Int J Clin Exp Med 2017;10(12):16657-16662
www.ijcem.com /ISSN:1940-5901/IJCEM0062430

*Original Article*

# Hoarseness and laryngeal lesions may be poor prognostic factors for pneumomediastinum in dermatomyositis with interstitial lung disease

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Received July 27, 2017; Accepted November 5, 2017; Epub December 15, 2017; Published December 30, 2017

**Abstract:** Pneumomediastinum (PnM) is a rare complication of interstitial lung disease (ILD) and dermatomyositis (DM) that can be fatal. The relationship of hoarseness, laryngeal lesions with the occurrence and prognosis of PnM in patients with ILD and DM is not clear. In this study the clinical records of patients with ILD and DM were retrospectively reviewed, focusing mainly on the presence of hoarseness, laryngeal lesions and PnM. All published cases of DM that were complicated by PnM in English were also reviewed and analysed. There were 1841 patients with a diagnosis of ILD in which there are 44 patients with DM were identified. There were statistically differences in average age and sex ratio between the patients with or without DM. In all of the 1841 patients there were 11 patients developed into PnM; 8 patients were reported hoarseness. The incidence of PnM and hoarseness are significantly higher in patients with ILD and DM than patients with ILD only ($P<0.01$). There was a significant difference in prognoses and the occurrence of PnM between patients with and without hoarseness or laryngeal lesions ($P<0.01$). Twenty-eight case reports of patients diagnosed with PnM in DM were identified in the English literature including our 3 cases. All of the patients with laryngeal lesions died, whereas 3 of the patients with only bronchial lesions survived. To conclude, our results support the concept that hoarseness and laryngeal lesions may be associated with the occurrence and poor prognosis of PnM in patients with DM and ILD.

**Keywords:** Pneumomediastinum, dermatomyositis, hoarseness, interstitial lung disease

## Introduction

Dermatomyositis (DM) is a generalized inflammatory connective tissue disease that is characterized by myositis and typical cutaneous findings. The lungs are commonly affected, usually by interstitial lung disease (ILD), infection, or dysfunction of the respiratory muscles [1, 2]. Pneumomediastinum (PnM) is a rare complication of ILD and DM that can be fatal. Although the pathogenesis of PnM has not yet been fully described, lesions in the superior airway and cutaneous ulcer may indicate the formation of PnM and be associated with its underlying mechanism [3-6]. We encountered several patients with ILD and DM who exhibited hoarseness and PnM, in whom laryngoscopy revealed presence of lesions in the vocal folds. Three of these patients died of respiratory failure. We wonder whether laryngeal lesions could also indicate the formation of PnM in those patients. As hoarseness and laryngeal lesions are relatively easy to be detected by the doctor, they could be very helpful for us to adjust the therapeutic regimen at the early beginning of PnM if they were prognosis factors for patients with DM and PnM.

We reviewed our own patients with ILD and DM to determine whether voice changes and laryngeal lesions are association with PnM. We also searched articles in the Medline database. The reports of patients with PnM in DM were reviewed to determine whether voice changes and vocal fold lesions are symptoms that indicate the formation of PnM or affect prognoses in PnM patients.

**Table 1.** Compare of Patients of ILD with and without DM

| | ILD | ILD with DM | *p* Value |
|---|---|---|---|
| Number | 1841 | 44 | |
| Male/Female | 905/936 | 14/30 | *P*=0.023 |
| Age* | 63.15 (12.37) | 51.05 (10.38) | *P*<0.01 |
| Hoarse | 8 | 4 | *P*<0.01 |
| Pneumomediastinum | 11 | 3 | *P*=0.004 |

*Data shown as mean (SD).

## Material and methods

*Medical record review*

We reviewed the clinical records of patients who were diagnosed with ILD, DM and patients diagnosed with PnM and ILD, who underwent medical treatment from January 2000 to December 2015. All DM diagnoses were achieved according to the criteria of Bohan and Peter [7]. These included symmetric muscle weakness, high serum muscle enzyme levels, myopathic changes on electromyography (EMG), typical histological findings on muscle biopsy, and characteristics of dermatologic manifestations. The diagnosis of ILD and PnM were according to the results of a chest X-ray and a high-resolution chest CT. Laryngeal lesions were according to the results of laryngoscope or bronchoscope that were conducted on all patients with hoarseness.

*Literature review*

We searched articles with key words used were dermatomyositis and pneumomediastinum in the Medline database from 2000 to 2015. We placed particular focus on the diagnosis of the patients; the presence of hoarseness and findings on laryngoscopy or bronchoscopy; and the outcomes. Only articles published in English were selected for review.

*Statistical analysis*

We used Independent Samples Test to compare the distributions of ages and genders in the included patients and the chi-square test or Fisher's exact test to compare mortality rates across patients with different vocal performance and PnM. A value of $P<0.05$ was considered to indicate significance.

## Results

*Results for patients from medical record review*

A total of 1841 patients with a diagnosis of ILD in which there are 44 patients with DM were identified. The incidence of ILD complicated with DM was significantly higher in women than in men compared with the patients with only ILD ($P=0.023$). The average age of patients of ILD complicated with DM was significantly younger than the patients of ILD without DM ($P<0.01$). In all of the 1842 patients there were 11 patients developed into PnM, 3 of the 11 patients also diagnosed with DM and died of respiratory failure; there were 8 patients were reported hoarseness in the 1842 patients, 4 of the 8 patients complicated with DM. The incidence of PnM and hoarseness are significantly higher in patients with ILD and DM than patients with ILD only ($P<0.01$). There was no significantly different of age and sex ratio between patients with or without PnM (**Table 1**).

On laryngoscopy, 4 of the 8 patients with hoarseness showed congestion of the vocal folds, 1 patient showed laryngeal cyst, other 3 patients showed white change on both of the vocal folds (**Figure 1**). All of the 3 patients with hoarseness and white changes on both vocal folds complicated with DM and developed into PnM. All of the 3 patients subsequently died of respiratory failure. There was a significant difference in prognoses and the occurrence of PnM between patients with and without hoarseness or laryngeal lesions ($P<0.01$) (**Table 2**).

*Results for literature review*

We identified 25 case reports of PnM patients with DM in the English literature. Sufficient clinical information was provided for all included patients, as shown in **Table 3** [8-25]. **Table 3** also includes the 3 patients encountered at our hospital. Two of the 28 patients had ADM, and the others had DM. In all, 22 of them had DM with ILD. Voice symptoms were described in 5 of the cases included in our analysis, and 4 of these reported hoarseness, while 1 reported dysphonia. A total of 10 patients underwent bronchoscopy or laryngoscopy, and 3 were found to have normal mucous membranes,

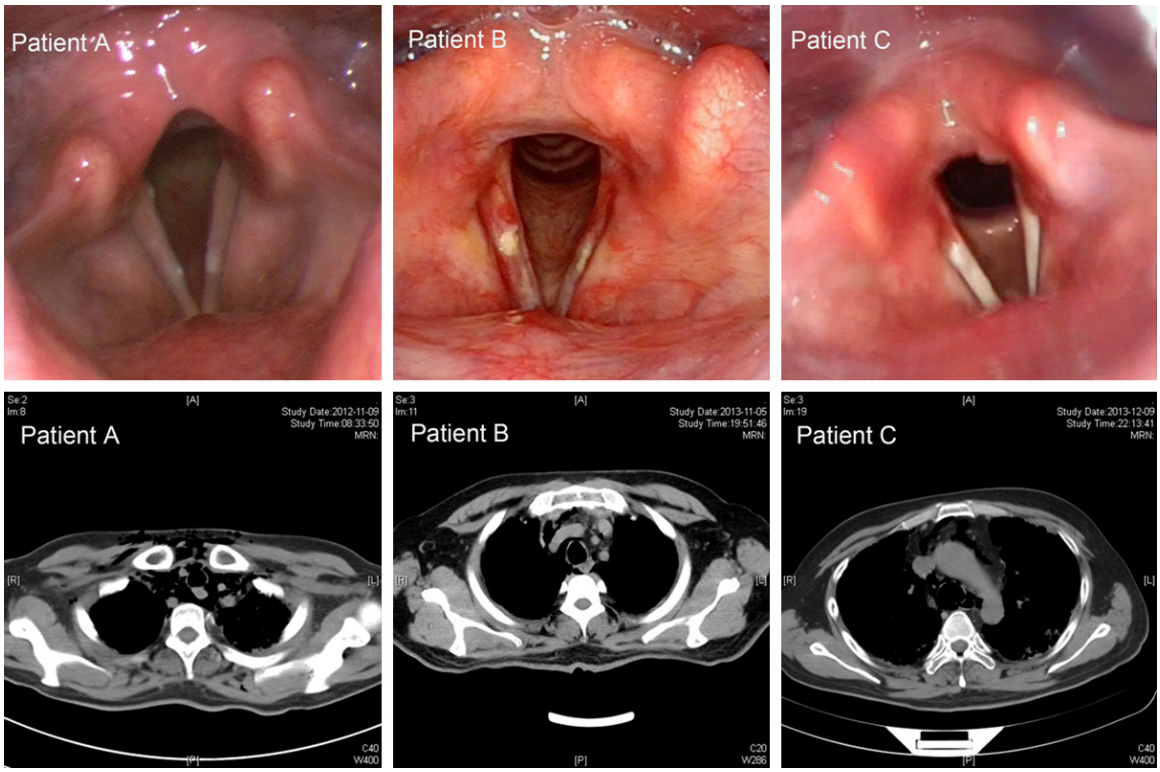


**Figure 1.** Patient A developed hoarseness after bronchoscopy and showed symmetrical white plaques on 1/3 of the vocal folds. Patient B was diagnosed with oral mucous Candidiasis based on a throat swab and exhibited multiple white plaques and diffused erosion on both of his vocal folds. He was found to have normal infrapharyngeal and tracheal mucous membranes. Patient C exhibited diffuse white changes on both of his vocal folds, but no infection or other symptoms. All of the three patients developed PnM.

**Table 2.** Comparison of patients with and without laryngeal lesions in ILD complicated with DM

| | Laryngeal lesions | Without laryngeal lesions | *p* Value |
|---|---|---|---|
| Number | 4 | 40 | |
| Hoarse | 4 | 0 | |
| Lagynscopy# | 3/1 | 0/0 | |
| Outcome (died/alive) | 3/1 | 40/0 | *P*<0.01 |
| Pneumomediastinum | 3/1 | 40/0 | *P*<0.01 |

#Data shown as white changes on the vocal folds/congestion.

while pathological changes were found in the mucous membranes of the bronchus or larynx in 7 cases. All 4 of the patients with laryngeal lesions died, whereas the 3 patients with only bronchial lesions survived (**Table 3**).

## Discussion

PnM is a rare but fatal complication of ILD and DM. Although its prevalence is not precisely known, it has a reported incidence of 1.3%-8.3% in DM according to different authors [3, 26], and its incidence in our study was 4.6%. The mechanisms that contribute to the initiation of PnM in DM patients are not clear. Several pathological situations are thought to potentially give rise to PnM. The first of these is the notion that PnM occurs following the rupture of previously damaged intra-alveoli or a subpleural cyst that developed from interstitial fibrosis, resulting in raised pressure in the lung [27]. ILD is the disease that is commonly associated with DM and thought to attributable to PnM in this situation. DM with PnM was complicated by ILD in 19 out of 25 of the cases in the literature reports, demonstrating that ILD is a common underlying condition during the development of PnM. The second is involves the weakening of the alveolar walls by corticosteroids during the course of treatment for DM [20]. The third potential mechanism is the rupture of an airway lesion as a result of underlying pulmonary vasculitis, and laryngeal or tracheobronchial mucosa lesions could be the manifestations of vasculitis [3, 4]. Hence, the app-

**Table 3.** Review of previously published and three present patients with DM complicated with pneumomediastinum

| Author | Diagnosis | Sex | Age (Y) | Larynscopy/Bronchoscopy | IId | Voice | Outcome |
|---|---|---|---|---|---|---|---|
| Alexander et al. [8] | DM | F | 60 | NA | No | NA | Alive |
| Tang et al. [9] | ADM | F | 52 | NA | No | NA | Alive |
| Saraya et al. [10] | ADM | F | 31 | NA | No | NA | Died |
| Cozzani et al. [11] | DM | M | 30 | NA | Yes | NA | Alive |
| Sandhya et al. [12] | DM | F | 10 | NA | Yes | NA | Alive |
| | DM | M | 33 | NA | Yes | Hoarse | Alive |
| | DM | M | 25 | NA | Yes | NA | Alive |
| Rodrigues et al. [4] | DM | F | 41 | Pale symmetrical lesions in the mucosa of the false vocal cords in the larynx | Yes | NA | Died |
| Onishi et al. [13] | DM | F | 46 | NA | Yes | NA | Died |
| Dogra et al. [14] | DM | M | 9 | NA | Yes | NA | Alived |
| Machuca et al. [15] | DM | M | 38 | Focal inflammation and no infectious process on the bronchial mucosa | NO | NA | Alive |
| Lee et al. [16] | DM | F | 25 | NA | No | NA | Alive |
| Park et al. [17] | DM | F | 45 | NA | Yes | NA | Alive |
| Masrouha et al. [18] | DM | M | 66 | Normal | YES | Dysphonia | Alive |
| Kim et al. [19] | DM | F | 38 | NA | Yes | NA | Alive |
| Yoshida et al. [20] | DM | M | 38 | NA | No | NA | Alive |
| Terao et al. [21] | DM | M | 16 | NA | Yes | NA | Alive |
| Powell et al. [22] | DM | M | 34 | NA | Yes | NA | Alive |
| Neves et al. [23] | DM | M | 45 | NA | Yes | NA | Alive |
| Korkmaz et al. [24] | DM | M | 28 | NA | Yes | NA | Alive |
| Barvaux et al. [25] | DM | M | 42 | Normal | Yes | NA | Alive |
| Kono et al. [3] | DM | M | 30 | Studded white plaques on the bronchial mucosa | Yes | NA | Alive |
| | DM | M | 25 | Normal | Yes | NA | Died |
| | DM | M | 23 | NA | Yes | NA | Alive |
| | DM | F | 59 | Bronchial stenosis caused by old tuberculosis | Yes | NA | Alive |
| Patient A | DM | F | 39 | Symmetry white plaque on the 1/3 of the vocal folds | Yes | Hoarse | Died |
| Patient B | DM | M | 36 | White plaques and diffused erosion on both of his vocal folds | Yes | Hoarse | Died |
| Patient C | DM | M | 44 | Diffused white change on both of his vocal folds | Yes | Hoarse | Died |

earance of ulcerous, pale, symmetrical lesions in the superior airway could be an important indication that a patient with DM could develop PnM. And our report could also prove the opinion based on the data analysis that there was a significant difference in the occurrence of PnM between patients with and without laryngeal lesions ($P<0.01$).

The mechanism by which the vocal folds became altered in our patients remains unclear because no biopsies were performed. Based on the clinical manifestations, we believe that vasculitis, infection may be the most likely causes. From the literature review and our cases reported, all 4 in 28 patients with PnM, who with symmetrical laryngeal lesions died, whereas all 3 patients with lesions only in the bronchial mucosae survived after therapy. This shows that no matter what the causes are, the vocal fold lesion itself may indicate the poor prognoses of PnM developed from DM. So,

laryngoscope should be done in patients with PnM developed from DM, especially in patients with hoarseness.

In summary, PnM is a rare and severe complication of DM and ILD. Hoarseness and laryngeal lesions may indicate the formation of PnM and a poor prognosis in patients who develop PnM. In patients with DM and ILD, the voice should be paid attention and a laryngoscopy should be performed when a patient is found to have developed hoarseness and dyspnoea.

## Acknowledgements

The research was supported by National Natural Science Foundation of China (Grant No. 81470682).

## Disclosure of conflict of interest

None.

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