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# ACTIVATION OF OPPOSITE PROCESSES – OSTEOPOROSIS AND OSTEOGENESIS IN ANKYLOSING SPONDYLITIS USING THE CLINICAL CASES

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#### Abstract

Ankylosing spondylitis (AS), despite the development of modern science of rheumatic diseases, remains an insufficiently studied pathology. Paradoxical for AS is the simultaneous activation of two opposing processes: osteoneogenesis and osteoporosis (OP). We have described two clinical cases of patients with AS, diagnosed in the cardio-rheumatology department of the University Hospital of Semey Medical University, where the opposing processes of osteoneogenesis and OP coexist and predispose to pathological fracture of the spine.

Risk factors for OP such as duration of the disease, persistent high activity, C-reactive protein, BASDAI and BASFI indices and reduced bone density values, along with a high process of osteogenesis - an immobilized spine due to ankylosis, prolonged use of non-steroidal anti-inflammatory drugs and the lack of effect of basic therapy led to a fracture spine in the clinical case of patient C. and suggests a high risk of fracture in the case of patient M.

To address the problem of pathological fractures in AS patients, early monitoring of bone mineral density, further studies of the clinical use of DXA to assess the risk of fractures, and timely use of medications for the prevention and treatment of OP in AS are required.

**Keywords.** Osteoporosis, ankylosing spondylitis, bone mineral density, dual-energy x-ray absorptiometry (DXA), pathological vertebral fracture.

#### Резюме

# АКТИВАЦИЯ ПРОТИВОПОЛОЖНЫХ ПРОЦЕССОВ – ОСТЕОПОРОЗА И ОСТЕОГЕНЕЗА ПРИ АНКИЛОЗИРУЮЩЕМ СПОНДИЛОАРТРИТЕ НА ПРИМЕРЕ КЛИНИЧЕСКИХ СЛУЧАЕВ

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Анкилозирующий спондилит (АС) несмотря на развитие современной науки ревматических заболеваний остается недостаточно изученной патологией. Парадоксальным для АС является одновременная активизация двух противоположных процессов: остеонеогенеза и остеопороза (ОП). Нами описаны два клинических случая пациентов с АС, диагностированным в условиях кардиоревматологического отделения Университетского госпиталя НАО «Медицинский Университет Семей», где представленные противоположные процессы остеонеогенеза и ОП сосуществуют и предрасполагают к патологическому перелому позвоночника. Такие факторы риска ОП как длительность болезни, персистирующая высокая активность, С-реактивный белок, индексы BASDAI и BASFI и сниженные величины костной плотности наряду с высоким процессом остеогенеза – обездвиженным позвоночником вследствие анкилозов, продолжительного приема нестероидных противовоспалительных препаратов и отсутствия эффекта базисной терапии привел к перелому позвоночника в клиническом случае пациентки С. и предполагает высокий риск перелома в случае пациента М. Для решения проблемы патологических переломов у пациентов АС требуется ранний мониторинг минеральной плотности костной ткани, дальнейшие исследования клинического

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применения DXA для оценки риска переломов и своевременное применение медикаментозных средств для профилактики и лечения ОП при АС.

**Ключевые слова.** Остеопороз, анкилозирующий спондилит, минеральная плотность кости, двухэнергетическая рентгеновская абсорбциометрия, патологический перелом позвонка.

### Түйіндеме

# КЛИНИКАЛЫҚ ЖАҒДАЙ МЫСАЛЫНДАҒЫ АНКИЛОЗДАУШЫ СПОНДИЛИТ КЕЗІНДЕГІ ОСТЕОПОРОЗ БЕН ОСТЕОГЕНЕЗ – ҚАРАМА-ҚАРСЫ ҮРДІСТЕРДІҢ БЕЛСЕНДІРІЛУІ

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Анкилоздаушы спондилоартрит (АС) ревматикалық аурулардың заманауи ғылымының дамуына қарамастан толық зерттелмеген патология болып есептеледі. АС үшін қарама-қарсы екі үрдістің: остеогенез бен остеопороздың бір мезеттегі белсендірілуі парадоксальды болып табылады. Біздің мақалада КеАқ «Семей медицина университеттінің» Университеттік госпиталінде анықталған АС екі науқас сипатталған, онда омыртқаның патологиялық сынығына әкеліп соқтырған қарама-қарсы екі үрдіс – остеогенез бен остеопороздың бір мезетте дамуының әсері ретінде көрініс тапқан. Остеопороздың ауру ұзақтығы, персистирлеуші жоғарғы белсенділік, Среактивті белок, BASDAI және BASFI индекстері, сүйек тығыздығының төмендеуі тәрізді қауіп факторларымен остеогенездің жоғарылаған үрдісі – анкилоз салдарынан омыртқа қозғалғыштығының жойылуы, стероидты қабынуға қарсы препараттарды ұзақ уақыт қабылдау және базисті емнің тиімсіздігі С. науқаста омыртқаның сынуына және М. науқаста сынудың жоғарғы қауіптілігіне әкеледі. Патологиялық сынықтың АС науқастарында алдын алу үшін сүйек тінінің тығыздығын ерте мониторлау, сыну қаупін бағалау мақсатында DXA клиникалық қолданылуын ары қарай зерттеу және остеопороздың алдын алу мақсатында емдік препараттарды уақытылы қабылдау шараларын жүргізу қажет.

**Түйінді сөздер.** Остеопороз, анкилоздаушы спондилоартрит, сүйектің минеральды тығыздығы, екіэнергетикалық рентгендік абсорбциометрия, омыртқаның патологиялық сынығы.

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#### Introduction

Ankylosing spondylitis (AS), despite the development of modern science of rheumatic diseases, remains an insufficiently studied pathology. Open questions of the etiology of the disease, pathogenetic mechanisms of the development of chronic progressive inflammation of the axial skeleton, the development of enthesopathies, and systemic manifestations.

In later stages of the disease, the combination of persistent inflammation and structural damage can lead to decreased bone mass and disruption of bone microarchitecture, affecting bone strength. Pathological bone formation is one of the signs of spondyloarthritis. With AS, progressive ankylosis develops, which significantly

aggravates the course of the disease and leads to disability [1].

A feature of the pathomorphology of AS is the simultaneous activation of two opposing processes: osteoneogenesis and osteoporosis (OP). Inflammation in AS is associated with trabecular bone loss, leading to the development of OP, but also with bone formation, leading to the development of ankylosis in the spine and peripheral joints. So, what is primary in AS is inflammation or osteogenesis or is it a single pathogenetic mechanism with elements of a physiological protective response - a question that is still relevant today [2,4].

The pathogenesis of bone loss at local and systemic levels predominantly involves inflammatory status, cytokine

release, and autoantibody production. Indeed, inflammation of the spine leads to loss of trabecular bone mass and leads to an increased risk of fractures. *Briot K. et al.* determined that the presence of MRI changes defined as osteitis increased the risk of low bone mineral density (BMD) fivefold in the spine, and was also the single best determinant of low BMD in the hip [12,18].

An increased risk of vertebral fractures has been described among patients with AS [12], with an estimated prevalence of morphometric vertebral fractures as high as 31% [18]. These high rates have been associated with inflammatory activity and structural damage, which can lead to overall bone loss especially in areas affected by bone marrow edema and osteitis [10], leading to decreased spinal flexibility [15,17]. Davey-Ranasinghe et al suggested that all patients with AS should undergo DXA examination of the femoral neck or lateral pelvis within the first 10 years after diagnosis, since new bone formation and systemic osteoporosis co-occur in patients with ASA [3].

Thus, osteoporotic vertebral fractures should be considered in any ASA patient with neck and/or back pain that has changed in intensity or pattern from baseline.

We have described two clinical cases of patients with AS, diagnosed in the cardiorheumatology department of the University Hospital of Semey Medical University, where the opposing processes of osteoneogenesis and osteoporosis coexist and predispose to pathological fracture of the spine.

#### Clinical case 1.

Patient C., 70 years old. Upon admission, complaints of pain in large joints, mainly in the hip, limitation of movements due to pain, heaviness when walking, pain in the spine, general weakness.

History of the disease. According to the patient, articular syndrome has occurred since 2011. In 2015, a diagnosis was made: Ankylosing spondylitis, Grade 3. Systemic osteoporosis. HLA-B 27 positive. Periodically receives treatment from a local doctor: NSAIDs in the form of tablets, calcium supplements, chondroprotectors, B vitamins. She does not take basic medications, she stopped them on her own.

Musculoskeletal system: "posture of the supplicant", moves with the help of a cane. Severe kyphoscoliotic deformity of the spine, limited range of motion in the cervical, thoracic, and lumbar regions, palpation of the spinous processes and paravertebral points is painful. The intercostal spaces are narrowed, the course of the ribs is oblique. Joints of the hands without visible deformation, palpation is painless. The shoulder joints are painful on palpation, with severe stiffness. Pain in the hip joints and iliosacral joints. The knee joints are deformed and moderately painful on palpation.

Disease Activity Index (BASDAI) – 5; functional disease index (BASFI) - 8, disease activity index (ASDAS) - 2.5; presence of human leukocyte antigen B27 (HLA-B27) – positive; erythrocyte sedimentation rate (ESR) – 35 mm/hour and C-reactive protein (CRP) – 25.5 mg/L. This patient underwent radiography of the thoracolumbar and cervical spine in direct and lateral projection (Fig. 1,2).

Conclusion based on radiography of the thoracolumbar spine. Spondylopathy due to systemic osteoporosis. Pathological fracture of bodies Th7-Th8-

Th10, L5, (Genant-2). Fish-like deformation of all vertebrae. Ankylosing spondylitis, Grade 3. Bilateral sacroiliitis.

**X-ray densitometry:** BMD of the femoral neck -0.41 mg/m, BMD of the lumbar spine -0.71 mg/m.



Figure 1. X-ray of the thoracic spine.

Kyphotic curvature of the thoracic region, changes in the shape of the vertebrae like "fish" and wedge-shaped deformities in the T7-T10 segment. The height of the intervertebral discs is sharply reduced in all segments; between the vertebral bodies in T7-T12, brackets are identified that block the motion segments, osteoporosis.

(Figure 1. An x-ray of the thoracic spine in 2 projections No. 4257-8 reveals kyphotic curvature of the vertebrae, fish-shaped changes in the shape of the vertebrae and wedge-shaped deformity in the Th7-T10 segment. The height of the intervertebral discs is sharply reduced in all segments; between the vertebral bodies in Th7-Th12, brackets are identified that block the motion segments, osteoporosis)

## Clinical case 2.

Patient M., 45 years old. Upon admission, complaints of pain along the entire spine, limitation of movements due to pain in all parts of the spine, mostly in the cervical spine, morning stiffness during the day, pain in the shoulder joints, more on the right, pain in and swelling of the right knee joint, weight loss

History of the disease. According to the patient, the disease began with pain in the cervical spine. Previously, he received treatment from a neurologist with a diagnosis of spondylosis, and took NSAIDs. Diagnosis: Ankylosing spondylitis was diagnosed in 2016. He received hospital treatment for the first time in 2019, due to increased pain, limited movement in the spine, pain in the knee joints (dz: Ankylosing spondylitis, peripheral form, late stage, high activity, with extra-axial (arthritis of the left knee joint) manifestations, x-ray stage IV. Osteoporosis). He took Sulfasalazine from 2019-2022, without effect. Constantly took NSAIDs in various dosages.

Musculoskeletal system: Movement is difficult, he has a limp. The "posture of the supplicant". Severe thoracic kyphosis, cervical lordosis.

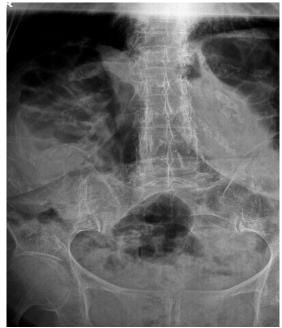




Figure 2. X-ray of the lumbar spine.

Diffuse osteoporosis. The height of the intervertebral discs is reduced in all segments, the L5 body has a wedge-shaped deformity. The endplates of the vertebral bodies are sclerotic, brackets are defined between the bodies of all vertebrae L1-L4, blocking the motion segments, the sacroiliac joints are narrowed and sclerotic. (Figure 2. Diffuse osteoporosis. The height of the intervertebral discs is reduced in all segments, the L5 body has a wedge-shaped deformity. The endplates of the vertebral bodies are sclerotic, between the bodies of all vertebrae L1-L4 there are brackets blocking the motion segments, the sacroiliac joints are narrowed and sclerotic).

Pain on palpation of the cervical, thoracic, lumbar spine. Sharply limited movement in all planes in the cervical, thoracic, lumbar spine, positive "platform" symptom, smoothness of lumbar lordosis, defence of the back muscles. Soreness of the sternoclavicular joints. Pain on palpation of the left shoulder joint, limitation of movement due to pain in the form of severe stiffness.

The head is in a forced position, tilted to the left. Pain on palpation and swelling of the right knee joint.

Disease Activity Index (BASDAI) -6; disease functional index (BASFI) -9, disease activity index (ASDAS) -3; presence of human leukocyte antigen B27 (HLA-B27) - positive; erythrocyte sedimentation rate (ESR) - 17 mm/hour and C-reactive protein (CRP) - 18.87 mg/L. This patient underwent radiography of the thoracolumbar and cervical spine in direct and lateral projection (Fig. 3,4,5).





Figure 3. X-ray of the cervical spine:

Reduction of the height of the intervertebral discs in all segments of the spine; brackets are determined between the vertebral bodies, blocking the motion segments. The joints of the spine are narrowed and sclerotic. (Figure 3. Reduction of the height of the intervertebral discs in all segments of the spine; brackets are determined between the vertebral bodies, blocking the motion segments. The joints of the spine are narrowed and sclerotic).



Figure 4. X-ray of the thoracic spine.

Kyphotic curvature of the thoracic region, decreased height of the intervertebral discs in all segments, brackets are identified between the vertebral bodies, blocking the motion segments.

Osteoporosis.

(Figure 4. Kyphotic curvature of the thoracic region, decreased height of the intervertebral discs in all segments, brackets are identified between the vertebral bodies, blocking the motion segments. Osteoporosis).

Conclusion based on radiography of the cervical, thoracolumbar spine and sacroiliac joints: straightening of physiological lordosis and severity of thoracic kyphosis, reduction in the height of intervertebral discs in all segments of the spine, brackets are identified between the vertebral bodies, blocking the motion segments. The joints of the spine are narrowed and sclerotic. Osteoporosis. Ankylosis of the sacroiliac joints on both sides.

X-ray densitometry: BMD of the femoral neck – 0.76 mg/m, BMD of the lumbar spine – 0.92 mg/m.

#### Discussion.

In the presented clinical cases in patients with active ASA, the disease is characterized by two paradoxical processes - AP and increased bone formation (syndesmophytes and ankylosis). AP, which led to pathological fractures in patient S., has a complex genesis and is considered both a manifestation of ASA disease and as postmenopausal. The standard method for assessing a vertebral fracture is x-ray of the thoracolumbar spine. However, there is no gold standard for defining osteoporotic vertebral fracture [7].

A number of methods have been developed for interpreting spinal radiographs, including the semi-quantitative Guenant method [8], which has been used as the standard in a number of key osteoporosis studies. However, the current preference is for DXA, which has much less radiation than standard radiography, and a number of studies have shown good agreement between the two methods [15].

Several cross-sectional studies have shown that hip bone density is associated with osteoporotic fractures independent of lumbar spine BMD measurements in postmenopausal women. Prospective studies have also shown that hip bone density predicts fractures in postmenopausal women and older men [5].

In the presented clinical cases, both patients underwent DCA in two anatomical zones - the lumbar spine and the femoral neck. It is necessary to take into account the presence of syndesmophytes, which can cause a pseudo-increase in



Figure 5. X-ray of the sacroiliac joints.

Ankylosis of the joints on both sides, the L1-L4 vertebral bodies are connected with staples, the height of the intervertebral spaces is reduced.

(Figure 5. X-ray of the pelvic: ankylosis on both sides, the L1-L4 vertebral bodies are connected with staples, the

mineral density, and extraspinal bone can level out osteoporosis in the spine.

height of the intervertebral spaces is reduced).

It is known from the literature that vertebral fractures do not occur uniformly along the spine, but, as shown in postmenopausal and senile osteoporosis, they occur more often in the midthoracic and thoracolumbar regions. In addition to load (height, weight, muscle forces, movements such as bending), other factors play a role in fracture, for example: spinal curvature and heterogeneity of BMD between vertebrae, and spinal stiffness in ASA may also contribute to the risk of fracture [6,11].

Risk factors for AP such as duration of the disease, persistent high activity, C-reactive protein, BASDAI and BASFI indices and reduced bone density values, along with a high process of osteogenesis - an immobilized spine due to ankylosis, prolonged use of non-steroidal anti-inflammatory drugs and the lack of effect of basic therapy led to a fracture spine in the clinical case of patient S. and suggests a high risk of fracture in the case of patient M. Thus, OP and osteogenesis coexist in AS and solving the problem of pathological fractures requires early monitoring of bone mineral density with the use of medications for the prevention and treatment of OP.

The densitometry results of our clinical cases are consistent with the studies of Kang KY et al. High disease activity associated with inflammation and new bone formation, spinal dysfunction and mobility as assessed by BASFI and BASMI was found to be associated with low levels of bone density at the femoral neck (DXA of the hip) in patients with AS [18].

However, the clinical use of DXA to assess fracture risk in patients with AS has not been well studied. Based on a meta-analysis [19] of prospective population-based cohorts from countries around the world studying hip DXA in predicting fracture risk, a threshold value for bone degradation was determined. However, it is unclear whether this threshold can be used in patients with AS of any ethnicity, since ethnicity influences the predictive ability of hip DXA for fracture [14].

We think that further research is needed into the clinical use of hip joint DXA to assess fracture risk in patients with AS.

**Limitations of the study.** We did not examine the influence of treatment and laboratory parameters on the development of osteoporosis in patients with AS.

**Conflict of interest**: The authors declare that there is no conflict of interest, and that no part of this article has been published in the open press and is not under consideration by other publishers.

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