

Asymptomatic Atlantoaxial Subluxation in Rheumatoid Arthritis

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Abstract- This cross-sectional study is conducted to determine the prevalence of asymptomatic cervical spine subluxation in rheumatoid arthritis patients by plain radiographs and its relation to demographic and clinical characteristics, disease activity measures and medications. 100 rheumatoid arthritis patients (18 male and 82 female) were selected randomly, according to the American college of Rheumatology Criteria, who were under follow up in the rheumatology clinic. A complete history was taken, and physical examination has been done with focus on the cervical spine to determine their demographic data, disease duration, age of disease onset, drug history, swollen and tender joint counts, and ESR, Hb, CRP, RF levels. The disease activity of patients with rheumatoid arthritis was measured using the disease activity score 28. Radiographs of the cervical spine included lateral views taken in flexion, extension, neutral position of the neck and anteroposterior and odontoid projection view. Asymptomatic cervical spine subluxation was found in 17 of the 100 patients (17%). The prevalence of, anterior atlantoaxial subluxation, atlantoaxial impaction and subaxial subluxation was 10(10%), 5(5%) and 6(6%), respectively. Posterior subluxation was not detected. The only characteristic that showed meaningful relationship with cervical spine subluxation was CRP ($P=0.036$). Our results showed that patients with RA, who have cervical spine subluxation cannot be distinguished on the basis of symptoms. Cervical spine involvement is common and may be asymptomatic, indicating routine cervical spine imaging is needed in patients with RA.

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Introduction

Rheumatoid arthritis (RA) is a chronic multisystemic disease of unknown cause. The characteristic feature is persistent inflammatory synovitis usually involving peripheral joints in a symmetrical distribution. Synovial inflammation causes cartilage destruction and bone erosion. Subsequently, joint deformity occurs. The axial skeleton, with the exception of the cervical spine, is affected later and less frequently (1).

The prevalence of RA in most populations is twice in women than men. Women had prevalence of 1.37% and in men 0.74% (2). It typically presents between the ages of 30 and 50 years (3).

The etiology of RA is not fully understood but involves a complex interplay of environmental and genetic factors. Most commonly pathogenic factors are heredity, infectious agents, and sexual factors (4).

Most commonly, the onset symptoms of joint pain and swelling are insidious, occurring over weeks to months. However, a minority of patients may present with an abrupt explosive onset (5).

After the small joints of the hands, the most common region to be involved in rheumatoid arthritis is the cervical spine. This can lead to severe pain and disability, as well as a variety of neurologic sign and symptoms although some patients with significant radiographic evidence of disease may be asymptomatic (6).

One of the most important forms of cervical spine involvement in RA is subluxation that has different subgroups: Atlantoaxial subluxation (AAS) in 50% of patients, atlantoaxial impaction (AAI) in 35% of patients, subaxial subluxation (SAS) in 15% of patients (6).

The most common presentation is pain (especially in the neck and occipital area) and seen in 40-80% of patients. Neurologic manifestations (radicular pain,

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paresthesia, weakness and motor disorders ...) are seen in 12-50% of patients. The most important complication is sudden death which is worrisome (6).

According to these studies, it is important to screen rheumatoid patients for cervical spine subluxation with plain radiographs before causing severe complication and treat it properly (6).

Materials and Methods

This cross-sectional study was carried out in six months with 100 RA patients (18 male and 82 female) diagnosed according to the American college of Rheumatology Criteria (ACR) who were under follow up in the rheumatology clinic or admitted in Rheumatology ward.

All of the patients that selected randomly underwent a complete history taking and physical examination with a focus on the cervical spine by a rheumatologist to determine their demographic data, disease duration, age of disease onset, swollen and tender joint counts. ESR, Hb, CRP, RF levels were checked in the follow-ups. The disease activity of patients with RA was measured using the disease activity score 28 (DAS28). Questionnaires about possible symptoms related to cervical spine disease were completed. The exclusion criteria in this study were symptomatic patients and previously diagnosed subluxation.

Radiographs of the cervical spine included lateral views taken in flexion, extension, neutral position of neck and anteroposteriorly and odontoid projection view after taking a consent form.

A diagnosis of aAAS is made if the distance between the anterior aspect of the dens and the posterior aspect of the anterior arch of atlas is more than 3 mm during flexion. Atlantoaxial impaction is measured using the McGregor line. This line is contracted from the base of the hard palate to the outer cortical table of the occiput. The tip of the odontoid is measured perpendicular to this line. Superior migration is considered present if the tip of the odontoid is 4.5 mm above this line. SAS is diagnosed if a vertebra has moved 3mm or more in relation to the next vertebra when measured from the posterior line of the vertebral bodies. In addition, the posterior atlantodental interval is measured from lateral view radiographs.

The distance of 14mm is determined to be critical as it has been reported to predict paralysis in rheumatoid patients with cervical spine involvement.

Cervical spine radiographs were evaluated by a radiologist.

Results

Mean age (SD) of the 100 patients was 53.05 ± 15.51 years and mean duration of RA 10.57 ± 9.80 was years. Eighty two of patients (82%) were female, 65(65%) were RF positive, and 16(16%) patients had radiographic erosions in their hands. At the time of evaluation 81(81 %) were taking DMARDS, 76(76%) MTX and 88(88%) steroids. 60 patients took these drugs in combination. Asymptomatic cervical spine subluxation was found in 17 of the 100 patients (17%) (Table 1).

Table 1. Prevalence of asymptomatic cervical spine subluxati in 100 patients who were under follow up in rheumatology clinic or admitted in ward

Subluxation	N(%)
Prevalence of disorders	17(17%)
aAAS(>3mm)	10(10%)
AAI	5(5%)
SAS (2:3mm)	6(6%)
No subluxation	83(83%)

The prevalence of aAAS, AAI and SAS was 10 (10%), 5 (5%) and 6 (6%), respectively. Posterior subluxation was not detected. A patient may have more than one disorder. The youngest patient was a 20 year old male who was diagnosed as juvenile RA since 10 years ago. The oldest one was a 77 year old female with 35 year's duration of RA. Twelve patients with subluxation (70.6%) and seventy patients without subluxation (84.3%) were female

The mean duration of RA in patients with

subluxation was not significantly different from patients without subluxation (12.53 and 10.17 years, respectively; $P=0.28$) (Table 2).

While disease activity (measured by DAS 28), ESR and Hb showed no significant association with cervical spine subluxation, a noticeable relationship was found between cervical spine subluxation and CRP ($P= 0.036$) (Table 3). Only two of 16 patients with erosive disease, had subluxation.

Table 2. Clinical characteristics at the time of evaluation in 100 patients with and without cervical spine subluxation

Characteristics	Patient with cervical spines subluxation	Patients without cervical spines subluxation	P value
	(n=17)	(n=83)	
Duration of RA (Years) ¥	12.53(10.42)	10.17(9.68)	0.368
RF δ positive	11(64.7%)	54(65.1%)	0.592
No with erosive Disease	2(11.8%)	14(16.9%)	0.459
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Values are mean (SD), n(%), ¥RA: rheumatoid arthritis, δRF: Rheumatoid factor

Table 3. Disease activity measures at the time of evaluation in 100 patients with and without cervical spine subluxation

Characteristics	Patient with cervical spines subluxation	Patients without cervical spines subluxation	P value
	(n=17)	(n=83)	
Hb (g/dl) δ	11.72±1.88	11.99±1.99	0.614
ESR(mm/h) ¥	36.94±24.85	41.41±30.83	0.576
CRP*	13±76.5	41±49.4	0.041
DAS 28£	11±64.7	54±65.1	0.978

Values are mean (SD), n(%), ¥Hb: Hemoglobin, δESR: Erythrocyte sedimentation rate 0, *CRP: C-reactive protein, £DAS 28: Disease activity score 28

Discussion

Rheumatoid arthritis, well recognized as a chronic, progressive, systemic inflammatory disease primarily affecting synovial joints, results in disabilities.

Cervical spine involvement is common and potentially severe in patients with rheumatoid arthritis (7).

Collin D Net al, 1991, believed that asymptomatic cervical spine subluxation in patients with RA is highly prevalent. 49% of the patients showed evidence of AAS. 38% also showed evidence of AAI or SAS (8). Kauppi *et al.*, reported a 35% prevalence of AAI, and Grauer *et al.*, reported a 41 % prevalence of. Cervical spine instability in rheumatoid patients who had undergone total hip or knee replacement (8,9).

Neva *et al.*, also reported 44% cervical spine subluxation in patients with RA on a waiting list for orthopedic surgery (9).

The high incidence of atlantoaxial subluxation reported by Conlon *et al*, 1966, Mathews *et al*, 1969 and Meikle *et al*, 1971, emphasized the need for further knowledge about the natural history of this condition (10-12).

The incidence of cervical instability is 5-7% according to Campbell *et al.*, 1995 and Riise *et al.*, 2001, being more severe in those with erosive disease. The atlantoaxial joint is more prone to subluxation, most commonly in an anterior direction. Only 255 of patients

with AAS have symptoms or signs as mentioned by Arawwawala D (13). Younes *et al.*, concluded that C I-C2 pannus was the most common lesion (62.5% of cases), followed by atlantoaxial subluxation (AAS, 45%). The most common AAS pattern was anterior subluxation (25%), followed by lateral subluxation (15%) then by vertical, rotatory, and subaxial subluxations (10% each). Cervical spine involvement was found in 29 (72.5%) patients and was asymptomatic in 5 (17.2%) patients (14).

Zikou AK *et al.*, 2005, believed that cervical spine radiological involvement is a frequent finding in patients with RA, but the severity of the disease is rather mild, possibly related to the ethnic background (15).

According to Naranjo A *et al.*, 2004, AAS is frequent in RA patients, particularly in those with markers of erosive disease. AAS was found in 88 out of 736 patients with available cervical radiographs. The presence of AAS was highly associated with RA duration of more than ten years, disease onset before age 50, eye involvement, and previous RA related surgery. No association was found with rheumatoid factor. Multivariate analysis showed that a disease onset before the age of 50, the number of previous DMARD, and, above all, were important independent factors associated with AAS (16).

Another study by Kauppi MJ *et al.*, 2009, demonstrated that RA patients with sustained clinical disease activity are at increased risk of developing

aAAS. The development of aAAS during the first five years of RA was rare among the patients treated with a combination of DMARD for at least 2 years from the diagnosis. Intensive treatment with traditional DMARD prevents or retards the development of aAAS in patients with recent-onset RA (17).

Vesela *et al.*, performed a study on patients with rheumatoid arthritis in Czech to identify typical pain symptoms and their relationship to radiologic findings at the C1/C2 level. Four hundred patients with RA were selected randomly and examined by plain X-ray. Cervical spine involvement was found in 45.8% of these patients. Cervicocranial syndrome was the most common symptom of any spine involvement at the C1/C2 level and was present in 54.6%. Cervicocranial syndrome was typical for ventral subluxation 3-6 mm and was found in 52.9%. A distance of 8 mm or more was associated with mild pain. The pain intensity at the C1/C2 level decreased with increasing distance of ventral atlantoaxial subluxation (18).

Our main observation was that 17% of patients with RA, who were under follow up in the rheumatology clinic or admitted in the ward of Hafez Hospital, had subluxation of the cervical spine. The prevalence of aAAS, AAI and SAS, was 10(10%), 5(5%) and 6(6%), respectively. Posterior subluxation was not detected. A patient may have more than one disorder.

Our results showed lower prevalence of cervical spine subluxation than previous studies; may be due to different sampling; we only selected asymptomatic patients from who were under follow up in the rheumatology clinic or admitted in the ward. So we selected the rheumatoid patients in general. However, in previous studies the patients were selected from whom waiting for orthopedic surgery.

Another problem that can be considered as a limitation is that magnetic resonance imaging (MRI) was not included in our study that can help us to confirm the diagnosis.

Our result demonstrated that patients with RA, who have cervical spine subluxation cannot be distinguished on the basis of symptoms.

Cervical spine involvement is common and may be asymptomatic, indicating that routine cervical spine imaging is indicated in patients with RA. Standard radiography including dynamic views constitutes the first-line imaging method of choice. Sensitivity and comprehensiveness of the assessment are greatest with MRI. MRI and CT are often reserved for selected patients (14).

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