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# Hydralazine-induced lupus and vocal fold paralysis

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**Abstract**
Systemic lupus erythematosus (SLE) is a multi-system autoimmune disorder that can affect the upper airway. Hydralazine has been known to cause a lupus-like syndrome that can produce the clinical manifestations of SLE. We discuss a case of hydralazine-induced lupus, presenting with acute laryngeal oedema and right vocal fold paralysis. Cessation of hydralazine therapy resulted in reversal of paralysis.

**Key words: Lupus erythematosus, systemic; Vocal fold paralysis; Hydralazine**

## Introduction

The actual prevalence of laryngeal involvement in SLE is not known but it is a rare event. The symptoms can range from hoarseness of voice to respiratory obstruction. It is a potentially life-threatening complication and may occur in patients with active or inactive disease. It is an indication for close observation and steroid therapy (Korbet *et al.*, 1984).

Certain drugs can cause clinical manifestations very similar to SLE. Hydralazine, a potent vasodilator used in hypertension, is most notable in this group. The symptoms are usually reversed once the offending agent is stopped.

## Case report

A 60-year-old Caucasian female presented with hoarseness of voice and inspiratory stridor. She had complained of hoarseness for two months but the stridor had started two days before presentation. Her past medical history included hypertension, for which she was taking 50 mg of hydralazine three times a day. She had previously been seen by her general practitioner (GP) for stiffness and pain in her fingers, which was diagnosed as 'arthritis' and was taking coproxamol. She was otherwise fit and well. Examination showed marked oedema of the right hemilarynx resulting in airway obstruction, that required tracheostomy. Direct laryngoscopy revealed paralysis of the right vocal fold in the paramedian position and marked oedema involving the right vocal fold, false cord, aryepiglottic fold and arytenoid, biopsies of which showed inflammatory oedema with exudate. Passive mobilization of the crico-arytenoid joint during direct laryngoscopy did not show fixation. A CT scan of the larynx showed swelling involving the right supraglottic region.

Haematological investigations on admission showed normocytic normochromic anaemia (haemoglobin 10.8) and an elevated ESR of 80 mm/hr. The leukocyte count was normal ($6.1 \times 10^9$/l). She was given hydrocortisone on admission and later started on a tapering dose of prednisolone over a period of two weeks. Her laryngeal swelling subsided and she was decannulated after 10 days. She was discharged home two weeks after admission, but the vocal fold paralysis persisted. Due to persistently elevated ESR, further immunological investigations were performed. Anti-nuclear antibodies were elevated at 400 i.u./ml (N.V. 0–24 i.u./ml) and anti-double stranded DNA antibodies 151 i.u./ml (N.V. 0–100 i.u./ml). Rheumatoid factor was within normal limits and the rest of the tests were also normal.

Because of the clinical and immunological picture, it was concluded that she was suffering from hydralazine-induced lupus. Hydralazine was stopped. When reviewed after a month, the pain and stiffness of her fingers was better and the ESR had dropped to 50 mm/hr. On indirect laryngoscopy, the vocal fold paralysis persisted. However, four months later the paralysis was found to have completely recovered and the ESR was within the normal range.

## Discussion

SLE is an immunologically-induced syndrome that causes widespread damage to connective tissue, blood vessels, mucous membranes and serosal surfaces. It can involve the skin, joints, kidney, gastrointestinal system, central nervous system, blood and immunological systems. Such a widespread disorder can also involve the upper airway (Smith *et al.*, 1978). The first case of laryngeal involvement in SLE was reported by Scarpelli in 1959. This patient had severe laryngeal oedema and died after an unsuccessful attempt at endotracheal intubation (Scarpelli *et al.*, 1959). Table I shows the cases of laryngeal involvement in SLE reported in the English literature (Table I).

SLE may affect the larynx by an active mucosal, submucosal or serosal process. In the acute phase, mucosal ulceration, oedema and submucosal haematoma can cause hoarseness and throat pain. Late effects of mucosal disease include corditis, mucosal thickening and laryngeal scarring (Smith *et al.*, 1978). Perichondritis, crico-arytenoid arthritis or actual vocal fold paralysis may occur in cases of serosal involvement. Korbet *et al.* described a case of arytenoiditis causing left vocal fold paresis during steroid dose reduction in a patient with inactive SLE (Korbet *et al.*, 1984). In 1986, Curley *et al.* described a patient with active SLE, who had crico-arytenoid joint involvement with oedema of the arytenoid region and posterior commissure producing bilateral vocal fold paresis. Toomey *et al.* (1974) reported a case of acute epiglottis in a patient with SLE.

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TABLE I
LARYNGEAL INVOLVEMENT IN SLE PATIENTS

| Authors | Age/Sex | Laryngeal disease | Treatment | Outcome |
|---|---|---|---|---|
| Scarpelli *et al.* (1959) | 21/M | Laryngeal oedema | Attempted intubation | Died of airway obstruction |
| Montgomery and Lofgren (1963) | 25/F | Vocal fold fixation | Prednisone | Resolved |
| Gilliam and Cheatum (1973) | 24/F | Vocal fold oedema | Tracheostomy, prednisone | Resolved |
| Toomey *et al.* (1974) | 45/M | Acute epiglottitis | Tracheostomy | Died 1 month later of cerebral bleed |
| Smith and Ferguson (1976) | 63/F | Subglottic stenosis | Prednisone | Tracheostomy |
| Sinclair *et al.* (1976) | 27/F | Right vocal fold nodule | Excision, Prednisone | Improved |
| Smith *et al.* (1977) | 36/F | Oedema of vocal folds | Steroids | Several recurrences |
| Smith *et al.* (1978) | 28/F | Laryngeal oedema, glottic web | Tracheostomy, steroids, excision of web | Improved with prolonged steroid therapy |
| | 36/F | Cricoarytenoid arthritis | Steroids | Improved |
| Schwartz and Grishman (1980) | 28/F | Rheumatoid nodules in vocal folds | Excision of nodules | Sicca syndrome, SLE later |
| Shalit *et al.* (1982) | 21/M | Acute epiglottitis | Endotracheal intubation, penicillin | Resolved |
| Weiser *et al.* (1984) | 60/M | Mass lesion of epiglottis | Hydralazine stopped | Resolution of mass |
| Burgess and Render (1984) | 59/F | Vocal fold paralysis, oedema of vocal folds | Tracheostomy, steroids | Oedema improved, vocal fold paralysis persisted |
| Korbet *et al.* (1984) | 51/F | Left vocal fold paralysis, artenoiditis | Steroids | Resolution |
| Asherson and Hughes (1985) | 28/F | Left vocal fold paralysis | Unknown | Pulmonary hypertension |
| | 24/F | Left vocal fold paralysis | Captopril | Pulmonary hypertension |
| Curley *et al.* (1986) | 31/F | Cricoarytenoid arthritis | Hydralazine stopped, steroids | Resolved |
| Aszkenasy *et al.* (1987) | 41/F | Left vocal fold paralysis | Steroids | Heart failure. Death |
| Maxwell and Silver (1987) | 63/F | Cricoarytenoid arthritis | Hydralazine stopped, prednisone | Resolved |
| Petri *et al.* (1988) | 50/M | Laryngeal nocardiosis | Steroids, antibiotics, tracheostomy | Resolution 8 months later |
| Sharma *et al.* (1988) | 24/M | Left vocal fold paralysis | Prednisolone | Recovered |
| Saluja *et al.* (1989) | 35/F | Bilateral vocal fold paralysis | Steroids | Recovered |
| Gordon and Dunn (1990) | 52/F | Right vocal fold paralysis | Prednisolone | Recovered |
| Espana *et al.* (1990) | 27/F | Right vocal fold paralysis | Prednisone, Azathioprine | No improvement after 1 year |
| Kraus and Guerra-Bautista (1990) | 33/M | Right vocal fold paralysis | Steroids, Cyclophosphamide | Recovered |
| Teitel *et al.* (1992) | 37/M | Left vocal fold paralysis, Oedema of larynx | Methyl prednisolone | Resolved |
| | 26/M | Laryngeal oedema | Methyl prednisolone, antibiotics, tracheostomy | Resolved |
| | 29/F | Acute epiglottitis | Methyl prednisolone, antibiotics, intubation | Resolved |
| | 26/F | Laryngeal oedema | Steroids, antibiotics | Resolved |
| Raz *et al.* (1992) | 29/F | Acute laryngeal oedema | Steroids | Recurrence |
| | 22/F | Acute laryngeal oedema | Steroids, tracheostomy | Resolved |
| Munianin *et al.* (1992) | 55/F | Right vocal fold paralysis | Prednisone | Recovered |
| Woo *et al.* (1995) | 31/F | Vocal fold nodules | Excision | Improved |
| Tsunoda and Soda (1996) | 51/F | Vocal fold nodule | Prednisolone | Resolved |

Paralysis of the vocal fold in SLE can occur due to direct involvement of the larynx in the disease process or secondary to pulmonary hypertension. The paralysis in the latter condition is always left-sided and is thought to be due to direct compression of the recurrent laryngeal nerve by the dilated pulmonary artery (Aszkenasy *et al.*, 1987). By virtue of its involvement of the nervous system, SLE can also cause peripheral neuritis and, hence, paralysis of the recurrent laryngeal nerve. Gordon and Dunn in 1990 reported a case of right vocal fold paralysis in the absence of pulmonary hypertension or laryngeal lupus. The cause of paralysis was thought to be due to vasculitis and neuritis affecting the right recurrent laryngeal nerve.

The syndrome of drug-induced lupus is a well known entity which produces clinical and immunological manifestations similar to spontaneous SLE. Although medications such as isoniazid, chlorpromazine and methyldopa have been incriminated, the data are strongest for hydralazine and procainamide (Schur, 1993). Slow acetylators are more likely to develop the syndrome and antinuclear antibodies (Harland *et al.*, 1980). The disease can begin a few months after the medication is commenced. The risk is present after long-term therapy with over 100 mg of hydralazine daily, or less in women (British National Formulary, 1997). About 14 per cent of patients taking hydralazine develop anti-nuclear antibodies, while only four to 12 per cent develop lupus (Harland *et al.*, 1980). Unlike spontaneous SLE, drug-induced lupus is reversible, once the offending agent is stopped.

Our case is unique because the vocal fold paralysis occurred as a result of drug-induced lupus. We believe that the cause of the paralysis was the direct involvement of the larynx by the disease process, which completely recovered after stopping the hydralazine therapy.

## Summary

Laryngeal involvement in drug-induced lupus is a rare event and is one of the few reversible causes of vocal fold paralysis. We recommend that upper airway symptoms occurring in patients taking such medications should always be investigated to rule out possible immunological involvement.

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