Radiological and Laryngoscopic Assessment of Patients with Autoimmune Polyarthritis

Original Article Asmaa El-Dessouky Rashad¹, Ahmad Abdelmonem Ragab¹, Dina Salem Fotoh Soliman², Samah Samy Youssef², Shimaa Abdelhamid Hassanein³, Hanan Anwar¹

¹Department of Otorhinolaryngology, ²Department of Rheumatology, Physical Medicine and Rehabilitation, ³Department of Radiology Faculty of Medicine, Menoufia University, Egypt.

ABSTRACT

Objectives: This study aimed to assess the laryngeal affection [laryngoscopy and computed tomography (CT)] in systemic polyarthritis patients [rheumatoid arthritis and systemic lupus erythematosus (SLE)] as well as their correlation to disease duration.

Patients and Methods: A cross-sectional study including 35 consecutive patients with poly arthritis (24 cases (68.6%) with rheumatoid arthritis and 11 cases (31.4%) with SLE who were diagnosed according to the American College of Rheumatology (ACR) criteria. Sociodemographic data, clinical data and laryngopharyngeal complaints were obtained. All cases were examined using videolaygoscopy and computerized tomography (CT).

Results: The patients' age ranged from 21 to 51 years; they were mainly females (94.3%). laryngeal complaints were presented in 80% of the studied patients; difficult swallowing (20%), dyspnea (8.6%), dysphonia (73.3%) and globus pharynges was (71.4%) and had significantly longer duration in SLE patients. On videolaryngoscopy, 31 cases (88.6%) had laryngeal abnormalities; 7 cases (20%) had nodule, all nodules were bilateral. Interarytnoid reaction was noted in 28 cases (80%), arytenoid edema in 27 cases (77.1%) and exaggerated vascular markings in 13 cases (37.1%), no cases showed vocal folds immobilization. On CT imaging, calcification was reported in 29 cases (82.9%).

All laryngeopharyngeal findings weren't related to duration of the disease, except, cases with joints calcification had longer disease duration.

Conclusion: Larygoparyngeal affection is common in autoimmune polyarthritis diseases, and it occurs irrespective to disease duration, joint radiological affection is also prevalent, so laryngopharyngeal and phoniatric assessment and radiological follow up of such cases seems to be beneficial for patient outcome.

Key Words: Laryngeal, rheumatoid arthritis, rheumatoid nodule, systemic lupus erythematosus.

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Corresponding Author: Asmaa El-Dessouky Rashad, Phoniatric Unit, Otorhinolaryngology Department, Faculty of Medicine, Menoufia University, Egypt, Tel.: 01002727331 E-mail: Asmaa_rashad1983@yahoo.com

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INTRODUCTION

Poly arthritis means that five or more joints in your body are affected by arthritis and inflammation. It's most often associated with autoimmune diseases such as rheumatoid arthritis (RA)^[1] and SLE had polyarthralgia and polyarthritis as the most common joint problems. In fact, over 50% of lupus patients possess this ailment upon their initial diagnosis with a negative impact on both quality of life and overall prognosis^[2].

In auto immune poly arthritis disease (RA & SLE), Musculoskeletal involvement is one of the most obvious manifestations, affecting up to 90% of patients. In SLE, it is the onset symptom in 60–80% of cases and documented in disease flares in up to 60%^[3,4] Transient joint complaints are usually presented mainly in the form of arthralgia or arthritis, with persistent pain, swelling, morning stiffness, and debility. The most frequently affected joints are the metacarpophalangeal and interphalangeal, wrist, and knee, also, tenosynovitis or tendonitis could be present^[5]. The prevalence of laryngeal involvement in Rheumatoid Arthritis (RA) and SLE had very variable range, it ranges from 13 to 75% in different studies. The specific manifestations include the cricoarytenoid arthritis and the presence of rheumatoid nodules in the vocal folds (Bamboo Nodes)^[6]. Severe nodulosis observed at the upper lip of the vocal fold or anywhere in the larynx may cause change in voice quality (dysphonia)^[7].

Laryngeal manifestations in autoimmune poly arthritis patients are usually subclinical and benign^[8] Initial symptoms are hoarseness, globus pharyngeus and the sensation of having a foreign body in the throat. Afterwards, patients experience odynophagia, sore throat, cough and dyspnea. Dysphonia happens to 12% to 27% of the patients with RA.

Musculoskeletal (MSK) involvement is one of the most frequent and the earliest locations of disease^[9].

These disorders affect joints and periarticular soft tissues, tendon sheaths and tendons, bones, and muscles, they are chronic diseases characterized by progressive tissue damage. identifying a potential related dysphonia could be relevant for the appraisal and management of this disease^[10]. In recent decades, novel treatments have greatly extended the life span of SLE patients. This creates a high demand for identifying the overarching symptoms associated with SLE and developing therapies that improve their life quality under chronic care^[11].

The connection between voice issues the studied diseases to be related to the only joint in the throat: the cricoarytenoid joint. The cricoarytenoid joint, located in between the cricoid and paired arytenoid cartilage in the larynx, are diarthrodial joints that tighten the vocal cords when they come together for speech and move apart for breathing^[12].

This study aimed to detect the rate and type of laryngeal symptoms and larngoscopic and CT findings in systemic polyarthritis patients (rheumatoid arthritis and SLE) as well as their correlation to disease duration.

METHODS

A cross-sectional study including 35 consecutive cases of poly arthritis and attending Rheumatology, Physical medicine and Rehabilitation department and radiology department were conducted.

CASE SELECTION

The patients who fulfilled at least four criteria of the updated American College of Rheumatology criteria^[13] were diagnosed as confirmed SLE cases.

RA patients were definitely diagnosed when they fulfilled the 2010 American College of Rheumatology (ACR) classification criteria for RA and their age was > 18 years^[14].

Patients who were definitely diagnosed with rheumatoid arthritis or SLE, patients who were aged (20–60) years, and those who were under medical treatment for any estimated period after establishing diagnosis were included in this study. But those who were smokers, had a history of laryngeal surgery, a history of neck trauma, head and neck cancer, or post-radiotherapy cases, as well as those who were known as professional voice users or had a history of voice abuse or strain, were excluded from the study.

The institutional ethics committee approval was obtained from Institutional Review Board under number (9/2024ENT2). From all the patients included in the study, informed consent was received from each patient after assuring confidentiality of their data.

Sample size calculation

According to Hamdan *et al*, 2007 who found that the percentage of thickening of true vocal cord is 2.27% among rheumatoid arthritis patients. The sample size is calculated using statistics and sample size pro program version 6, at a power of the study 80% and confidence level 95%, α error=0.05. It is two tailed study, using the following formula.

$$n \geq \frac{Z_{1-\alpha_{2}}^{2} \times p(1-p)}{d^{2}}$$

n:Sample size, Z = 1.96, *p*:expected proportion, *d*:marginal error= 0.05.

 \div The estimated sample size was 35 polyarthritis patients.

All included patients were subjected to:

• History taking including, demographic data (age, gender, special habits), clinical history including disease duration especially laryngeal and articular symptoms and its duration (change of voice, Loss of voice, Pain in the throat, A sensation of tenderness at the back of the throat, A constant urge to clear the throat, and breathing difficulties).

• Videolaryngoscopic examination. For laryngeal assessment, the patients were subjected to videolaryngoscopy, which was carried out with the 8mm 70° rigid telescope, coupled to the halogen Sigmed[®] FL250 light source and a Toshiba[®] micro camera. Stroboscopy was not utilized. The 10% lidocaine spray was used in the patients' oropharynx when needed. The videolaryngoscopy exams were always done by the same examiner.

• Non contrast Computerized tomography (CT) scan of the neck and laryngeal cartilages. A non-contrast Ct examination of the neck was conducted for all included patients 128 multi-detector CT scanner (revolution, GE, USA). Patients were scanned in the supine position with the head rested in the neutral position at the table, both arms placed next to the body and shoulders pulled down. Patients were asked to breathe quietly and, not to swallow during the scan. A scout was then taken from the mid-chest to vertex, then the scan extent was from the hard palate till the aortic arch in a craniocaudal direction. The scan parameters were (tube voltage of \leq 120 kVp, automated current adjustment mode, field of view (FOV): 140-200 mm, slice thickness: \leq 0.75 mm, interval: \leq 0.5 mm).

Images were transferred to a dedicated workstation where it was analyzed in soft tissue and high-resolution bone reconstruction algorithm in multi-planar reconstruction viewing mode where the axis of centralization were perpendicular to the larynx.

Evaluation of the images of the larynx was performed by an experienced radiologist in head and neck images for cricoarytenoid joint as well as the arytenoids and cricoid cartilage morphology and any abnormality^[15].

Statistical analysis

Statistical package for social science (SPSS) version 27 software (SPSS Inc., Chicago, IL, USA). was used to compare the collected data. The data either qualitative or quantitative were described as frequency and percentage (qualitative data) or mean, standard deviation and range (quantitative data). Significant difference was tested in qualitative data using Chi square or Fisher's Exact tests accordingly. Mann Whitney U test is the test of two not normally distributed quantitative data settings while the 3 data categories were compared by Kruskal Wallis test. Significance level was considered when *P value* <0.05.

RESULTS

A cross-sectional study including 35 patients with autoimmune polyarthritis (24 cases, 68.6% rheumatoid arthritis) and (11 cases, 31.4% SLE) was conducted.

The age was 37.66 ± 10.27 and ranged from 21 to 51 years with non-significant difference between RA patients and SLE patients, the total patient group was mainly females (94.3%) who were mainly house wives. the

duration of the disease ranged from 3 months to 14 years in which SLE had significantly longer duration among our participants (*P value* = 0.008). surprisingly, 80% of the studied group had laryngeal complaint which varies from cough (22.9%), difficult swallowing (20%), dyspnea (8.6%), change in voice presented in 26 cases (73.3%) and globus pharyngeous was reported in 25 cases (71.4%) with its duration was significantly longer in SLE patients (*P value* = 0.002) (Table 1, Figure 1, 2).

Videolaryngoscopic examination revealed laryngeal abnormalities in 31 cases (88.6%); 7 cases (20%) had nodule, all nodules were bilateral and equal on both sides. Interarytnoid reaction was noted in 28 cases (80%), arytenoid edema in 27 cases (77.1%) and 13 cases (37.1%) had exaggerated vascular markings, no cases showed vocal folds immobilization (Table 2).

CT imaging revealed that 27 cases (77.1%) had normal joint space, 6 cases (17.1%) had relatively narrow joint space, while only 2 cases (5.7%) had narrow joint space. Calcification was reported in 29 cases (82.9%), this calcification was mainly nodular in shape (82.8%) and mostly affected arytenoid joint (58.6%) (Table 3).

Laryngeopharyngeal findings presented in autoimmune poly arthritis patients were not related to duration of the disease as all of these findings showed non-significant association with disease duration, affection of joint space on CT examination was also not significantly related to disease duration but joint calcification was related to longer disease duration (P value = 0.002) (Table 4).

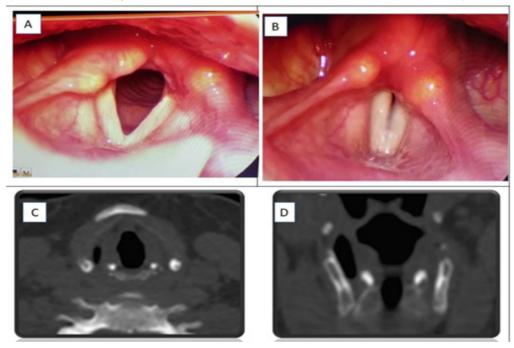


Fig. 1: (A) and (B) laryngoscopic examination demonstrating mild arytenoid edema. (C) CT scan axial cut bone window of the same patient at the level of cricoarytenoid joint showing sclerotic foci at the joint and (D) coronal view showing diffuse calcification and sclerosis of the arytenoid side of the joint.

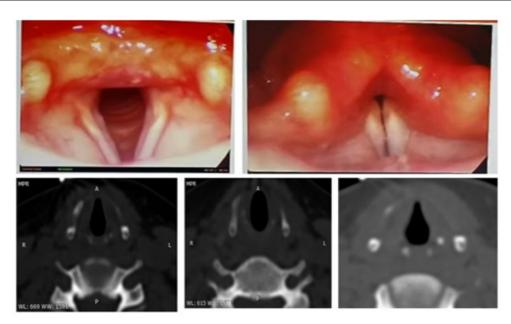


Fig 2: laryngocopy reveled bilateral mild arytenoid edema and CT scan cuts demonstrated bilateral small calcific nodules at the aryepiglottic folds while at the level of CAJ showing bilateral sclerotic foci.

	Total group $N = 35$	RA <i>N</i> = 24	SLE <i>N</i> = 11	Test (p value)
Age (years) Mean ±SD Range	37.66±10.27 21 - 51	36.17±9.44 21 - 50	40.91±11.69 21 - 51	<i>U</i> = 1.39 (0.16)
Sex Male Female	2 (5.7) 33 (94.3)	2 (8.3) 22 (91.7)	0 (0.0) 11 (100)	FE=0.97 (1.0)
Occupation House wife Students Employee Farmer Worker Doctor	27 (71.4) 3 (8.6) 3 (8.6) 1 (2.9) 1 (2.9) 2 (5.7)	17 (70.8) 1 (4.2) 3 (12.5) 1 (4.2) 1 (4.2) 1 (4.2)	$\begin{array}{c} 8 \ (72.7) \\ 2 \ (18.2) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 0 \ (0.0) \\ 1 \ (9.1) \end{array}$	$X^2 = 4.34$ (0.50)
Clinical findings Duration of disease Mean ±SD Range	4.904.73± 0.25 – 14	3.56±4.45 0.25 – 14	7.82±4.12 1 – 12	U = 2.59 0.008*
Laryngeal complaint	28 (80.0)	20 (83.3)	8 (72.7)	FE=0.53 (0.65)
Cough	8 (22.9)	6 (25.0)	2 (18.2)	FE = 0.20 1.0
Dyspnea	3 (8.6)	3 (12.5)	0 (0.0)	<i>FE</i> = 1.5 0.54
Difficult in swallowing	7 (20.0)	5 (20.8)	2 (18.2)	FE = 0.03 1.0
Voice changes	26 (74.3)	18 (75.0)	8 (72.7)	FE = 0.02 1.0
Course of voice changes Intermittent Persistent	N=26 19 (73.1) 7 (27.9)	N=18 11 (61.1) 7 (38.9)	N = 8 8 (100) 0 (0.0)	FE = 4.26 (0.06)
Globus pharyngeus	25 (71.4)	17 (70.8)	8 (72.7)	FE = 0.01 (1.0)
Duration of globus pharyngeus (year) Mean ±SD Range	N = 25 4.55±5.70 0.33 - 18	N=17 1.98±2.02 0.33 - 6	N=8 10.0 \pm 7.23 1 - 18	U = 2.95 0.002*

 Table 1:Sociodemographic data and clinical data among the studied group:

RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SD= standard deviation, U=Mann Whitney U test, FE= Fisher's Exact test, X^2 = Chi squared test, *= significant P value (<0.05).

 Table 2: Videolaryngoscopic finding among the studied cases:

	Total group $N = 35$	RAN = 24	SLE N = 11	Test (p value)
Videolaryngoscopic finding				FE = 0.72
Present	31 (88.6)	22 (91.7)	9 (81.8)	(0.58)
Presence of nodule	7 (20.0)	7 (29.2)	0 (0.0)	FE = 4.01
				(0.07)
Side of nodule	N = 7	N = 7		
Bilateral	7 (100)	7 (100)		
Equality of nodule	N = 7	N = 7		
Equal	7 (100)	7 (100)		
Nodule, level number	N = 7	N = 7		
One level	3 (42.9)	3 (42.9)		
Two level (bamboo)	4 (57.1)	4 (57.1)		
Interarytnoid reaction	28 (80.0)	19 (79.2)	9 (81.8)	FE = 0.03
				1.0
arytenoid edema	27 (77.1)	18 (75.0)	9 (81.8)	FE = 0.20
				1.0
Side of arytenoid edema	N = 27	N = 18	N = 9	FE = 6.75
Left	9 (33.3)	9 (50.0)	0 (0.0)	(0.01)
Bilateral	18 (66.7)	9 (50.0)	9 (100)	
VF immobility				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	
No	35 (100)	24 (100)	11 (100)	
Concomitant finding				<i>FE</i> = 9.48
Negative	22 (62.9)	13 (54.2)	11 (100)	(0.002)*
Exaggerated vascular markings	13 (37.1)	11 (45.8)	0 (0.0)	

N = number, FE = Fisher's Exact test, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, U = Mann Whitney U test, FE= Fisher's Exact test, X^2 = Chi squared test *= significant P value (<0.05), ** = highly significant p value (<0.001)

Table 3: Radiological findings by CT among the studied cases:

Radiological findings	Total group N = 35	RA N = 24	SLE N = 11	Test (p value)
	N (%)	N (%)	N (%)	
Joint space	·			X ² = 1.92
Normal	27 (77.1)	19 (79.2)	8 (72.7)	0.38
Relatively narrow	6 (17.1)	3 (12.5)	3 (27.3)	
Narrow	2 (5.7)	2 (8.3)	0 (0.0)	
Calcification				FE = 0.01
	29 (82.9)	20 (83.3)	9 (81.8)	(1.0)
Location of calcification	N = 29	N = 20	N = 9	
Cricoid	5 (17.2)	5 (25.0)	0 (0.0)	$X^2 = 10.86$
Arytenoid	17 (58.6)	11 (55.0)	6 (66.7)	0.01*
Arytenoid & cricoid	4 (13.8)	4 (20.0)	0 (0.0)	
Arytenoid & cricoid & aryepiglottic fold	3 (10.3)	0 (0.0)	3 (33.3)	
Shape of calcification	N = 29	N = 20	N = 9	$X^2 = 2.72$
Nodular	24 (82.8)	15 (75.0)	9 (100)	0.26
Sheet like	3 (10.3)	3 (15.0)	0 (0.0)	
Nodular & sheet like	2 (6.9)	2 (10.0)	0 (0.0)	
Side of calcification	N = 29	N = 20	N = 9	<i>FE</i> = 1.51
Left	3 (10.3)	3 (15.0)	0 (0.0)	0.53
Bilateral	26 (89.7)	17 (85.0)	9 (100)	

RA = rheumatoid arthritis, SLE = systemic lupus erythematosus; N = number, X^2 = Chi squared test, FE= Fisher's Exact test; *= significant P value (<0.05).

	Duration of	Duration of the disease		Durler
	Mean ±SD	Range	U test	P value
Videolaryngoscopic finding				
Present	5.21±4.92	0.25 - 14	0.45	0.68
Absent	2.50±1.73	1 - 4	0.45	0.08
Presence of nodule				
Yes	4.29±6.64	0.25 - 14	1 (2	0.11
No	5.05±4.28	0.5 - 12	1.62	0.11
Interarytnoid reaction	5.71±4.91	0.25 - 14	1.95	0.051
	1.64 ± 1.62	0.5 - 4		
Arytenoid edema	4.91±4.50	0.25 - 12	0.04	0.97
5	4.87±5.81	0.5 - 14		
Concomitant finding				
Negative	4.75±5.77	0.25 - 14	1.29	0.20
Exaggerated vascular markings	4.98±4.15	0.5 - 12	1.29	0.20
Radiological findings				
Joint space				
Normal	4.85±4.51	0.25 - 14	K	
Relatively narrow	6.30±6.24	0.6 - 12	0.76	0.68
Narrow	$1.33{\pm}0.0$	1.33 - 1.33		
Calcification				
Yes	5.79±4.73	0.5 - 14	3.17	0.002*
No	0.58 ± 0.34	0.25 - 1	- ,	

 Table 4: Duration of disorders in relation to laryngeal disorders and radiological abnormalities:

U= Mann Whitney U test, K = Kruskal Wallis test; *= significant P value (<0.05), ** = highly significant p value (<0.001); U = Mann Whitney U test, K = Kruskal Wallis test, *= significant P value (<0.05).

DISCUSSION

laryngeal joints, despite of life supporting crucial function, it is forgotten joints during long management plan of systemic poly arthritis patients (RA &SLE) with limited researches about its affection.

Video-laryngoscopic examination revealed laryngeal abnormalities in a significant percentage (88.6%) of patients with autoimmune polyarthritis. Remarkably, 91.7% of RA patients displayed these abnormalities, with nodules being the most prevalent finding, detected in 7(29.2%) of RA cases.

This high rate of affection is coincident with that detected by Beirith *et al*^[6] who found 72.3% of his sample had laryngeal affection, but rate of nodule 2.13%.

This work revealed that the frequency of laryngopharyngeal complaint was 80% and videolaryngoscopic abnormalities were presented in 88.6% of the studied patients. Rate of dysphonia was 74.3% in total group and 75% & 72.7% for RA and SLE patients respectively. laryngopharyngeal complaint was 83.3% and 72.2% in RA and SLE patients respectively, and videolaryngoscopic abnormalities were presented in 91.7% and 81.1% for RA and SLE patients respectively. Beirith *et al*^[6] revealed that the prevalence of dysphonia and videolaryngoscopy changes was respectively 12.8% and 72.4%. Autoimmune diseases in general and rheumatoid arthritis in particular can cause dysphonia or change in voice quality secondary to either functional or anatomical laryngological alterations^[16].

de Macedo et al [9] interpreted the cause of laryngeal affection in SLE cases as a part of generalized tissue damage and documented that tissue damage scores in different organ systems correlated with dysphonic symptoms, suggesting that some features of SLE-related dysphonia are due to tissue damage. While Bayar et al [17] reported that about 66% of the laryngeal symptoms in RA patients are related to cricoarytenoid joint involvement. Also, Peters et al^[18] suggested cricoarytenoid arthritis is a potential cause of acute obstruction of the airways. In the same context, the current work; 82.9% of the studied cases showed calcification in larynx joints (cricoid, arytenoid) joints, even calcification was noted in 10.3% of cases in Arytenoid, cricoid & aryepiglottic folds, these findings may play a role in the high rate of related laryngeal manifestations.

The current study revealed that, no cases have been presented with vocal fold immobilization among the studied patients, this is in line with the study of Aljawi and Hantzakos^[19] who reported that Vocal fold paralysis and mononeuropathy have not been widely reported as a manifestation of SLE. also, Leszczynski et al^[20] documented that, vocal cords palsy is a rare complication in the course of systemic lupus erythematosus (SLE). also, Hyland et al^[21] reported the same observation regarding rheumatoid arthritis and it rarely presented as vocal fold immobilization or inspiratory stridor and if occur. it presented late in the disease process of RA. On the other hand, Teitel et al^[22] found that in SLE patients, 28% had laryngeal edema and 11% had vocal cord paralysis. Vocal fold paresis or paralysis wasn't almost detected in most researches, this can be explained by inflammatory and articular nature of larvngeal affection that rarely affect the nerves. Link et al^[23], tried to interpret the cause of vocal fold immobilization in RA as cervicomedullary compression (CMC) that may result from destructive arthritic changes and inflammatory pannus formation at the occipito-atlantoaxial joint in patients with rheumatoid arthritis (RA).

This current study reported arytenoid edema in the 77.1% of total patients; 75% in RA patients and 81.8% in SLE patient, this was obviously of higher rate than of Teitel *et al* ^[22] study.

Regarding the relation between duration of the disease and the presence of laryngeal affection, the current results showed non-significant relation between the disease duration and any of laryngeal findings except calcification of larynx joint, and that was understandable, as calcification takes time to be established. supporting these findings, those of Hart^[24] and Stojanovic& Belic ^[25] who documented that, the damage of laryngeal anatomical structures and physiological functions happens in the early phases of rheumatoid arthritis.

CONFLICT OF INTEREST:

There are no conflicts of interest.

CONCLUSION

Rheumatoid arthritis and SLE are autoimmune systemic diseases with a wide clinical presentation. The emergence of subtle airway symptoms and or change in voice quality in these patients should alert the primary caring physician and specialists to the presence of laryngeal involvement. A thorough laryngoscopic and radiological evaluation is recommended to rule out cricoarytenoid joint involvement. A multidisciplinary approach is needed to provide adequate laryngeal rehabilitation and alleviate the patient's suffering. An early diagnosis of laryngeal involvement may prevent drastic complications.

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