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The Risk of Depressive Symptoms Increases in Radiographic Axial Spondyloarthritis Patients with Acute Anterior Uveitis

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ABSTRACT

Background This study aimed to assess the psychological status of radiographic axial spondyloarthritis (r-axSpA) patients with/without acute anterior uveitis (AAU) and to investigate whether the emotional status was different and associated with disease activity and other clinical variables.

Patients and Methods This cross-sectional study included a total of 145 r-axSpA in-patients who fulfilled the modified New York criteria for ankylosing spondylitis. AAU was established by ophthalmologists. Clinical variables were collected from patient charts. All patients received a comprehensive rheumatologic assessment for disease activity, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score (ASDAS). The Short Form (SF)-36 Health Survey, the revised Self-Rating Anxiety Scale (SAS) and the revised Self-Rating Depression Scale (SDS) were applied to all participants by psychiatrists.

Results Fifty-seven patients were diagnosed as having the first onset of AAU. Compared with the group of r-axSpA without AAU, the risk of depressive symptoms was higher in the group of r-axSpA with AAU ($p = 0.008$). However, there was no significant difference in terms of the risk of anxious symptoms between these groups ($p = 0.868$). In addition, r-axSpA patients with AAU had higher scores of ASDAS-C-reactive protein (ASDAS-CRP) but lower scores of ASDAS-erythrocyte sedimentation rate (ASDAS-ESR) ($p = 0.032$ and $p = 0.019$). Furthermore, there was a negative correlation between SDS scores and duration in r-axSpA patients with AAU. Among all patients, the group of r-axSpA with depressive symptoms had increased CRP levels and ASDAS-CRP scores and lower vitality in SF-36.

Conclusion The risk of depressive symptoms increases in r-axSpA patients with AAU. Moreover, r-axSpA patients with uveitis had a higher disease activity as measured by ASDAS-CRP. Physicians should pay more attention to depressive symptoms and AAU in addition to the disease of r-axSpA itself.

Introduction

Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease that mainly involves the sacroiliac joint and the spine [1]. It comprises the whole spectrum of patients with and without radiographic sacroiliitis-radiographic axSpA (r-axSpA, formerly known as ankylosing spondylitis, AS) and non-radiographic axSpA (nr-axSpA), respectively [2, 3]. It has been shown that r-axSpA and nr-axSpA are part of the same disease spectrum and that patients with r-axSpA and nr-axSpA are largely similar with regard to clinical presentation, burden of disease, including the presence of comorbidities, treatment received and response [4, 5]. Furthermore,

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even the same clinimetric tool and measurement tool of disease activity, Ankylosing Spondylitis Disease Activity Score (ASDAS), is widely used in both r-axSpA and nr-axSpA [6]. axSpA can mainly result in different degrees of functional impairment and also affect all life activities, including social, economic, psychological and even sexual functions [1, 7–9].

Uveitis is known to be the most common extraarticular clinical manifestation of r-axSpA. Up to 40 % of patients with r-axSpA experience unilateral acute anterior uveitis during the disease process [10]. Though axSpA-associated uveitis is typically acute, unilateral, recurrent, and carries a relatively good prognosis [10], it may cause extra burden of psychological status. It was found that there was an increased risk of depression and anxiety among patients with r-axSpA [11]. However, there have been few reports about the effects of uveitis on the psychiatric status in r-axSpA. The aim of this study was to assess the psychological status of r-axSpA patients and identify the roles of acute anterior uveitis (AAU) in the emotional status of r-axSpA patients.

Patients and methods

Ethic committee approval

This study was approved by the Ethics Committee of our hospital (Approval number: K57–1). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Study design

145 in-patients were enrolled in this study. All of them were classified as r-axSpA according to the modified New York criteria. The diagnosis of AAU was made by ophthalmologists. The uveitis in r-axSpA patients were all unilateral and all the r-axSpA patients with AAU were hospitalized because of the first onset of AAU. 145 r-axSpA patients were classified into two groups: r-axSpA with AAU and r-axSpA without AAU. Exclusion criteria were: (1)comorbidity (cardiac, respiratory, gastrointestinal, neurological, endocrine, neoplasm, etc); (2)infection influencing r-axSpA activity or their functional or psychological status; (3)history of anxiety or depression prior to r-axSpA onset; (4)other diseases that can cause uveitis.

Clinical data and laboratory tests

All demographic data were gathered from the patient charts. The C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and human leukocyte antigen (HLA)-B27 were also collected.

Assessment tools

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to measure disease activity. This instrument consists of six questions assessing the patient's fatigue, spinal pain, joint pain/swelling, areas of localized tenderness, pain severity, and duration of morning stiffness in the last week. Higher scores indicate increased disease activity, while scores of ≥ 4 indicate higher disease activity [12].

ASDAS was also used to measure disease activity. This composite index combines BASDAI items 2, 3, and 6 with CRP or ESR value. Values over 3.5 indicate very high disease activity, while values below 1.3 are considered inactive disease [13].

The Short-Form 36 (SF-36) questionnaire was used to assess the general health from the following eight scales: physical functioning (PF), role of physical problems (RP), role of emotional problems (RE), social functioning (SF), mental health (MH), vitality (VT), body pain (BP) and general health (GH) [14]. High scores denote better health.

The revised Self-Rating Anxiety Scale (SAS) was used to evaluate the level of anxious symptoms during the week prior to the survey. Scores ≥ 50 indicate anxious symptoms. The scores between 50–59 indicate mild, 60–69 indicate moderate and equal to or more than 70 indicate severe [15].

The revised Self-Rating Depression Scale (SDS) was used to assess depressive symptoms during the week prior to the survey. Scores ≥ 53 indicate depressive symptoms. The scores between 53–62 indicate mild, 63–72 indicate moderate and equal to or more than 73 indicate severe [16].

Statistical analysis

Data were expressed as mean ± standard deviation (SD) or median (min-max). The chi-square test was used to assess categorical variables. Normally distributed variables were compared using independent and randomized paired t-tests. Non-normally distributed variables were compared using Mann-Whitney U test. Pearson's rank correlation coefficient and Spearman's correlation coefficient were used to examine the correlation between two groups of normally-distributed variables and non-normally distributed variables, respectively. A p value of < 0.05 was considered as statistically significant. Statistical Package of Social Science (SPSS) version 24.0 was used to perform statistical analysis.

Results

A total of 145 r-axSpA patients were included in the study. Among r-axSpA patients, the male sex rate, the positive rate of HLA-B27 and the smoking rate were 84.83 %, 94.48 %, 24.83 %, respectively. The median age was 35 (16–69) and the median symptom duration was 6 (0.1–30 years). 57 and 88 patients were finally classified as r-axSpA with and without AAU, respectively. The baseline data of these two groups is listed in ▶ **Table 1**. There were no significant differences in terms of sex, age, duration, HLA-B27, body mass index (BMI), smoking, education, ESR, CRP, BASDAI, SAS or SDS between two groups. Compared to r-axSpA patients without AAU, r-axSpA patients with AAU had higher scores of ASDAS-CRP but lower scores of ASDAS-ESR.

The rate of anxious and depressive symptoms in our cohort was 15.17 % and 22.07 %, respectively. ▶ **Table 2** lists the comparison of clinical parameters in r-axSpA with and without anxious/depressive symptoms. Compared to the group without depressive symptoms, the group with depressive symptoms had higher CRP levels and ASDAS-CRP scores. As for Short Form-36, the VT scores decreased in the group with depressive symptoms.

Compared to r-axSpA patients without AAU, there was a higher risk of depressive symptoms in r-axSpA patients with AAU (14.77 % vs. 33.33 %). However, there was no significant difference in terms of the risk of anxious symptoms between the two groups (14.77 % vs. 15.79 %) (▶ **Fig. 1**). Among r-axSpA patients with AAU screened positive for depressive scores, all 19 patients had mild, none had

▶ **Table 1** Characteristics of clinical data in r-axSpA subgroups.

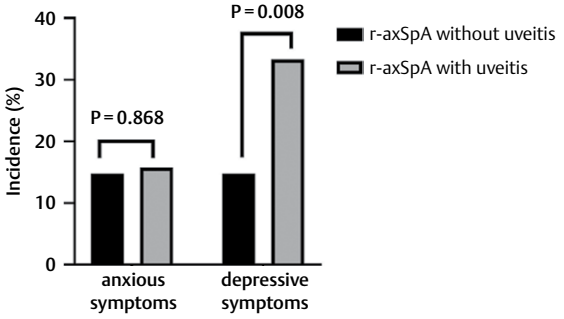
	r-axSpA with uveitis (n = 57)	r-axSpA without uveitis (n = 88)	p
Age (years) [a]	38.00 (16.00–69.00)	34.71 (19.0–65.0)	0.053
Male (%)	47.00 (82.46%)	76.00 (86.36%)	0.522
Duration (years) [a]	6.85 (0.20–30.00)	5.60 (0.10–20.00)	0.145
HLA-B27 positive (%)	53.00 (92.98%)	84.00 (95.45%)	0.524
BMI (kg/m^2) [b]	23.21 ± 3.89	23.69 ± 3.47	0.440
Smoking (%)	18.00 (31.58%)	18.00 (20.45%)	0.130
High-educated (%)	27.00 (47.37%)	45.00 (51.14%)	0.658
ESR (mm/H) [a]	21.00 (2.00–105.00)	16.50 (2.00–141.00)	0.358
CRP (mg/L) [a]	5.90 (0.07–95.18)	8.00 (0.04–172.34)	0.835
ASDAS-ESR[a]	1.61 (0.61–4.89)	2.11 (0.74–3.65)	**0.019**
ASDAS-CRP[b]	2.01 ± 0.92	1.70 ± 0.79	**0.032**
BASDAI[a]	1.42 (0.40–5.00)	1.30 (0.40–4.20)	0.332
SAS score[a]	36.00 (25.00–62.00)	33.00 (25.00–65.00)	0.403
SDS score[a]	32.00 (25.00–61.00)	33.00 (25.00–66.00)	0.960
Treatment			
TNF-α inhibitors (%)	47.37%	46.59%	0.927
IL-17 inhibitor (%)	52.63%	53.41%	0.927

r-axSpA: radiographic axial spondyloarthritis; HLA-B27: human leukocyte antigen-B27; BMI: body mass index; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; TNF-α: tumor necrosis factor-α; IL-17: interleukin-17; [a]: median (min-max); [b]: mean ± standard deviation

▶ **Table 2** Comparison of depressive and anxious symptoms with clinical parameters in r-axSpA patients.

	With depressive symptoms (n = 32)	Without depressive symptoms (n = 113)	p	With anxious symptoms (n = 22)	Without anxious symptoms (n = 123)	p
ESR (mm/H) [a]	24.00 (2.00–105.00)	18.00 (2.00–141.00)	0.079	14.00 (3.00–75.00)	19.00 (2.00–141.00)	0.465
CRP (mg/L) [a]	19.36 (0.07–103.31)	6.40 (0.04–172.34)	**0.008**	5.40 (0.30–34.81)	7.62 (0.04–172.34)	0.285
ASDAS-ESR [a]	2.21 (0.74–3.63)	1.73 (0.61–4.98)	0.086	1.57 (0.77–2.81)	1.76 (0.61–4.89)	0.272
ASDAS-CRP [b]	2.15 ± 0.85	1.73 ± 0.84	**0.013**	1.58 ± 0.77	1.87 ± 0.87	0.149
BASDAI [a]	1.35 (0.40–4.10)	1.40 (0.40–5.00)	0.941	1.20 (0.40–3.20)	1.40 (0.40–5.00)	0.207
SF-36						
PF [a]	100 (80–100)	100 (75–100)	0.718	100 (80–100)	100 (75–100)	0.684
RP [a]	100 (0–100)	100 (0–100)	0.226	100 (0–100)	100 (0–100)	0.778
BP [a]	81 (32–100)	90 (22–100)	0.170	100 (41–100)	90 (22–100)	0.540
GH [a]	80 (30–100)	80 (15–100)	0.410	76 (15–92)	80 (20–100)	0.101
VT [a]	82.5 (20–100)	90 (54–100)	**0.043**	85 (30–100)	85 (20–95)	0.188
SF [a]	100 (80–100)	100 (50–100)	0.386	100 (80–100)	100 (50–100)	0.905
RE [a]	100 (0–100)	100 (0–100)	0.120	100 (0–100)	100 (0–100)	0.987
MH [a]	90 (52–100)	88 (56–100)	0.796	88 (52–100)	88 (56–100)	0.109

r-axSpA: radiographic axial spondyloarthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; SF-36: Short Form-36; PF: Physical functioning; RP: role physical; BP: bodily pain; GH: general health; VT: vitality; SF: social functioning; RE: role emotional; MH: mental health; [a]: median (min-max); [b]: mean ± standard deviation



▶ **Fig. 1** Comparison of the risk of psychological status between two groups.

▶ **Table 3** Correlation analysis between SAS/SDS scores and clinical parameters in r-axSpA patients with uveitis.

	SAS score [a] r	p	SDS score [a] r	p
Age (years) [a]	0.043	0.752	0.035	0.796
r-axSpA Duration (years)[a]	−0.175	0.192	−0.268	**0.044**
ESR (mm/H) [a]	0.001	0.992	0.080	0.555
CRP (mg/L) [a]	0.135	0.318	0.175	0.194
ASDAS-ESR [a]	−0.089	0.512	−0.006	0.964
ASDAS-CRP [b]	0.009	0.945	0.077	0.570

SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; r-axSpA: radiographic axial spondyloarthritis; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; [a]: median (min-max); [b]: mean ± standard deviation

moderate or severe elevation of depressive scores. Among r-axSpA patients without AAU screened positive for depressive scores, 10 had mild, 3 had moderate and none had severe elevation of depressive scores.

In addition, duration of r-axSpA since diagnosis correlated with SDS scores but not SAS scores. Additionally, age, ESR, CRP, ASDAS-ESR and ASDAS-CRP did not correlate with the SAS or SDS scores (▶ **Table 3**).

Discussion

In this paper, the risk of depressive symptoms increases in r-axSpA patients with AAU. Additionally, r-axSpA patients with depressive symptoms have increased CRP levels, higher disease activity scores of ASDAS-CRP and lower VT scores.

It has been found that psychological problems, including anxiety and depression, were common in the population of r-axSpA and r-axSpA might increase the risk of a subsequent newly diagnosed depressive disorder [11, 17–20]. It was reported that both the anxiety and the depression rate were significantly higher than those in the healthy controls [21]. In this study, the rate of anxious and depressive symptoms in r-axSpA were up to 15.2 % and 22.1 %, respectively. However, there were still few reports about the effect of uveitis on the psychological function in r-axSpA. It was suggested in this study that the rate of depressive but not anxious symptoms was higher in r-axSpA patients with AAU than that in r-axSpA patients without AAU. Several studies suggested that the depressive symptoms in r-axSpA could be caused by the physical impairment and inflammation [20].

Uveitis might be one factor that could induce the depression. It was reported that 28/104 (26.92 %) of patients with non-infectious ocular inflammatory disease (including severe posterior and panuveitis patients) screened positive for depression [22]. Other findings also revealed depression could be easily noted in uveitis patients, although different questionnaires were used for the assessment of depression. Uveitis patients with a depression frequently had ankylosing spondylitis (5/6) and they scored significantly worse on vision-related quality of life, suggesting that the presence of a systemic disease has a high influence on this outcome. In addition, low vision was found to be associated with depression [23, 24]. Thus, the increased risk of depressive symptoms in this study might be attributed to the combined consequence of r-axSpA itself and low vision caused by AAU.

The scores of ASDAS-ESR and ASDAS-CRP were all more than 1.3 in two groups, indicating moderate disease activity. Interestingly, r-axSpA patients with AAU showed higher ASDAS-CRP scores but lower ASDAS-ESR scores. These findings might be partly attributed to the low level of agreement between ASDAS-CRP and ASDAS-ESR [25]. Finally, there was negative correlation between the SDS scores and duration in r-axSpA patients with AAU in this study.

There are still limitations to this study. First, it was a cross-sectional study and the sample was relatively small. Longitudinal cohort studies with larger samples should be needed to ascertain whether more other factors participate in the increased risk of depressive symptoms. Second, these patients should be followed up on for enough time to check whether they could fulfill ICD-10 or DSM-IV criteria and finally be defined as anxiety or depression. The status of uveitis in r-axSpA patients should be also continuously monitored to investigate whether the activity of uveitis is related to the severity of depression. Third, the depressive symptoms should be monitored for longer time to check whether they will alleviate when r-axSpA and AAU get into remission and whether they will improve when CRP levels reduce.

In conclusion, this study revealed the increased risk of depressive symptoms in r-axSpA patients with AAU and the correlation between disease activity and psychological status in r-axSpA. These results provide crucial implications for physicians to understand the quality life of r-axSpA patients. Future studies should focus on the intervention of the abnormal psychological status in r-axSpA patient with AAU.

Conflict of interest

The authors declare that they have no conflict of interest.

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