

# Angioedema of the larynx

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## ABSTRACT

**Objective:** To clarify the clinical manifestations of laryngeal edema in patients with angioedema.

**Study design:** Retrospective study.

**Setting:** University hospital.

**Methods:** Patients with angioedema who visited the otolaryngology clinic in our institution were examined (including the face, lips, tongue, pharynx, larynx and neck) for the presence of oral cavities and upper airway edema. In addition, the etiology of the angioedema in each patient was surveyed.

**Results:** Twenty patients (12 men, 8 women; mean age, 63 years) were diagnosed with angioedema, visiting our clinic on a total of 27 occasions (one patient visited our clinic three times and five patients visited us twice each with each visit regarded as a separate patient). An edema was observed in the pharynx in 22 (81%), the tongue in 20 (74%), the arytenoids in 15 (56%), the lip in 11 (41%) and the epiglottis in 8 patients (30%). Edema of the larynx, including the arytenoids and/or epiglottis, was present in 16 of the 27 patients (59%) receiving treatment. The etiology of the angioedema was identified in 11 patients as follows: C1 inhibitor deficiency (3), of which two showed hereditary angioedema and one acquired; renin-angiotensin system inhibitors (4), estrogen (1) and diet (3). Two patients underwent tracheotomy and another one underwent tracheal intubation for airway management.

**Conclusion:** More than 50% of patients with angioedema who initially consult at an otolaryngology clinic are found to have a laryngeal edema; therefore, examination of the upper airway is recommended for all patients diagnosed with angioedema.

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## INTRODUCTION

Angioedema, which has the potential to obstruct the upper air way, is common disease in the USA and Europe. About fifty percent of patients with urticaria have angioedema, as described previously<sup>1,2</sup>).

Furthermore, hereditary angioedema (HAE) caused by C1 inhibitor deficiency is well known to be the severest type of angioedema<sup>3</sup>).

In contrast, angioedema, especially HAE, is a rare disease in Japan.

The incidence of urticaria-associated angioedema is only fifteen percent in Japan<sup>4</sup>), which is one-third that in the USA, and less than sixty cases of HAE have been identified in the country. For this reason, few reports on angioedema have been published by Japanese otolaryngologists, although angioedema has the associated risk of asphyxia.

The aim of this study is to evaluate the incidence of laryngeal edema in angioedema patients. To access the edema of upper air way, we hope to indicate the importance of angioedema management to otolaryngologists in Japan.

## METHODS AND MATERIALS

Clinical data for angioedema patients who visited the otolaryngology clinic of Fukushima Medical University Hospital from 1989 to 2010 were reviewed. Manifestations, regions of swelling and cause of angioedema were examined. We classified the head and neck edema into ten regions: the face, eyelids, lips, tongue, pharynx, epiglottis, arytenoid region, vocal cords, false folds and neck. All patients were examined with a digital laryngoscope.

ACEI = angiotensin-converting enzyme inhibitor

ARB = angiotensin type-2 receptor blocker

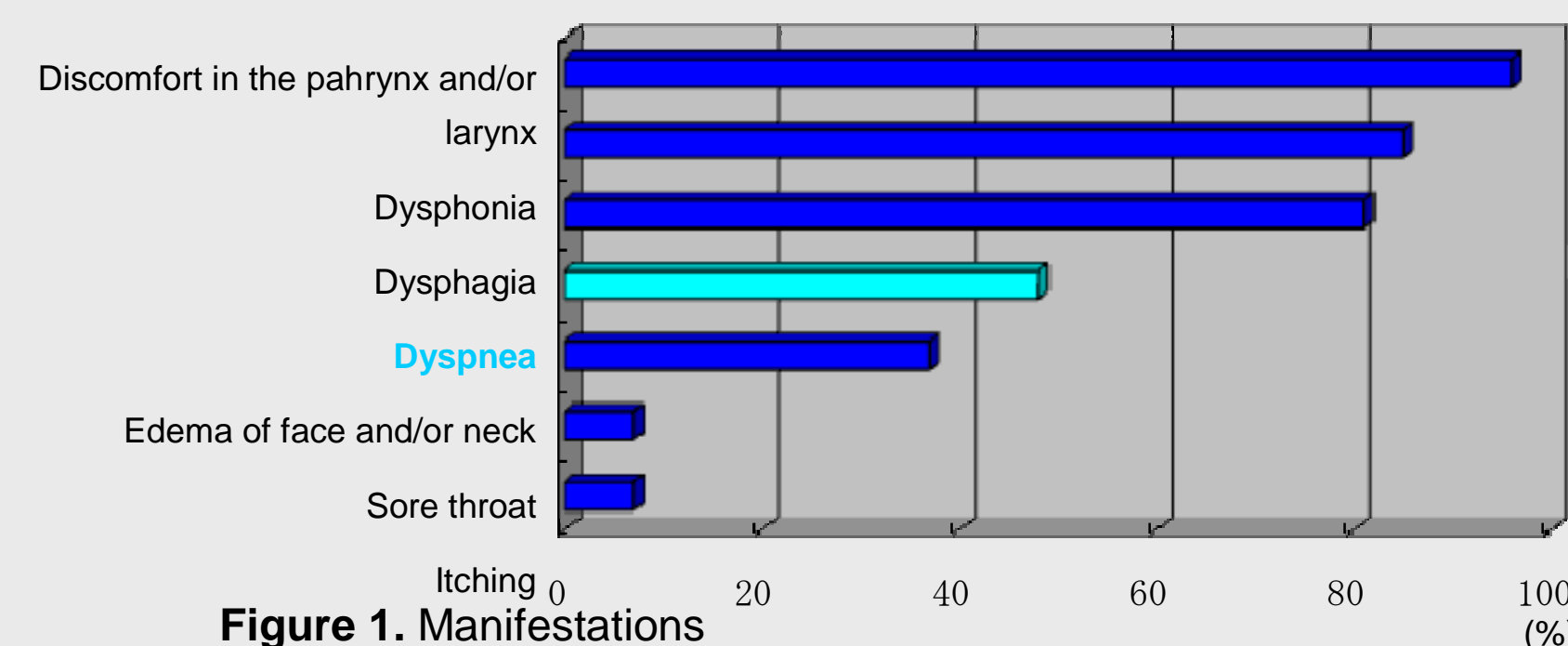


Figure 1. Manifestations

## RESULTS

Twenty patients were diagnosed angioedema on their first visit to our department. Twelve were men and eight were women, and their mean age was sixty-three years. They received treatment on twenty-seven occasions in total; one patient visited our clinic three times, five patients visited us twice each. As the symptoms differed at each examination, we regard each of the 27 examinations as individual patients for simplicity.

(1) Manifestations.

Manifestations are shown in Figure 1. The most common manifestation was discomfort in the pharynx and/or larynx. Dysphonia and dysphagia were recognized in over eighty percent of patients. In contrast, only a few patients complained of pain or itching. A remarkable result was that forty percent of patients showed dyspnea.

(2) Cause of angioedema.

Causes of angioedema were listed in Table 1. The cause was unknown in a majority of patients. In those patients for whom the cause was specified, drugs were the highest causal agent of angioedema. A notable result was that the causal drugs in 3 of 5 cases were angiotensin-converting enzyme inhibitors. Diet as a cause included one case each of peach, shrimp and tomato. C1-inhibitor dysfunction containing HAE was observed in three cases.

(3) Region of Swelling.

An example of a laryngeal edema is shown in Figure 2.

Edema of the head and neck were classified into ten regions as shown in Figure 3. The region most frequently affected was the pharynx including the tonsils, base of the tongue and soft palate. The second most commonly affected area was the tongue. The arytenoid region, which was the part of the larynx most frequently affected, showed edema in fifty-six percent of cases. Laryngeal edema, including the epiglottis, arytenoids, vocal cords and false folds, demonstrated the presence of edema in fifty-nine percent of cases.

Cause	The number of patients
Unkown	9
Drugs	5
(ACEI)	(3)
(Others)	(2)
Diet	3
C1-INH dysfunction	3

Table 1. Cause of angioedema



Figure 2. An example of a laryngeal angioedema (a case of HAE)

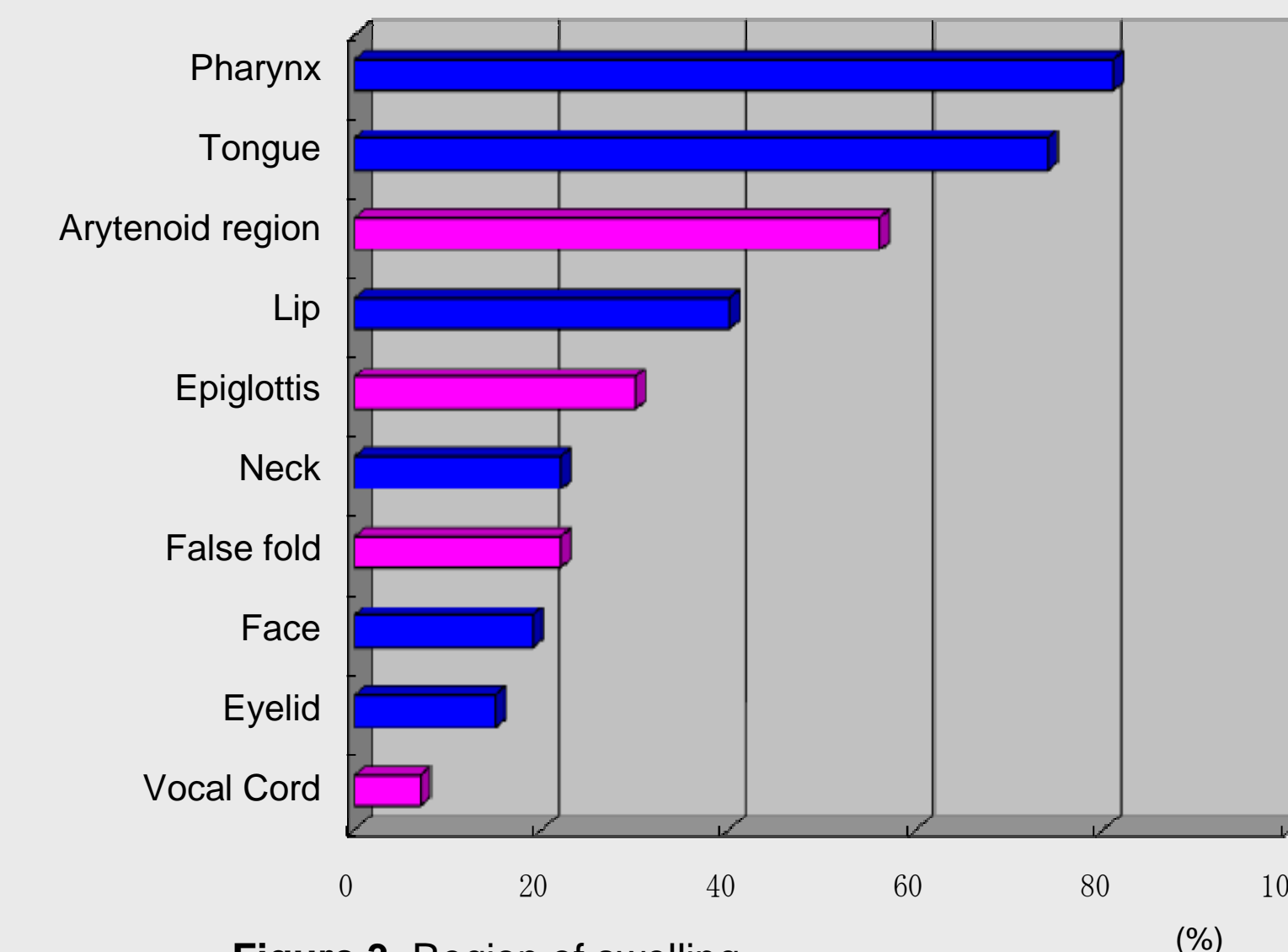


Figure 3. Region of swelling  
Total rate of laryngeal edema was 59%.

## DISCUSSION

This study presents three noteworthy results.

First is the fact that the most common manifestation requiring treatment by an otolaryngologist is not facial or lip edema, but discomfort in the pharynx or larynx. In this study, patients with angioedema were only selected when they received their initial treatment at the Department of Otolaryngology, thus mucosal manifestations may be more frequent than dermal symptoms. In addition, forty-eight percent of patients complained of dyspnea. Thus we should take good care to examine the upper airway when treating angioedema.

The next remarkable result is that laryngeal edema was present in fifty-nine percent of the angioedema patients. Zingale et al. reported the rate of laryngeal edema in angioedema ranged from twenty to thirty-five percent<sup>3</sup>). Our results indicated there were more cases with laryngeal edema than cases with dyspnea (laryngeal edema 59%, dyspnea 48%). It is recommended that angioedema patients should be examined for laryngeal edema.

The final notable result is that ACE-related drugs are important etiologic agents of angioedema in Japan. In our study, four cases were caused by ACE-related drugs; ACEI in three cases, and ARB in one case. According to Byrd et al., the incidence of angioedema due to ACE-related drugs varies from 0.1 to 6 percent<sup>5</sup>). Our results showed sixteen percent of angioedema cases to be caused by ACE-related drugs. There are few cases of HAE in Japan, so that the percentage of angioedema attributed to ACE-related drugs increases in Japan.

## CONCLUSIONS

We evaluated laryngeal edema in patients with angioedema who sought initial treatment at our otolaryngology clinic.

The most common Complaint was pharyngeal or laryngeal discomfort and 48% of patients complained of dyspnea.

ACE-related drugs were found to be important agents of angioedema in Japan.

Laryngeal edema was demonstrated in 59% of patients. It was found that the rate of laryngeal angioedema was higher than those shown in previous reports. It is recommended that all cases of angioedema should be examined for laryngeal edema.

## REFERENCES

1. Champion RH, Roberts SO, Carpenter RG, et al. Urticaria and angio-oedema. A review of 554 patients. *Br J Dermatol.* 81(8):588-97, 1969
2. Frigas E, Park MA. Acute urticaria and angioedema: diagnostic and treatment considerations. *Am J Clin Dermatol.* 10(4):239-50, 2009
3. Zingale I.c., Beltrami I., Z., et al.: Angioedema without urticaria: a large clinical survey. *CMAJ.* 175: 1065-1070, 2006
4. Tanaka T, Kameyoshi Y, Hide M. Analysis of the prevalence of subtypes of urticaria and angioedema *Arerugi.* 55(2):134-9, 2006
5. Byrd JB, Adam A, Brown NJ. Angiotensin-converting enzyme inhibitor-associated angioedema. *Immunol Allergy Clin North Am.* 26(4):725-37, 2006