American Journal of Medicine and Medical Sciences 2025, 15(1): 255-258
DOI: 10.5923/j.ajmms.20251501.50

The Significance of Annexine A1 Level Changes in the Course of Axial Spondylarthritis

M. Sh. Karimov, D. N. Ikramova, A. A. Eshmurzaeva, Kh. S. Akhmedov

Tashkent Medical Academy, Tashkent, Uzbekistan

Abstract This article presents the results of a study on the relationship between the level of anneksin A1 (ANXA1) in the blood of 62 patients with different clinical stages of axial spondylitis (AS) and the degree of disease activation. According to the results obtained, against the backdrop of a decrease in ANXA1 levels in the blood serum of patients with AS, exacerbation of the disease is observed.

Keywords Axial spondylarthritis, Activation, Annexin A1

1. Introduction

Currently, understanding of the mechanism of corresponding structural changes in the structure of the spine in axial spondylitis (AS) has been formed, and according to modern understanding [17], not only autoimmune, but also hyperinflammatory processes occupy a special place. Furthermore, considering the association of the disease with a person's primary histological adaptation complex of type I (AGM-I) based on the general pathogenesis, AS is considered to belong to the category of "AGM-I-associated diseases" [15]. The origin of AS is associated with the immune system response and the expression of pro-inflammatory cytokines, particularly TNF-α, IL-17, and IL-23, whose hyperscretion is observed based on a specific genetic predisposition of T-cell immunity. Increased levels of these pro-inflammatory cytokines in the corresponding tissues contribute to the development of an inflammatory process associated with increased prostaglandin E2 (PgE2) and type 2 cycloxygenase (COH-2) [12].

According to the literature [11], the activation of the pathological process is accompanied by structural changes in the spinal tissues, which arise due to cascade changes. These changes, initially occurring at the molecular stage, subsequently lead to pronounced anatomical and physiological disorders in the spine and exacerbation of AS [13]. Increased pain in the spine in this disease corresponds to the radiological stage of the disease, and an increase in the number of visits to the doctor during this period is observed during the period of exacerbation of the disease and the development of irreversible ankylosing spinal disorders [5]. Therefore, the isolation of biomarkers that allow for early diagnosis of AS and assessment of structural changes in the spine is of scientific interest.

Received: Dec. 23, 2024; Accepted: Jan. 17, 2025; Published: Feb. 3, 2025
Published online at http://journal.sapub.org/ajmms

In the literature of subsequent years, patients with HLA-B27 develop specific cytotoxic T-lymphocytes with a TRBV9 segment on the receptor, which are also called "autoreactive T-lymphocytes" [16].

This segment is involved in the recognition of foreign antigens. When the immune system is disrupted, cytotoxic T-lymphocytes activate and attack healthy cells. As a result, the spine, sacro-ilial junction, and other organ tissues are inflamed and AS develops.

In recent years, scientists' focus on the protein Anneksin A1 (ANXA1) has been linked to its role in the immune system [4]. Because it is synthesized by immune system cells under the influence of glucocorticoids [3]. Based on this, ANHA1 indirectly exhibits immunosuppressive, anti-inflammatory, and anti-allergic properties. However, it suppresses the activity of phospholipase A2, contributing to a decrease in prostaglandin and leukotriene production. Furthermore, ANXA1 enhances the suppression of prostaglandin biosynthesis by inhibiting types 1 and 2 cyclooxygenase [14].

Along with this, ANXA1 binds to specific receptors on the leukocyte membrane and attempts to inhibit various manifestations of its activity. Consequently, ANXA1 suppresses processes such as the adhesion ability of epithelial cells, leukocyte migration from blood to target tissue, chemotaxis, phagocytosis, and oxidative metabolism. ANXA1 plays an important role in inhibiting the production of various pro-inflammatory mediators, including lysosomal enzymes, cytokines, and plasminogen activators, by neutrophils, macrophages, and mast cells.

It is well-known that the clinical course and joint syndrome of many rheumatic diseases largely depend on morphological changes, the inflammatory process, and geographical factors [2]. Certainly, the varying development of rheumatic diseases and their distinctive progression patterns lead to specific changes in the joints [9]. Among these conditions, AS is characterized by diverse progression patterns, manifesting

through various clinical and radiological changes as well as functional states. This, in turn, results in the exacerbation of structural disorders in the spine, ultimately leading to a deterioration in the patients' quality of life [1].

Therefore, taking into account the role of ANXA1 in the inflammatory process, the proposed method aims to establish its role in the early detection of changes in the developing tissues of the spine in AS, as well as to determine its prognostic significance in structural changes.

The aim of the study is to determine the change in ANXA1 against the background of disease activation in patients with AS.

2. Research Materials and Methods

This study involved 62 patients with various clinical stages of ankylosing spondylitis (AS), with an average age of 43.2±5.3 years and a mean disease duration of 2.4±1.4 years. The control group consisted of 10 healthy individuals (average age 41.5±4.4 years) approximately matched to the selected patients by age and sex. For the purpose of the study, patients with AS were divided into 3 groups (Table 1): Group I (n=21) included patients in the non-radiographic stage of AS; Group II (n=21) included patients in the established stage of AS; and Group III (n=20) included patients in the late stage of AS. Group II (n=21) - expressed stage of AS; Group III (n=20) included patients with late stages of AS.

The control group consisted of 10 practically healthy individuals (40.5±3.1). To assess the inflammatory and functional activity of the disease, a visual analogue scale (VAS) [8,10] and acute phase inflammation indicators, ASDAS (Ankylosing Spondylitis Disease Activity Score), recommended by the international ASAS (Assessment Ankylosing Spondylitis Work Group), and BASFI (Bath Ankylosing Spondylitis Functional Index) indices were used to assess functional spinal disorders.

An enzyme-linked immunosorbent assay (ELISA, Russia) was used to determine serum anneksin A1 (ANXA1) levels in patients with AS.

Criteria for excluding patients from the study:

1) Patients without confirmed diagnosis of AS according to the ASAS (Assessment Ankylosing Spondylitis Work Group) criteria;
2) Severe concomitant pathology (renal, liver, heart failure, high uncontrolled hypertension, decompensated diabetes, etc.), injuries;
3) Malignant tumors, alcohol abuse, mental illnesses, as well as dementia and cognitive impairment;

The research results were statistically processed using the Microsoft Office Excel 2016 software package.

Table 1. Groups description

Groups		Gender		Average age of patients
		Male	Female	
Group I (n=21)	abs	18	3	40,3±2,5
	%	85,7	14,3	
Group II (n=21)	abs	19	2	42,1±5,1
	%	90,5	9,5	
Group III (n=20)	abs	18	2	45,2±3,4
	%	90	10	

3. The Results Obtained and Their Discussion

The majority of patients participating in this study, 88.7%, were men. The duration of the disease was 2.5±1.1 years, and according to medical history, the average age of patients at the time of the onset of the first symptoms was 40.2±2.6 years. The average period before the diagnosis was established with the onset of the first symptoms was 12.5 months.

It is known that AS, accompanied by various stages of joint-bone system disorders, leads to bone erosion and discomfort of the joint surface against the backdrop of a systemic inflammatory process. This process, in turn, is associated with changes in the properties of the morphological substrate, leading to the intensification of structural changes [6,7].

Table 2. Patients with AS who participated in the study clinical and laboratory indicators

Indicators	Group I (n=21)	Group II (n=21)	Group III (n=20)	p
Disease duration, years	0,4±1,2	2,6±2,1	6,4±2,8	$p^{I-II}<0,05$; $p^{I-III}<0,05$; $p^{II-III}<0,05$
Pain, VAS, cm	5,4±0,8	8,5±1,2	9,3±1,7	$p^{I-II}<0,05$; $p^{I-III}<0,05$; $p^{II-III}>0,05$
Morning swoon duration, min	44,5±9,6	36,2±10,1	40,9±11,5	p>0,05
DAREA	8,6±1,4	9,2±2,1	14,5±3,2	$p^{I-II}>0,05$; $p^{I-III}<0,05$; $p^{II-III}<0,05$
ASDAS	5,2±2,2	6,1±2,1	8,2±1,9	$p^{I-II}>0,05$; $p^{I-III}<0,05$; $p^{II-III}>0,05$
BASFI	4,5±0,6	7,1±0,9	9,2±1,2	$p^{I-II}>0,05$; $p^{I-III}<0,05$; $p^{II-III}<0,05$

Naturally, it is known that the degree of systemic inflammation correlates with structural changes. Therefore, considering the involvement of ANXA1 in the inflammatory process and its immunosuppressive properties, assessing the relationship between its level and structural disorders is of practical importance. It should be noted that the level of ANCHA1 in the patients included in the study varied widely. As shown in Figure 1, the total ANXA1 level in all three groups of patients was significantly ($p<0.05$) lower than in the control group. It should be noted that ANXA1 decreases from the early stages of AS.

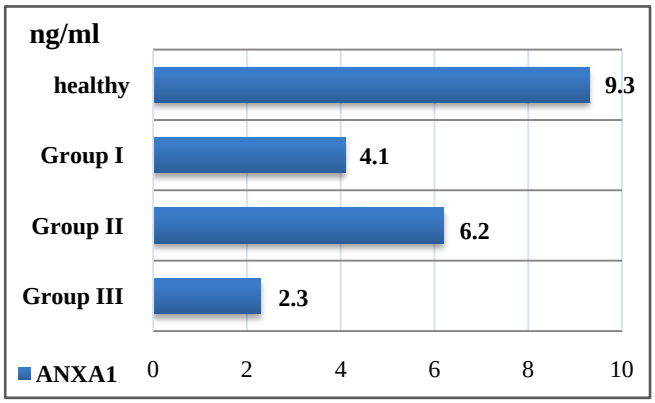

Figure 1. Changes in ANXA1 levels in groups

At the same time, the levels of ANCHA1 differed significantly between the groups. As shown in Figure 1. In Group I, its total value was 4.3±1.1 ng/mL, while in Group II it decreased by 1.5 times ($p<0.05$). In group III, it decreased by 2 times compared to group I and by 1.5 times compared to group II. However, the progression of the disease to subsequent stages in patients with AS is accompanied by a decrease in ANXA1 levels.

In turn, according to the results obtained, the assessment of the duration of AS indicates the presence of certain reliable differences. The assessment of ANXA1 levels in the blood serum of patients with AS also indicates that the duration of the disease has a specific dynamic. As shown in Figure 2, a decrease in the indicator ($p<0.05$) was observed from the early stages of the disease, and a pronounced decrease was observed with increasing duration.

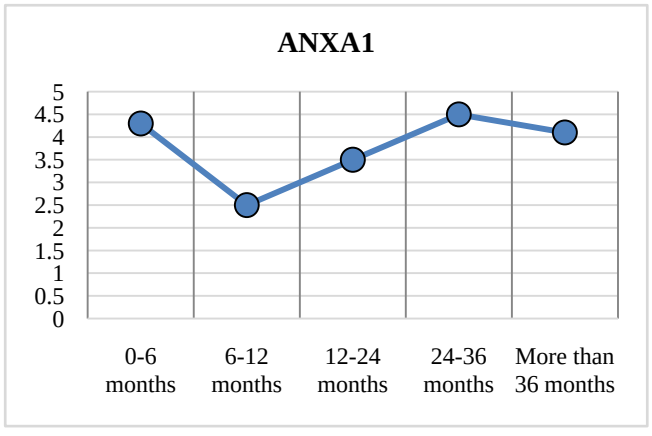

Figure 2. Changes in ANXA1 levels depending on the duration of AS

It is known that changes in the structure of the spine in AS are associated with specific changes in the inflammatory process. In this case, due to the expression of pro-inflammatory cytokines by immune cells, particularly TNF-α and IL-17, erosions are observed in the bones, followed by the formation of enthesitis and syndesmophisms [6]. Therefore, the change in ANXA1 in relation to the inflammatory process observed in AS was carried out based on an analysis of the correlational relationships between them.

Correlation analysis, as shown in Figure 3, showed that ANXA1 in the control group had a positive correlation with ASDAS and VAS, while in all groups with AS it had a moderate negative correlation. Furthermore, the positive correlation between TNF-α and IL-17, also recorded in the control healthy group, turned into a strong negative correlation in all patient groups.

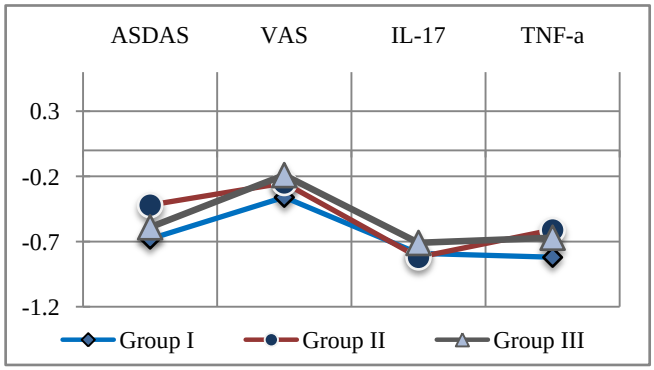

Figure 3. The correlation between ANXA1 and the inflammatory process

Thus, against the backdrop of a decrease in serum ANXA1 levels in patients with AS, exacerbation of disease activation is observed.

REFERENCES

[1] Braun J., Sieper J. Ankylosing spondylitis. Lancet. 2007; 369 (9570): 1379–1390.

[2] Akhmedov K. et al. Changes in the immune system with rheumatoid arthritis in the background of the influence of environmental factors of the external environment // International Journal of Advanced Science and Technology. – 2020. – T. 29. – №. 5. – C. 1907-1917.

[3] Chapman L. P. et al. Evidence for a role of the adenosine 5′-triphosphate-binding cassette transporter A1 in the externalization of annexin I from pituitary folliculo-stellate cells // Endocrinology. – 2003. – T. 144. – №. 3. – C. 1062- 1073.

[4] Chen J. et al. Annexin A1 attenuates cardiac diastolic dysfunction in mice with inflammatory arthritis // Proceedings of the National Academy of Sciences. – 2021. – T. 118. – №. 38. – C. e2020385118.

[5] De Winter J.J., van Mens L.J., van der Heijde D., et al. Prevalence of peripheral and extra-articular disease in ankylosing spondylitis versus non-radiographic axial spondyloarthritis: a meta-analysis. Arthritis Res. Ther. 2016; 18 (1): 196.

[6] Hartl A., Sieper J., Syrbe U., et al. Serum levels of leptin and high molecular weight adiponectin are inversely associated with radiographic spinal progression in patients with ankylosing spondylitis: results from the ENRADAS trial. Arthritis Res. Ther. 2017; 19 (1): 140.

[7] Landewe R., Dougados M., Mielants H., et al. Physical function in ankylosing spondylitis is independently determined by both disease activity and radiographic damage of the spine. Ann. Rheum. Dis. 2009; 68 (6): 863–867.

[8] Landewe R., Machado P., Landewe R., et al. Both structural damage and inflammation of the spine contribute to impairment of spinal mobility in patients with ankylosing spondylitis. Ann. Rheum. Dis. 2010; 69 (8): 1465–1470.

[9] Ramiro S., van der Heijde D., van Tubergen A., et al. Higher disease activity leads to more structural damage in the spine in ankylosing spondylitis: 12-year longitudinal data from the OASIS cohort. Ann. Rheum. Dis. 2014; 73 (8): 1455–1461.

[10] Raychaudhuri S.P., Deodhar A. The classification and diagnostic criteria of ankylosing spondylitis. J. Autoimmun. 2014; 48–49: 128–133.

[11] Robinson P. C. et al. Axial spondyloarthritis: concept, construct, classification and implications for therapy // Nature Reviews Rheumatology. – 2021. – Т. 17. – №. 2. – С. 109-118.

[12] Sieper J., Poddubnyy D. Axial spondyloarthritis. Lancet. 2017; 390 (10089): 73–84.

[13] Van Tubergen A., Ramiro S., van der Heijde D., et al. Development of new syndesmophytes and bridges in ankylosing spondylitis and their predictors: a longitudinal study. Ann. Rheum. Dis. 2012; 71 (4): 518–523.

[14] Dacquisto F., Perretti M. Annexin A1 antibody. – 2016.

[15] Karateev D.E. How to stop the progression of structural changes in ankylosing spondylitis. Effective pharmacotherapy. 2019; 15 (40): 26–34.

[16] Lila A.M. et al. Resolution of the Expert Council "New approaches to the treatment of axial spondyloarthritis" // Modern rheumatology. – 2024. – Vol. 18. – No. 3. – P. 134-139.

[17] Rumyantseva D.G. et al. Ankylosing spondylitis and non-radiological axial spondylitis: two stages of the same disease? // Therapeutic archive. – 2017. – T. 89. – No. 5. – pp. 33-37.

Copyright © 2025 The Author(s). Published by Scientific & Academic Publishing
This work is licensed under the Creative Commons Attribution International License (CC BY). http://creativecommons.org/licenses/by/4.0/