly. As inflammatory chronic poly-arthritis, most of the cases of Rheumatoid Arthritis present with constitutional symptoms with typical presentation but a group of patients may produce difficulties for diagnosis due to a variety of atypical presentations. Knowledge about atypical presentations & onset of rheumatoid arthritis is very important to prevent disabling complications of rheumatoid arthritis resulting from joint failure as well as from non musculoskeletal involvement.

Introduction

Rheumatoid arthritis is a common rheumatological disease all over the world but history of it's evolution is not clear yet. The term rheumatoid arthritis was first coined by Sir Alfred Garrod in 1876. The first convincingly clear description of the disease was that of Landre Beauvais in 1800. The term rheumatoid arthritis was officially adopted by the Empire Rheumatic Council in 1922 and by American Rheumatic Association only by 1941[1].

Though rheumatoid arthritis is thought of as a prototypical autoimmune disease its aetiology still is not clearly known. During the past decades, important contribution of imunogenetic susceptibility and triggering or persisting microbial infection is thought to play some important role in initiation of its pathogenesis. Rheumatoid synovitis leads destruction of articular cartilage and bony erosions and joint deformity. But the course of disease is not same in all people even not in the same individual. In some the disease may be progressive, devastating, in some it may follow course of exacerbation and remission and in some it may be of mild variety.

As inflammatory chronic polyarthritis, rheumatoid arthritis patients presents with constitutional symptoms with typical presentations. But a group of patients may produce difficulties for diagnosis due to a variety of atypical presentations like long lasting constitutional symptoms before joint manifestations, extra articular manifestation which are not directly related to musculoskeletal system. Patient may present with unusual weight loss. With refractory rheumatoid arthritis[2-3], cachecxia, fever of unknown origin[4]. For this, diagnosis may be delayed subsequently patients suffer

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from irreversible musculoskeletal damage. Again patient may present with complications. Therefore recognition of these atypical presentations in very important which requires high index of clinical suspicions.

Atypical presentation

A typical presentation of RA is inorderly developed polyarthritis symmetrically involving small joints. Particularly in the hands and wrist. The presentation is countered as atypical or unusual when a patient presents with symptoms different from symmetric pain in hands and wrists. Atypical rheumatoid arthritis does not fulfill the criteria of Rheumatoid Arthritis (RA) but may be included under this category. It is possible with newer imaging techniques such as magnetic resonant image (MRI) or ultrasound (USG) that sub-clinical synovitis may be present. This presentation accounts for less than 1percent to 2 percent of RA patients and the prognosis for this patient is generally good. Because the patients do not fulfill the American College of Rheumatology criteria for RA, they would be excluded from clinical trial and limited evidence based information is available on their treatment response.

Palindromic rheumatism is an example of an inflammatory arthritis that is characterized by flare ups of synovitis occurring at intervals from weeks to months[5]. The joint involvement is generally oligo-articular in contrast to symmetrical arthritis and different joints may be involved in separate flare ups. This flare ups generally last for two to three days and then resolve without any evidence of radiographic damage. Approximately 50% of this patients progress to classic RA over time. Developments of RA occur after chronic Hepatitis C infection. A patient with RA who had preceding evidence of non - A, non - B Hepatitis showed positive serological test for anti-hepatitis C antibody. The manifestation of RA, including progressive poly arthritis and positive serum rheumatoid factors, emerged after the amelioration of hepatitis and persisted for more time indicating that the poly arthritis in this patient was not the prodrome of hepatitis. This HLA-DR 4 and HLA-Dw 54 which are found to be strongly associated with RA in Japan suggested that HCV may trigger the development of RA especially in genetically susceptible individuals[6]. Being relatively common, RA is likely to occur with many other types of chronic diseases. A striking asymmetry or event unilateral involvement has been describe in patients with poliomyelitis, meningioma, encephalitis, neurovascular syphilis, strokes and cerebral palsy[7,8]. Joints are spared on the paralyzed side, and the degree of protection demonstrates a rough correlation with the extension of paralysis[9]. The protective effect on the affected side is less if a neurological deficit develops in a patient who already as RA[10]. Physical trauma in the preceding 6 months is significantly associated with the onset of RA[11].

Incase of late-onset rheumatoid arthritis pitting oedema of the hands at onset is a good prognostic indicator[12]. A patient effected by rheumatoid arthritis (RA) that developed myasthenia gravis (MG) after 20 years of illness. The peculiarity of this case concerns both the rare association between these diseases and the fact that the patients had never assumed disease modifying anti-rheumatic drugs. These treatments have been associated in some clinical reports with the onset of MG during the clinical course of RA[13].

Fever of unknown origin (FUO) is always a diagnostic challenge FUO was best explained by the finding of late-onset rheumatoid arthritis (LORA), which is characterized by acute onset in elderly patients without the usual musculoskeletal manifestations of rheumatoid arthritis. Both the highly increased rheumatoid factor titer and perinuclear antineutrophilic cytoplasmic antibody level in the absence of an alternate explanation indicate that the FUO in this patient was caused by LORA[14].

Diminished autonomic nervous system response is observed in RA of recent onset, most clearly in patients with more severe pain. This suggests that it is associated with primary pathophysiological mechanisms[15]. In case RA smoking may increase the diseases severity, these associations were most pronounced in those with more than 20 pack-years of exposure Cigarette smoking is associated with both subcutaneous nodules and higher serum concentrations of IgA-RF in African Americans with RA, associations that may have important implications for long-term outcomes in this population[16].

Anaemia appeared as a frequent and dynamic manifestation in RA. Recovery and recurrence of anaemia was observed throughout follow up, leading to a longstanding and relatively high prevalence of the condition. Anaemic patients, particularly those with anaemia of chronic disease, seemed to have a more serious course of their RA compared with non-anaemic patients[17]. Onset of rheumatoid arthritis after surgical treatment of Cushing's disease, a patient with Cushing's disease who, shortly after trans-sphenoidal surgical

resection of an adrenocorticotropic hormone secreting pituitary microadenoma and specifically at the time of normalization of her serum cortisol level, developed a subacute episode of symmetric polyarticular synovitis. These patients may represent a natural illustration of the antinflammatory effects of supraphysiological levels of endogenous glucocorticoids[18].

New-onset rheumatoid arthritis after anthrax vaccination. Anthrax vaccine was licensed in 1970. Four cases of rheumatoid arthritis (RA) temporally related to anthrax vaccine have been reported. As the number of administered doses increases, a better understanding of its adverse events profile will be forthcoming[19]. Morning stiffness may influence on early retirement in patients with recent onset rheumatoid arthritis. Severe MS in the early course of the disease has a high impact on RA patients' decision to withdraw from working life. Great attention should be paid to the effective treatment of MS in early RA, to prevent patients from possible untimely decisions that will have long-lasting and costly consequences[20].

Rheumatoid arthritis is the most commonly reported host-related risk factor for septic arthritis. This risk is highest in severe, seropositive, long-standing (mean, 10 years) rheumatoid arthritis responsible for extraarticular symptoms and treated with systemic glucocorticoids. The clinical presentation of the joint infection is often atypical, leading to diagnostic wanderings. In 25% of cases, the infection is polyarticular, with 3.5 involved joints on average. Staphylococcus aureus is the most common causative organism. Despite its low incidence, polyarticular septic arthritis should be routinely considered in the differential diagnosis of rheumatoid flares[21].

A RA patient may present with cerebral vasculitis, Inflammatory vasculitis of the central nervous system is exceedingly rare in patients with rheumatoid arthritis (RA). The symptoms may be misleading. Most of the reported cases occurred in males with long-standing, nodular, destructive, rheumatoid factor-positive disease. Severe constitutional symptoms and prominent extraarticular manifestations of vasculitis were usually present. Patient may present with headache that was unresponsive to symptomatic treatment developed abruptly, together with gait disorders[22]. Rheumatoid arthritis may develop after treatment of other disease. A case of new onset rheumatoid arthritis in previously asymptomatic individual appeared during interferon beta-1B treatment in multiple sclerosis[23]. The presentation, severity and prognosis of rheumatoid arthritis (RA) differ depending on the age of disease onset. Elderly onset RA (EORA[24]: age of onset > 60 years) has been reported to differ from younger-onset RA (YORA) by a more balanced gender distribution, a higher frequency of acute onset often associated with systemic features, more frequent involvement of the shoulder girdle and higher disease activity. The female to male ratio was higher in the YORA group (4.4:1 vs 1.6:1; $p < 0.05$). The distribution of involved joints showed a significantly higher frequency of shoulder involvement in EORA (64% vs 38%; $p < 0.05$) and of feet involvement in YORA (25% vs 52%; $p < 0.05$). Hands and wrists were the most frequently involved joints in all patients[25].

The mode of onset of rheumatoid arthritis may be influenced by environmental factors. There was a statistically significant correlation between mode of the onset and seasonal variations ($P < 0.05$). Rheumatoid arthritis started abruptly more often in springtime, and more insidiously in autumn, whereas in summer and winter there was an equal number of patients with acute or insidious onset of the disease[31].

Atherosclerotic disease is increased in recent-onset rheumatoid arthritis play a critical role for inflammation. Rheumatoid arthritis (RA) patients have increased mortality and morbidity as a result of cardiovascular and cerebrovascular disease. The carotid intima-media thickness (cIMT) and plaque, measured by ultrasound, correlate closely with direct measurement of the local and systemic atherosclerotic burden[26].

The extent of inflammation predicts cardiovascular disease and overall mortality in seropositive rheumatoid arthritis. A retrospective cohort study emphasizes the importance of inflammation as an important risk indicator for CVD and mortality in RA. The positive impact of disease activity reducing treatment on CVD risk and survival is suggested[27].

Excess recurrent cardiac events occur in rheumatoid arthritis patients with acute coronary syndrome. Recurrent ischaemic events and death occur more often after ACS in rheumatoid arthritis. Atypical presentation is commoner in rheumatoid arthritis. There is an urgent need to develop identification and intervention strategies for ACS specific to this high risk group[28]. Breast-feeding may influence the onset of rheumatoid arthritis. In a recent study we demonstrated that the postpartum period, particularly after the first pregnancy,

is a time of increased risk for the development of rheumatoid arthritis (RA) which may reflect hormonal influences, specifically the high level of the proinflammatory hormone prolactin[29]. The onset of RA symptoms is reduced during pregnancy and increased in the postpartum period. These findings might be explained by a delayed clinical onset of RA that started during pregnancy, analogous with the ameliorating effect of pregnancy on the course of existing RA and the flare-up of disease activity in the postpartum period[30]. Pulmonary rheumatoid nodules, a rare disease onset in rheumatoid arthritis; Rheumatoid nodules are a benign differential diagnosis to neoplasia and infection, when round lesions are accidental findings on chest X-ray. Two cases are reported of rheumatoid lung nodules as presenting features of rheumatoid arthritis. In each case, the diagnosis was verified by open biopsy[31].

Conclusion

Reheumatoid arthritis is a chronic or subacute systemic inflammatory disorder principally involving the joints with a peripheral symmetrical nonsuppurative arthritis. Though, mainly it is a joint disease, it often involves many other organ systems of body beyond joints for which it sometimes is designated as rheumatoid disease. Only immunologic study can help a little for diagnosis of rheumatoid arthritis. Furthermore immunologic and other modalities of diagnostic helps are not available every where. Knowledge about atypical presentations & onset of rheumatoid arthritis is very important to prevent disabling complications of rheumatoid arthritis resulting from joint failure as well as from non musculoskeletal involvement.

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