

# Three cases of rheumatoid arthritis with laryngeal stridor

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**Abstract** The purpose of this is case-based review is to report a series of patients with rheumatoid arthritis who developed stridor and highlight this potentially life-threatening manifestation of the disease. We report three cases from the Rheumatology Department of University College Hospital, London and review the literature on the prevalence, clinical presentation, histopathological features and treatment of laryngeal involvement in rheumatoid arthritis. In two patients, emergency tracheostomy was necessary to maintain a patent airway. One patient improved with systemic corticosteroids without the need for surgical intervention. All patients were seropositive with anti-CCP antibodies and had long-standing erosive disease. Stridor in patients with rheumatoid arthritis is typically due to arthritis of the cricoarytenoid joints leading to fixation of the vocal cords in a midline position. Cricothyroid joint arthritis may be acute, chronic, or acute-on-chronic. Emergency tracheostomy may be life-saving in cases of acute stridor. Cricothyroid inflammation and airway compromise may respond to local or systemic corticosteroid therapy. Other causes of vocal cord paresis in rheumatoid arthritis include ischaemic neuropathy of the recurrent laryngeal and vagus nerves due to vasculitis or cervicomedullary compression due to rheumatoid involvement of the cervical spine.

**Keywords** Cricothyroid joint · Rheumatoid arthritis · Stridor · Tracheostomy · Vocal cord paresis

## Introduction

Laryngeal stridor is an uncommon but potentially life-threatening complication of rheumatoid arthritis (RA). Prompt recognition of stridor and early involvement of anaesthetic and otolaryngology specialists with a view to tracheostomy can be life-saving. We aim to increase awareness of this condition among rheumatologists, otolaryngologists and emergency physicians.

## Methods

We report three patients with RA (under the care of the Rheumatology Department of University College Hospital, London) who developed stridor. We review the literature on the prevalence, clinical presentation, histopathological features and treatment of laryngeal involvement in RA.

## Results

### Case 1

Patient 1 was a 50-year-old man with a 12-year history of erosive RA with nodules, complicated by episcleritis and scleromalacia. Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibodies were positive. He also had steroid-induced diabetes. He presented with acute respiratory distress and inspiratory stridor. He reported a 3-day history of sore throat and increasing dyspnoea, which

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was worse at night and when lying flat. His wife had noticed snoring. He was taking prednisolone 25 mg daily, gliclaside, omeprazole, alendronic acid, folic acid and ibuprofen. He had received rituximab 3 months prior to this presentation. At a clinic visit shortly before this presentation, his RA was active, with erythrocyte sedimentation rate (ESR) of 45 mm/h and C-reactive protein (CRP) of 20 mg/L. Previous treatments had included methotrexate, leflunomide, hydroxychloroquine, etanercept, and adalimumab.

The patient was given intravenous dexamethasone and adrenaline nebulisers, but deteriorated and so was intubated and ventilated. Rigid bronchoscopy showed bilateral impairment of vocal cord abduction, ulceration of the vocal cords and marked swelling of the aryepiglottic folds. An emergency tracheostomy was performed. Computed tomography (CT) of the neck and thorax showed lower lobe consolidation in the right lung, but no abnormality in supraglottic region or at level of cords. Vocal cord biopsy revealed inflammation and ulceration of the mucosa, no organisms on Gram staining, and no features of vasculitis or malignancy.

Repeat laryngoscopy 2 months later showed persistent supraglottic swelling and arytenoid oedema compromising the airway. Twenty months after the original presentation, the tracheostomy was removed. Further laryngoscopy showed normal vocal cord movements and minimal arytenoid swelling. The patient's voice was reasonable and he was able to eat and drink normally.

#### Case 2

Patient 2 was a 75-year-old woman with a 40-year history of erosive RA and secondary Sjögren's syndrome, for which she took methotrexate 15 mg weekly. RF and anti-CCP antibodies were positive. She reported a 2-year history of progressive dyspnoea, cough and increasingly hoarse voice. The latter was worse in the evenings and caused her considerable distress. Examination revealed inspiratory stridor. There was chronic severe deformity of her peripheral joints but no active synovitis. ESR was 22 mm/h and CRP <5 mg/L. A flow–volume loop revealed extra-thoracic large airway obstruction (see Fig. 1). CT of her thorax demonstrated minor bronchiectasis only. Laryngoscopy showed the left vocal cord fixed in adduction and significant reduction of right vocal cord abduction.

She underwent laser arytenoidectomy using a flexible bronchoscope as her severe hand arthritis precluded self-management of a tracheostomy. The procedure was complicated by post-operative swelling of the glottis leading to type 2 respiratory failure, necessitating an emergency tracheostomy. She was decannulated 10 days later. However, over the next 2 months, she once again

developed worsening stridor. A permanent tracheostomy was performed and fitted with a speaking valve. She subsequently remained free of upper airway symptoms. Her tracheostomy is managed with the help of full-time home carers.

#### Case 3

Patient 3 was a 75-year-old woman with RA diagnosed 9 years earlier. RF and anti-CCP antibodies were positive. She presented with dysphonia, dysphagia, mild dyspnoea, and 10 kg of weight loss over the previous month. Her arthritis had initially been well controlled on gold injections, but 10 months prior to presentation became active. However, she defaulted from follow-up and discontinued gold. On admission, she was cachectic, bed-bound, and unable to vocalise. She was febrile with crackles at the right lung base. There was a widespread vasculitic rash with small digital infarcts, ulceration over her sacrum and ankles, and a symmetrical deforming polyarthropathy but no active synovitis (Fig. 2a, b). ESR was 126 mm/h and CRP was 212 mg/L. Three sets of blood cultures, hepatitis B and C serology, ANCA, ANA, and ENA were all negative. A transthoracic echocardiogram showed no vegetations. A skin punch biopsy was consistent with rheumatoid vasculitis. A chest radiograph showed right basal opacification. CT of her neck/chest/abdomen showed right basal consolidation in keeping with aspiration pneumonia, but no evidence of a neoplasm. Laryngoscopy revealed bilateral paresis of the vocal cords.

She was given intravenous antibiotics, and feeding was commenced via a nasogastric tube. She had already been commenced on prednisolone 30 mg daily by the acute medical team for a presumptive diagnosis of chronic obstructive pulmonary disease in view of breathlessness and 'wheeze'. Her prednisolone dose was increased to 40 mg daily. The rash resolved over the next 7 days. Over the next 2 weeks, her vocal cord palsy improved. She was able to talk and eat normally and could mobilise.

#### Discussion

We report three patients with RA presenting with stridor due to bilateral vocal cord paresis. Patient 1 presented with acute onset stridor and life-threatening airway compromise necessitating tracheostomy. The onset of symptoms in the other two cases was more insidious, although patient 2 ultimately required a permanent tracheostomy and patient 3 developed aspiration pneumonia. All patients were seropositive with anti-CCP antibodies and had erosive disease.

Laryngeal stridor is an uncommon but well-described complication of RA. Although described as long ago as

**Fig. 1** Flow–volume loop showing extra-thoracic large airways obstruction in patient 2

### Spirometry

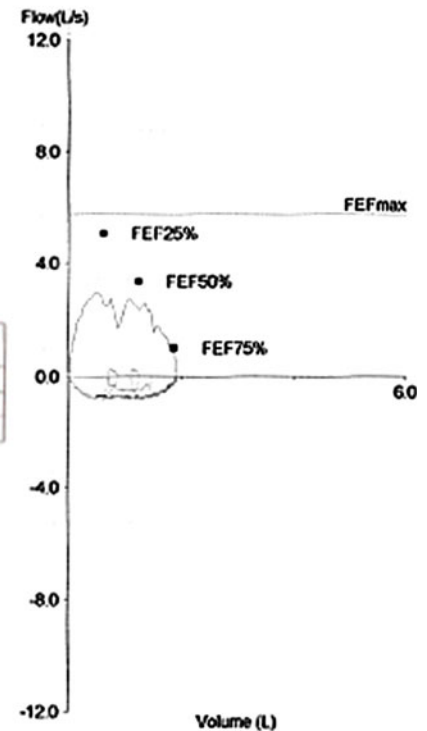
	Units	Predicted	Result	% Predicted
PEF	L/s	5.74	2.97 <	52 <
FEV1	L, btps	2.07	1.91	92
FVC	L, btps	2.50	1.92	77 <
FEV1/FVC	%	75.04	99.74	133 >
FEF50%	L/s	3.35	2.10	63 <
FEF75%	L/s	0.99	2.28	229 >

### Transfer Factor

	Units	Predicted	Result	% Predicted
TLco	mmol/min/kPa, stpd	7.13	6.44	90
VAsb	L, btps	5.10	4.67	91
KCO	mmol/min/kPa <sup>1/2</sup> , stpd	1.40	1.38	99

### Technician Notes

Good effort on all tests.



1880 [1], it received closer attention in the 1950s and 1960s [2–4]. Most cases are due to cricoarytenoid joint arthritis. The cricoarytenoid joint (CAJ) is diarthrodial, with a ligamentous capsule lined by synovium. Muscles, innervated by the recurrent laryngeal nerve branch of the vagus nerve, acting on the joint adduct and abduct the vocal cords. Therefore, either acute inflammation or chronic ankylosis of the joint can impair vocal cord movement. Symptoms vary according to whether there is unilateral or bilateral cricoarytenoid involvement and on the position in which the vocal cords become fixed. Typical symptoms of CAJ arthritis include hoarseness, dyspnoea, dysphagia, odynophagia, pain radiating to the ears, and fullness in the throat, particularly when swallowing or speaking [4]. When there is bilateral CAJ involvement and the cords become fixed in an adducted position, life-threatening acute airway obstruction can rapidly occur.

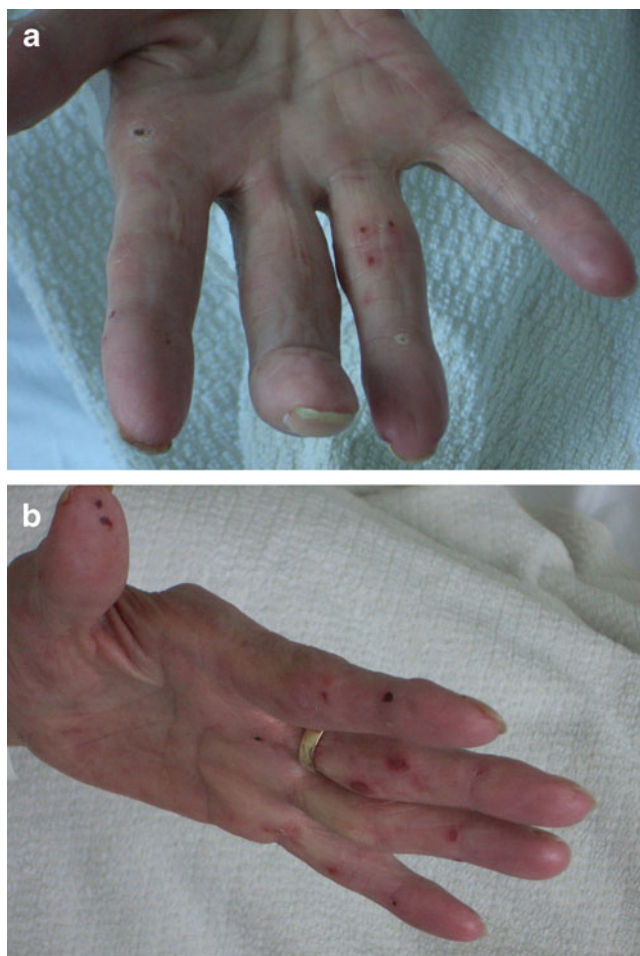
In less acute cases where the airway is not immediately threatened and the patient presents with mild exertional dyspnoea without stridor evident at rest, pulmonary function testing may point to the diagnosis. Bilateral paralysis of the vocal cords produces characteristic changes in the flow–volume loop (Fig. 1). Extra-thoracic airway obstruction is suggested by a forced expiratory flow at 50% lung volume/forced inspiratory flow at 50% lung volume greater than one, or forced expiratory volume in 1 second/peak expiratory flow rate greater than 10 ml/l/min [5].

Series from the 1960s suggested that CAJ arthritis was under-recognised. Montgomery found laryngeal involvement

in 26 of 100 RA patients [6]. Bienstock et al. investigated 64 RA patients, none of whom had presented with symptoms of CAJ arthritis [7]. On direct questioning, 27% had symptoms suggesting cricoarytenoid involvement. Seventeen percent had laryngoscopic signs of cricoarytenoid involvement. Grossman et al. found that 17 of 55 RA patients had laryngeal symptoms. Eighteen had signs of CAJ arthritis on mirror exam, of whom half were asymptomatic [8]. Erosions of the CAJs were demonstrated by low-dose radiography in 45% of RA patients [9].

Generally, stridor due to CAJ arthritis develops late in the course of RA, as in our three patients. The peripheral joint examination usually reveals significant deformity but there may be little active disease, as in patients 2 and 3 [4]. Some cases of stridor in rheumatoid patients appear to have been precipitated by upper respiratory tract infection. Presumably, in such cases, the increase in soft tissue inflammation is sufficient to close an already compromised airway. Kolman reported a patient with RA who developed stridor due to vocal cord palsy following extubation, treated successfully with tracheostomy [10].

In most reported cases, CAJ arthritis was diagnosed clinically. However, distinguishing vocal cord immobility due to CAJ arthritis from a recurrent laryngeal nerve palsy can be difficult. Laryngoscopic signs of acute CAJ inflammation include erythema and tense swelling of the aryepiglottic folds, and oedematous true and false cords, as in patient 1. However, these signs may be absent in chronic CAJ arthritis. Fixation of the joints favours CAJ arthritis



**Fig. 2** a and b Photographs of patient 3's hands revealing rheumatoid deformity and vasculitic rash

over a nerve palsy. However, disuse fixation of the CAJs can occur with long-standing nerve palsies. Bowing of the vocal cords during inspiration (due to abductors attempting to pull the cords laterally) is a sign that can distinguish CAJ arthritis from laryngeal nerve palsy [4, 11]. EMG has been used to distinguish denervation of the vocal cords from other causes of vocal cord immobility [11, 12]. CT may be helpful in identifying CAJ arthritis. Of note, only patient 1 had both active peripheral joint disease and laryngoscopic signs of acute CAJ inflammation; both these features were absent in patients 2 and 3.

Darke et al. described five RA patients with laryngeal stridor, of whom four required tracheostomy [13]. In three cases, laryngoscopy revealed bilateral abductor muscle paralysis. Necropsy was performed on two of these three. In one patient, the CAJs were entirely normal. In the other, the CAJ synovium was thickened and chronically inflamed, but the joints were freely mobile. However, in both patients, there was severe demyelination and degeneration of the recurrent laryngeal and vagus nerves with neural atrophy of the laryngeal muscles. In one patient, this was accompanied

by gross obliterative arteritis of the vasa vasorum. Thus, ischaemic neuropathy due to arteritis as part of the rheumatoid process may account for vocal cord abductor muscle paresis in some cases.

Other post-mortem series have not reproduced these findings. Bienstock et al. found typical rheumatoid changes at the cricoarytenoid joints in all seven RA patients who underwent autopsy in their series [7]. Histopathological changes included synovial proliferation, pannus, and destruction of the articular cartilage. One patient had a rheumatoid nodule in muscle adjacent to the cricoarytenoid joint. Montgomery described two RA patients with stridor who underwent necropsy; both had marked CAJ inflammation [4]. Grossman et al. found that five of 11 consecutive RA patients had CAJ involvement at autopsy [8]. Only two of five were symptomatic, indicating that even advanced CAJ arthritis can be clinically silent.

Erb et al. described a rheumatoid patient with dysphagia and stridor requiring emergency tracheostomy [14]. The patient had a large inflammatory laryngeal mass compromising the laryngeal lumen and destroying the adjacent cartilage. Biopsies showed chronic inflammatory synovitis and confluent rheumatoid nodules. Cervicomedullary compression due to rheumatoid involvement of the cervical spine is an uncommon and easily overlooked cause of vocal cord palsy [15]. Laryngeal amyloidosis is another rare cause of stridor in RA [16].

Prompt recognition of stridor is essential. Stridor is often misdiagnosed as asthma or chronic obstructive pulmonary disease [5], as initially occurred in case 3. However, careful examination reveals that the stridor is inspiratory whereas the wheeze of obstructive airways disease is predominantly expiratory. If the airway is severely compromised, endotracheal intubation may be attempted but is often difficult. In such cases, tracheostomy can be life-saving [5, 13, 17–19], as in case 1. Subsequent decannulation may be possible if CAJ inflammation responds to treatment and vocal cord mobility improves. However, patients may function well with a permanent tracheostomy [18], as patient 2 did.

When the airway compromise is less critical, as in case 3, tracheostomy may be avoided and conservative measures attempted. Successful treatment of stridor due to CAJ arthritis with systemic corticosteroids as occurred with patient 3 has been described [2, 20]. Habib et al. reported injection of the CAJ with depomedrone allowing subsequent successful removal of a tracheostomy [21]. This cannot be attempted in a patient without a tracheostomy as it may lead to further swelling and fatal airway obstruction. Arytenoidectomy, as in patient 2, sometimes accompanied by vocal cord lateralisation procedures, has been used [4].

In conclusion, upper airway obstruction due to vocal cord paresis is an unusual complication of RA. It typically occurs in long-standing disease [7], usually due to involvement of the

cricoarytenoid joints by the rheumatoid process. CAJ involvement may be asymptomatic for many years before presenting acutely as stridor. Prompt recognition of stridor is essential, and early involvement of anaesthetic and otolaryngology specialists with a view to tracheostomy can be life-saving. Laryngoscopy should be considered as part of the investigation of RA patients with stridor, or breathing difficulties where other causes have been excluded. It is likely that the incidence of CAJ arthritis will decline as better control of RA is achieved with the early aggressive use of standard DMARDs and biological therapies.

**Disclosures** None

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Written consent has been obtained from all patients to publish the above case descriptions.