Onset of Rheumatoid Arthritis: A Probable Role of Stressful Life Events

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This work aims to find support to the "life events approach" proposing that premorbid stressful life events may have a role in the precipitation of RA and to try to correlate these stressful life events with subsequent disease-related and psychological factors. 100 patients, including 60 RA patients and 40 patients with OA of the knees as a comparative group, represent the sample of the study. Psychological assessment was done by the Symptom Check List-90-Revised, besides a brief psychiatric history including history of stressful life events within one year prior to the onset of the disease. Major stressing life events may have a role in the precipitation of RA, being reported much more frequently in RA patients (38%) than in OA patient (7.5%) in the year before their illness. These results have been discussed in the light of recent research.

(Egypt.J. Psychiat.,1994, 17: 59-66).

Introduction

Whether a specific personality or alexithymia in any person predisposes to RA is an approach to the psychosomatic nature of RA, termed the trait approach, while the life events approach examines the association between major life events "stressor" (e.g. divorce and retirement) and the onset and exacerbation of RA (Bechkham *et al.*, 1987).

The most thorough evaluation of stress and RA onset and exacerbations was published by Rimon (1969) in his monograph of 156 pages, and was followed up by a series of studies. In his first study, 100 female RA patients underwent extensive study and psychological testing. 55% of them associated a major life conflict with their first symptoms of RA while 45% did not. In the former group, 65% of all subsequent RA exacerbations were associated with psychological stress versus 18% in the latter group.

In a subsequent study of 40 RA female patients referred for depression, Rimon (1974) found that rheumatological improvement was most marked between those in whom clinical manifestation of depression has disappeared, while the clinical state deteriorated or remained unchanged in the patients whose depression persisted.

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Rimon and Laakso (1984 b) conducted a 15-year follow up study of 74 of the RA patients studied originally by Rimon (1969). They found that in a group of patients, emotionally traumatic life stress was significantly associated with clinical exacerbations of the illness. Some patients had severe and persistent marital discord associated with a continuously active and progressive disease. In some of these, solution of a long - term family problem was accompanied by significant improvement.

In a subsequent paper Rimon and Laakso (1985) they classified RA patients into two groups; a major conflict group, which is less connected with genetic factors and more influenced by major psychodynamic conflict situations, and a non conflict group, more associated with hereditary predisposition and less influenced by environmental changes.

Aim of work:

This work aims to find support to the "life events approach" proposing that premorbid stressful life events may have a role in the precipitation of RA and to try to correlate these stressful life events with subsequent disease-related and psychological factors.

Subjects and Method

100 patients, including 60 RA patients and 40 patients with OA of the knees as a comparative group, were recruited from the Rheumatology and Rehabilitation outpatient clinics of El-Minia and Cairo University Hospitals over the year 1992, to form the study sample.

Criteria for diagnosing RA patients were the 1987 American Rheumatism Association (ARA) criteria (Arnett *et al.*, 1988). While criteria for diagnosing OA of the knees were the clinical and radiographic criteria developed by Altman *et al.*, (1986).

All cases were submitted to a detailed medical history and examination including relevant laboratory tests. Psychological assessment was done by the Symptom check List-90-Revised (SCL-90-R), the Arabic version (El-Behairy, 1984) of the earlier Hopkins Symptom Chick List (1976); besides a brief psychiatric history including history of psychological trauma or stress within one year prior to the onset of the disease. To exclude ordinary day stressors, we asked patients if the stressor was sufficiently strong that he considers it to be out of his ordinary everyday experiences.

Results

(A) Stressful Life Events Preceding the Onset:

Concerning stressful life events, table (1) and (2) enumerates the various stressors reported by RA and OA patients respectively about the onset of their diseases. Death of a dear person (father, mother, husband, son, sister, brother,.... etc) occupied the top of the list in both groups. It was reported by 8 of the 23 RA patients and by all 3 OA patients reporting positive stressful life events at onset. Other stressors concerning the RA group are shown in table (3) including divorce, family troubles, marriage and infidelity among others.

Overall, 23 RA patients (38.3%) and 3 OA patients (7.5%) reported stressful life events preceding the onset. The differences were very highly significant as shown in table (3).

Table (3) shows also the differences in family and past history of psychiatric disorders. Though OA patients had a higher incidence in past and family history than RA, patients the differences were not statistically significant. Depression, was the only psychiatric disorder reported by both groups in past

Table 1

Stressful Life Events Preceding Onset in RA Patients (N= 60)

Stressful Life Event	Frequency	Percent
Death of father	3	(5%)
Death of husband	2	(3.33%)
Death of sister	2	(3.33%)
Death of mother	1	(1.67%)
Divorce/ separation	3	(5%)
Second marriage of husband	2	(3.33%)
Marriage/ honeymoon	2	(3.33%)
Acute family troubles	4	(6.67%)
Infidelity of wife	1	(1.67%)
Imprisonment of brother	1	(1.67%)
Detainment of husband in a mental hospital	1	(1.67%)
Depressive attack	1	(1.67%)
Total	23	(38.33%)

Table 2

Stressful Life Events Preceding Onset in OA Patients (N= 40)

Stressful Life Event	Frequency	Percent
Death of two sons (twins)	1	(2.5%)
Death of father	1	(2.5%)
Death of brother	1	(2.5%)
Total	3	(7.5%)

Table 3

Stressful Life Events, Past and Family History of Psychiatric Disorders in RA and OA Patients

Variable	Rheumatoid Arthritis N = 60	Osteoarthritis N = 40	Difference X^2	P value
- Stressful Events				
Positive	23 (38.3%)	3 (7.5%)	11.86	0.0006
Negative	37 (61.7%)	37 (92.5)		
- Past history of Psychiatric disorders				
Positive	5 (8.33%)	5 (12.5%)		
Negative	55 (91.67%)	35 (87.5%)	0.12	0.73 (NS)
- Family history of Psychiatric disorders				
Positive	0 (0.0%)	2 (5%)	1.04	0.31 (NS)
Negative	60 (100%)	38 (95%)		

NS=Nonsignificant

Table 4

Association of Stressful Life Events and Past History of Psychiatric Disorder with Demographic Variables in RA Patients (N= 60)

Variable	Stressful Event (n= 23)		Past History of Psych. Disorder (n= 5)	
	Test	P value	Test	P value
Age	T= 1.45	0.15 (NS)	T= 1.1	0.27 (NS)
Sex	x^2= 0.36	0.55 (NS)	x^2= 0.34	0.56 (NS)
Marital status	x^2= 2.9	0.41 (NS)	x^2= 1.94	0.68 (NS)
Residence	x^2= 1.94	0.16 (NS)	x^2= 0.13	0.58 (NS)
Education	x^2= 2.41	0.30 (NS)	x^2= 11.8	0.003**2
Occupation	x^2=10.48	0.005**	x^2=5	0.08 (NS)
Economic Dependence	x^2=0.1	0.76 (NS)	x^2=0.22	0.64 (NS)
Family income/ Person/month	T= 0.83	0.41 (NS)	T= 0.47	0.63 (NS)

1- Tested as the difference between positive ad negative patients using a t-test for continuo variables and by χ^2-test for nominal variables, with or without continuity correction.
**1 Stressful life events were reported more by unemployed patients and less by housewiv and employed patients. Association between unemployment and Stressful life events at ons was highly significant (P< 0.01).
**2 All 5 patients reporting a past history of psychiatric illness were formally educated. T association was highly significant (P< 0.01).
NS Nonsignificant.

history. It is notable than non of the RA patients reported a family history of psychiatric disorders, while one OA patient reported a history of depressed brother and another a history of schizophrenic aunt.

(B) Association of Stressful Life Events at Onset and Past History of Psychiatric Disorders with Other Variables in RA Patients:

1- Demographic Variables:

Table (4) shows the association of stressful life events at onset and past history of psychiatric disorder with demographic variables. There were no significant associations except for a highly significant association between unemployment and stressful life events at onset and another between formal education and a past history of psychiatric disorders. It is notable that all 5 patients reporting a past history of psychiatric disorder (depression) were formally educated.

2- SCL-90-R Scales:

Table (5) shows that patients' reports of stressful life events and a history of

Table 5
Association of Stressful Life Events and Past History of Psychiatric Disorder with SCL-90-R Scales in RA Patients (N= 60)

SCL-90-R Scales	Stressful Event (n= 23)		Past History of Psych. Disorder (n= 5)	
	U	P value	U	P value
Somatization	387	0.56 (NS)	114.5	0.54 (NS)
Obsessive-compulsive	341.5	0.29 (NS)	96	0.27 (NS)
Interpersonal sensitivity	349.5	0.25 (NS)	121.5	0.67 (NS)
Depression	352.5	0.27 (NS)	114.5	0.54 (NS)
Anxiety	363.5	0.34 (NS)	81	0.13 (NS)
Hostility	290.5	0.04* (NS)	41.5	0.02*
Phobic anxiety	400	0.70 (NS)	135	0.95 (NS)
Paranoid Ideation	362.5	0.34 (NS)	89.5	0.20 (NS)
Psychoticism	356.5	0.29 (NS)	64.5	0.05*
Distress	340	0.19 (NS)	93.5	0.24 (NS)

1- Tested using the Mann-Whitney U-test for difference between positive and negative patients in scores of SCL-90-R scales.
* Statistically significant association.
NS Nonsignificant association.

psychiatric disorder were significantly associated with subsequent hostility, and that patients reporting a positive history of psychiatric disorder had significant higher psychoticism scores than patients not reporting it. Apart from this, there were no statistically significant associations.

Discussion

Contrary to the "trait approach" proposing that specific personality traits predispose to the development of RA, our findings support the "Life events approach" proposing that psychological stress may have a role in the precipitation of RA. 23 RA patients (38%) reported a psychologically meaningful stressor within one year before the onset of their disease (premorbid stressful life events), in comparison to 3 OA patients (7.5%), with a very highly significant difference between the two group (P< 0.001).

Loss (death of a dear person) was the most common stressor, being reported by more than a third of the 23 patients. Other stressors included conflict (family troubles; divorce) and frustration (marriage of husband; infidelity of wife). It is notable that stressors of a happy nature were also included (e.g. marriage; honeymoon).

Our findings are comparable to Shaheen *et al.*, (1987) who found premorbid stressful life events in 44% of 60 RA patients, most commonly loss, frustration and conflict.

Rimon (1969) and Baker and Brewerton (1981) found that 55% of RA patients reported stressful life events

within one year prior to the onset of their first symptoms of the disease, whom Rimon and Laakso (1985) called the major conflict group, as their disease was influenced by major psychodynamic conflict situations. The highest incidence of stressful life events was found by Abd El-Azim *et al.,* (1987) who found it in 85% of RA and 82% of OA patients. However they studied only 20 RA and 22 OA patients.

A possible cause for the slightly lower incidence found in our study is that we applied more stringent criteria; stressful life events was only considered positive if it was sufficiently strong to be out of ordinary everyday experiences.

None of these previous studies tried to correlate premorbid stressful life events with subsequent disease-related and psychological factors. In our study, premorbid stressful life events was not associated with any RA disease parameter, but was significantly associated with subsequent higher hostility and psychoticism scores and with unemployment. We can therefore deduce that the major conflict RA group become more hostile and socially alienated than the non-conflict group and are commonly unemployed. The association with unemployment can also be due to the significant association between unemployment and psychoticism.

The implications of these findings can be interpreted in the light of recent research in psychoneuroimmunology linking psychological stress with immune mechanisms, which may induce RA in genetically predisposed individuals (Wallace, 1987). Stress has been linked to several disturbances in the immune system (Dantzer and Kelley, 1989), but a recent study by Spratt and Denney (1991) found that a severe form of stress (bereavment) was associated with a significant increase in T helper cells and a decrease in T suppressor cells, with a great increase in the T_H/T_S cell ratio. This was typically found to occur in the blood of RA patients, and is thought to be related to the pathogenesis of RA (Duke *et al.*, 1982). Therefore it is possible that stress affects RA through altering T-cell number or functions.

The mediators of such effects may be opioid peptides (substance P; endorphins; enkephalins) which generally stimulate T-cell activities (Plotnikoff *et al.*, 1985). They were also implicated in the pathophysiology of RA (Levine *et al.*, 1985); Agro and Stanisz, 1992) and in the mediation of stress effects in the development of RA specifically (Famaey *et al.*, 1991).

Modification of these effects of stress on the immune system and RA might be brought about by learning, coping mechanisms, learned helplessness and social support.

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L'Attaque de l'Arthritis Rheumatoid Un Rôle Probable des Evénements Presants De La Vie

Ce travail vise à trouver un support à "l'approche des événements de la vie" en proposant que les évènements de la vie pressantes primalade peuvent avoir un rôle dans la précipitation de l' A. R. et pour essayer de correller ces évènements pressants de la vie avec les maladies subsequentes reliées et les facteurs psyhologicals. 100 patients, includants 60 A. R patients et 40 patients d' O. A des genoux comme étant un grouppe comparatif, représentent l'échantillant de l'étude. L'assessement psychological a été faite par le symptômes du check - liste - 90 - reviseé, à côté d'une histoire psychiatrique brief includant l'listoire des éuénements pressants de la vie un an avant l'attaque de la maladie. Les évènements majeurs et pressants de la vie peuvent avoir un rôle dans la précpitation de l'A.R et fûrent reportés plus fréquemment dans les patients de l'A.R (38%) que dans les patients de l'O.A (7,5%) dans l'année avant leur maladie. Ces résultats ont été discutées à la lumiére de la recherche récente.

بداية مرض الروماتويد المفصلى

(دور محتمل لأحداث الحياة الضاغطة)

أجرى هذا البحث على ستين مريضا بالروماتويد المفصلى ، واربعين مريضا بالتهاب المفصل العظمى بالركبة كمجموعة مقارنة. وقام الباحثون بإجراء دراسة إكلينيكية ونفسية بتركيز أكثر على وجود أحداث تمثل صدمة نفسية للمريض وتاريخ مرضى قديم وتاريخ عائلى مرضى خاص بالأمراض النفسية ، وأمكن تطبيق قائمة الأعراض ٩٠ المراجعة للقياس النفسى والتى وجدت تناسب مرضى الروماتويد لخلوها من أعراض المرض الإكلينيكية.

واستنتج الباحثون أن مصائب الحياة الكبيرة (الصدمات النفسية) قد تكون سببا مؤثرا فى ابتداء المرض ، حيث وجدت أكثرحدوثا بين مرضى الروماتويد (٣٨٪) منها بين مرضى التهاب المفصل العظمى للركبة (٧,٥٪) فى خلال السنة السابقة لبداية المرض . وقد نوقشت نتائج هذه الدراسة فى ضوء الأبحاث الحديثة .