Definition of Disease Flare in Ankylosing Spondylitis: The Patients' Perspective

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ABSTRACT. ***Objective.*** Ankylosing spondylitis (AS) is a systemic disorder occurring in genetically predisposed individuals. The disease course appears to be characterized by bouts of partial remission and flares. However, we have little understanding of what is a flare, why they occur, and what lasting effects they have on the patient. We examine the patient's perception of the factors important in defining flare.

Methods. Twenty group meetings of 7–12 participants were held over a one year period. A summary statement was written at the end of each discussion and patients were asked to sign the statement if they considered it to be an accurate summary of their answers, or to amend the statement where they disagreed.

Results. There were 214 patients questioned (169 men, 45 women; average disease duration 25 years; age of disease onset 22 years). Data show that the main symptoms of flare are pain (100% of groups), immobility (90%), fatigue (80%), and emotional symptoms (depression, withdrawal, anger) (75%). There are 2 types of flare: (1) localized: during which the symptoms affect one area; and (2) generalized: this is a severe event including all the above symptoms and a flu-like illness (fever, sweating) with hot, burning joints, muscle spasm, and increased sensitivity. All patients experience between one and 5 localized flares per year. Fifty-five percent of groups contained patients (n = 85) who experienced a generalized flare. The main perceived triggers of flare were stress (80%) and "overdoing it" (50%). Patients reported that a flare may last anywhere from a few days to a few weeks and relief from flare can be gained by analgesic injections (including opiates) from a doctor, relaxation, sleep, and cannabis (3 individuals). Three-quarters of the groups agreed that there was no longterm effect on the AS following a flare.

Conclusion. There are 2 forms of flare: (1) localized to one area or (2) throughout the entire body. Examining the differences between these types of flares may aid our understanding of the biological mechanism of the disease process of AS and allow us to help relieve the symptoms of flare, a highly painful and often depressing phenomenon. (J Rheumatol 2002;29:954–8)

Key Indexing Terms:
FLARE ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is a systemic disease that occurs in genetically predisposed individuals thought to have been exposed to specific environmental triggers. However, the disease course is poorly defined and there is a great deal of individual variation in terms of prognosis and outcome. Although we accept that a chronic disease can be punctuated by exacerbations and quiescent periods[1], there are also less well defined active "flares." However, an accepted definition of this phenomenon does not exist. In other rheumatic conditions such as systemic erythematosus lupus (SLE) and rheumatoid arthritis (RA) there are marked physical changes that can be quantified. For example, in SLE the SELENA (Safety of Estrogen in Lupus Erythematosus National Assessment)[2] definition of flare includes new/worse stomatitis, serositis, arthritis, fever, vasculitis, nephritis, anemia, or increase in dose of prednisolone. Flares may be predicted by erythrocyte sedimentation rate, anemia, and lymphopenia[3]. In RA, definitions make use of the number of swollen and tender joints[4,5]. However, in spondylitis many changes in disease activity that lead to flare will by their very nature be subjective and difficult to quantify objectively. For example, current measures of disease activity examine pain, fatigue, discomfort, tenderness, and morning stiffness, which are all measures that can be quantified only by the patients themselves. Clinical measures used to evaluate other conditions (i.e., inflammatory markers, swollen joints, etc.) have been found to be of limited value in AS. For example, inflammatory markers such as erythrocyte sedimentation rate (ESR), plasma viscosity, and C-reactive protein have been found to be raised in less than 50% of patients with severe disease[6].

We have learned to appreciate that patients' concerns are

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sometimes ignored. For example, in 1993[7] (and in 1996[8]) we focused on fatigue, showing this is a major symptom for many patients. Thus, this study examined patients' perspectives of factors defining a flare. This will allow us to define a flare in terms of symptoms relevant to the patient and what treatment may alleviate this condition, and to examine factors involved in activating the disease, and perhaps aid our understanding of the biological mechanism of pathogenesis in AS.

MATERIALS AND METHODS

Patients. Twenty group meetings of patients with AS (defined by the New York criteria[9]) attending the Bath Intensive Management Program were held over a one-year period. Patients are referred to the hospital program by their general practitioner and therefore may have had more severe disease than non-course AS patients. All participants in the program consented to participate. All meetings were held in the living room of the patients' accommodation and patients were assured that participation was voluntary and would not affect their treatment. Ethical approval was granted and no patients were paid for their participation.

Group Meetings. The sessions lasted 30–40 minutes and to enhance validity, a summary statement was written (by SB) at the end of each discussion. Participants were asked to sign the statement if they considered it an accurate summary of their deliberations, or to amend the statement where they disagreed. The group came to a consensus at the end of each session. The sessions were not all tape-recorded as some patients did not want to be identified on a recording. However, written notes (not including patient names) were taken for all meetings. The patients were asked 5 set questions: (1) Have you ever experienced a flare and how would you describe it? (2) What triggers a flare? (3) How long does a flare last? (4) Are there longterm sequelae of the flare? (5) How many times a year do you experience a flare?

Group discussion methods were used as opposed to a mailed survey of the 5 questions, to ensure that patients could discuss their experience of flare and therefore modify the definition of flare to accommodate all patients' perspectives. A single consensus definition of flare (including symptoms, duration, longterm effects, and frequency) was outlined by each group.

RESULTS

There were 214 patients (169 men, 45 women) enrolled in the 20 groups (7–12 patients per group). The average age was 47 yrs (± 14) with disease duration of 25 yrs (± 13) and age at onset 22 yrs (± 7.3).

Description of flare. From the compiled results (Table 1), the single worst aspect of a flare was pain (100% of groups). This was an acute pain that differed from normal baseline AS pain. Additional and related symptoms included immobility (90% of groups), which is unlike stiffness but was described as being "seized up," overwhelming fatigue (80% of groups), and emotional symptoms (70% of groups) such as depression, anger or fear accompanying the physical expression of flare.

Although all patients reported experiencing flares, there were 2 clearly different types identified (Table 2). The first type, which had been experienced by all participants, is a localized flare involving pain and immobility in one area such as the knee, neck, ankle, or localized area of the back. It may be accompanied by fatigue and some emotional symptoms. The joint may be hot and burning and there may be a cramp-like pain in the muscles. This localized flare may start in one area and move to other areas, although only one or 2 areas are involved at a time. The main symptom is a stabbing pain in one area.

The second type of flare is a generalized flare involving the whole body and had been experienced by roughly 40% of the patients questioned (85/214). This is an infrequent event consisting of all the normal symptoms of AS taken to the extreme. The pain was described variously as paralyzing and like the fluid has come out of the joints and they are scratching each other. There is an associated flu-like ill feeling described as face going grey, sweating, feel like vomiting, and running a temperature. The joints may be burning and inflamed (i.e., swollen, red, painful, and hot), with increased tenderness and sensitivity everywhere. The muscles go into spasm and feel knotted. The person feels crippled with the pain and immobility. Patients report chronic fatigue and emotional changes such as extreme depression.

Individuals who experienced these generalized flares reported that the localized episodes were not really a true flare. They reported that everyone will experience a localized increase in disease activity, but this is not comparable to a true flare, which is a generalized whole body reaction, an acute and devastating phenomenon.

Triggers. The 10 most cited triggers of flare are listed in

Table 1. Symptoms of flare.

Symptom	Percentage Describing Symptom	Patients' Description
Pain	100	Excruciating, incapacitating pain, can't tolerate even the chair, throbbing pain right deep inside Like a knife being jabbed into one area
Immobility	90	Like a lead man, feel crippled, seized up
Fatigue	80	Beyond exhausted, overwhelming, incapacitating
Emotional symptoms	70	Depressed instantly, devastated, debilitated, withdrawn, frustrated and frightened, angry and snap at people

Table 2. Types of flare.

	Localized Flare	Generalized Flare
Experienced,%	100	55 of groups (≈ 40% of individuals)
Frequency	Frequent (0–5 per year)	Rare and random
Duration	Days/weeks	Days/weeks
Symptoms	Acute and sudden pain in one area, which may move to other areas. Pressure in the painful area. Occasional swelling, inability to move joint, immobility, fatigue, bad temper, withdrawn.	Paralyzing and throbbing pain deep inside and in every joint. Immobility, fatigue, muscle spasm/cramp, burning or tightness in the muscle. Sweats, fever, flu-like illness, loss of appetite, grey pallor, shortness of breath, depression, anger.
Attitude	Adapt and learn to live with it	Devastating every time

Table 3. However, if the terms run down, overdoing it, and stress were categorized together, then 100% of groups described this as the primary trigger. General and localized flares appear to be triggered by the same factors: overdoing it, jarring of a joint, infection.

Duration of flare. Both local and generalized flares may last from a few days to a few weeks. However, 50% of the groups believed that for some individuals, in extreme cases it might last a month or more. A quarter of the groups specifically stated that if it lasted months, it was not a flare but something else (i.e., the disease process itself had become more aggressive and had turned into severe AS). In all cases the onset of flare was instantaneous with little or no warning. Similarly, when the flare was finished, it instantly lifted.

Longterm effects of flare. According to our patients, when the flare has gone, the AS typically returns to baseline (75% of groups). However, in the very short term (for a few days), the person may feel weak and fragile. A quarter of the groups thought that a bad flare could leave the person with some loss of function to specific joints (reduced neck mobility or increased stiffness of the fingers).

Frequency of flare. All groups felt that there was no specific frequency pattern. For the localized flares, it was variable but could be between one and 5 per year. For the generalized flares, this was extremely variable and dependent on the individual. One patient experienced a 5 year gap between generalized flares, while for another there were 2 flares within the same year, and for many patients there has been no exposure to this type of flare in the course of their disease. Frequency of flare does not alter with disease duration.

Table 3. Triggers of flare.

Number	Trigger	Percentage of Groups
1	Stress (physical and emotional)	80
2	Overdoing it (too much activity)	50
3	Weather (cold, damp)	45
4	Random	45
5	Jarring of a joint/a fall	30
6	Remaining in one position (driving long distance, someone else's bed/chair)	30
7	Colds and flu (physical activity of coughing/sneezing combined with being in bed)	25
8	Generally run down	15
9	Food poisoning	15
10	Allergies/intolerances (e.g., food allergies)	10

Treatment for flare. Relief from a flare was gained by parenteral analgesia, relaxation, and sleep. However, 75% of patients reported that sleep was almost impossible due to the pain. Cannabis was reported by 3 individuals in separate groups to provide significant relief, helping the muscles relax, decreasing the pain, and aiding sleep. The following is a case quote by a woman, age 32: "I was virtually incapacitated. I couldn't walk, only shuffle. I was awake for most of the night through the pain of even the slightest movement. I have had 3 such severe episodes, which lasted for a few days up to about 3 weeks."

DISCUSSION

There are 2 forms of flare in AS: (1) localized to one area and (2) throughout the entire body. Both types are triggered in the majority of cases by stress and are extremely painful, but are short term (duration: days to weeks), and do not appear to have long lasting effects. These findings may help patients and clinicians better understand what determines a flare in AS. In some cases, patients have been hospitalized with an apparently different and new illness and later realize that it was a flare of their AS. In addition, our results may improve the treatment and measurement of flares (for clinical trials) and increase our understanding of the biochemical processes involved in AS.

Future studies will examine the type of people who experience generalized flares compared to those who experience only the localized type. For example, differences in sex, family history, associated diseases (inflammatory bowel disease, psoriasis, iritis), radiological severity, and disease

duration may be relevant. Patients with severe and aggressive disease might be identified early on as having whole body flares. Understanding why some people are prone to generalized flares may give insight into the factors that determine the natural disease course and outcome of spondylitis. For example, bursts of cytokine activity may be involved in mediating flare, as suggested by an associated pyrexia.

Flare may involve muscle spasm, causing extreme pain, immobility, and fatigue. Muscle relaxation is reported to help ease flare and amitriptyline has been reported to reduce disease activity (pain and morning stiffness) in baseline (non-flare) AS[10]. Perhaps this hypothesis may be tested by offering patients who report numerous flares a muscle relaxant such as a benzodiazepine, to use at home at the onset of flare to evaluate the efficacy of such treatment.

Patients consistently reported that their normal medication (i.e., NSAID) did not have any effect on the symptoms of AS during a flare. Even increasing the dose of drugs did not seem to relieve the pain. Future studies with anti-tumor necrosis factor (TNF) treatment, other disease modifying drugs, and perhaps steroids may help relieve the symptoms of flare and may aid our understanding of the mechanisms involved in the disease. For example, anti-TNF has been shown to be effective in the management of exacerbations in flares in Crohn's disease (a disorder associated with AS)[11]. In 7 AS patients treated with this drug, there was evidence of regression in terms of clinical measures, magnetic resonance image readings, and quality of life assessments[12]. However, the discontinuation of anti-TNF is associated with relapse of disease at about 10 weeks following the last infusion[13].

The main symptoms of flare may be measured using the existing disease activity measures for AS. For example, the Bath AS Disease Activity index (BASDAI)[14] and Functional Index (BASFI)[15] would measure increased levels of fatigue, pain, stiffness and tenderness, and loss of function. Thus, with existing indices it may be possible to quantify flare activity. The symptoms of flare are pain, immobility, fatigue, and emotional changes. It could be argued that fatigue, emotional changes, and immobility are all outcomes of the pain and not symptoms themselves. However, patients did suggest that the emotional changes can precede the flare and that the immobility was not due to pain but a seizing-up of the muscle. Fatigue occurs in AS generally (not during flare) as a sudden onset event that is not necessarily accompanied by pain. Thus, we feel that these events appear not to be simply outcomes of the pain but are truly separate symptoms of flare.

The flare in AS does not show measurable changes as seen in other conditions such as RA (swollen joints, ESR changes, etc.). However, the main symptom, pain, does appear to be identical to that experienced in other forms of arthritis. The words used by patients to describe the quality of pain mirror those used in RA[16]. Sharp stabbing pain is used both to describe the localized flare of AS and to describe individual joint pain in RA[16]. However, the words burning, cramping, and throbbing are used to describe the generalized flare in AS and the overall pain in RA. Thus, the main symptom of flare is not unique in quality to AS but is similar to the experiences of patients with other forms of arthritis.

These results are based on patient recollection and not on prospective data. Some aspects of flare that are important at the time may not be recalled by these groups. In addition, the groups consisted of patients who were attending a 2 week intensive physiotherapy/education program. Therefore, it is possible that individuals referred to this course were more symptomatic and had more significant flares than the average patient with AS.

In conclusion, the majority of patients experiencing a flare describe it as a localized phenomenon of acute pain and stiffness accompanied by fatigue. This is an occurrence that patients report they are able to learn to live with. However, when combined with fatigue, flares present the patient with a worrying symptomatic complex. Some individuals experience an extreme and devastating whole-body illness accompanied by fever, sweats, extreme pain with sensitivity, and flu-like symptoms. This is a devastating and depressing phenomenon that undermines patients' confidence in their ability to cope with their AS. The approach to treatment for both types of flare is unclear and limited. The unpredictability of flare causes many emotional symptoms, but in terms of disease progression, there appears to be little longterm lasting damage to the joints caused by this phenomenon.

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