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Research Article

Angioedema: The Location of the Swelling Matters

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Abstract

Objectives: To explore the relationship among location of edema, patient characteristics, and disposition in patients who present to the Emergency Department (ED) with angioedema.

Methods: A retrospective analysis was conducted on adult patients who presented to the ED with angioedema. Patient data collection included age, sex, initial vital signs, physical exam findings, and ED treatment measures. For those patients who required admission, the specific disposition (observation, medical floor, progressive care, or critical care) was noted. Follow-up telephone calls were made to discharge patients to gather information regarding recurrence, adverse events, or further intervention. The location of edema was split into 4 groups: Group 1-external (lips and face); Group 2-internal (tongue, oropharynx, uvula); Group 3-both internal and external; and Group 4-absence of swelling. Statistical analysis was completed using Fisher's exact, multivariate logistic regression and Student t-tests. Group comparisons were evaluated using ANOVA and Levene's test. Chisquare analysis and Mann-Whitney rank tests were performed where appropriate.

Results: One-hundred ninety-nine patients were identified and included in the study. 120 patients (60.3%) were female. The majority of patients (134 patients, 67.3%) were discharged, with the remaining patients (65, 32.7%) requiring inpatient admission. Admitted patients had a mean age of 60.9 years, while non-admitted patients had a mean age of 51.4 years. For each one year increase in age, there was a 2% increase in odds of admission (odds ratio, 1.02; 95% confidence interval). External swelling was most evident in 82.9% of the discharged patients and evident in 17.1% of the admitted patients. The majority of admitted patients experienced either internal or both external and internal swelling (68%). The admitted patients were further categorized according to specific disposition: observation (4.6%), medical floor (46.2%), progressive care (43.1%), and critical care (6.2%). Of the 65 admitted patients, 7.7% required intubation and mechanical ventilation. Of the 134 discharged patients, 24 patients experienced recurrence of angioedema or allergic reaction, of which only four patients returned to the ED. A logistic regression test for the recurrence of angioedema within 48 hours and location of swelling revealed that group 3 patients, with both external and internal swelling, had a higher odds of recurrence when compared to the other groups (odds ratio, 4.81; P=.029).

Conclusion: The results of this study support the notion that the majority of patients with angioedema are safe to be discharged home, specifically when the swelling is primarily external. Those patients who have predominance of internal swelling and of older age are more likely to necessitate hospital admission, and their disposition may have variable placements within the hospital.

Introduction

Angioedema (AE) is a common presenting diagnosis to the Emergency Department (ED). Data regarding epidemiology of angioedema is limited. However, it is estimated that 10-20% of people have one episode of angioedema at some point in life [1]. It is characterized by localized swelling of the mucosa or submucosa of the skin [2]. It is oftentimes observed as external swelling, affecting the face or extremities, but can progress to internal swelling in the uvula and oropharynx. Swelling of the skin usually subsides within 24 hours; however, other symptoms may persist for two to three days [3,4]. Although the onset for angioedema may be sudden and can be classified as a drug or food-induced allergic reaction, most cases of angioedema are categorized as idiopathic.

The number of angioedema hospitalizations is increasing suggesting the prevalence may also be increasing. In recent years, hospitalizations due to a primary diagnosis of angioedema have increased from 9,724 cases in 2000 to 12,265 in 2004 [5]. One factor that has likely triggered this increase is the widespread use of Angiotensin-Converting Enzyme inhibitors (ACEi), which make up a common cause of drug-induced angioedema.

Many studies have been done on outcomes and management of angioedema patients who present to the ED. However, there is a dirth of information about what factors lead physicians to discharge certain patients while admitting others. This study explored these factors with special attention to examination of the oropharynx with the intention of clarifying a pathway for disposition of angioedema patients. Furthermore, for admitted patients, identifying what bed type (observation, medical floor, progressive care or critical care) was investigated.

Methods

An Institutional Review Board approved retrospective medical chart review was conducted on all patients who presented to a tertiary care Level 1 trauma center Emergency Department with an annual census of 120,000 visits between January 1, 2010 and December 31, 2010. Patients with a primary International Classification of Diseases (ICD) 9 code for angioedema were selected for the study.

All patient data was extracted from the EPIC medical record database. A data collection form was completed for each patient, and the following information was extracted from the medical charts: age, sex, past medical history of angioedema, allergen or causal agent, initial vital signs, physical exam findings, consultations, ED treatment measures (including intubation and cricothyrotomy), and time spent in the ED. For those patients who required admission, the management, duration of hospital stay, and bed classification were noted. The bed classification was categorized as follows: observation area (vitals taken every 4 hours with nurse/patient ratio of 1:6), regular medical floor (vitals taken every 4 hours with nurse/patient ratio of 1:6-8), medical progressive unit (vitals taken every 2 hours of all monitored beds with nurse/patient ratio of 1:4), intensive care unit (ICU; vitals taken every hour for all monitored beds with nurse/patient ratio of 1:2). Follow-up telephone calls were made to discharged patients in order to gather information about adverse events and/or recurrence of symptoms. These calls were made within one year of the index visit. The recurrence rate was further characterized into two groups as a repeat episode within the first twenty-four hours and within forty-eight hours. The location of the edema was split into four groups: Group 1 - external (lips and face), Group 2 - internal (tongue, oropharynx, and uvula), Group 3 - both internal and external, and Scale 4 - the absence of swelling. Group 4 was included as some patients presented with complaints of oropharyngeal swelling but this swelling was not appreciated on the examination of the provider, potentially secondary to symptom resolution prior to evaluation by the physician or that the degree of swelling was so mild that the physician noted a normal exam in the medical record.

For the analysis, standard statistical methods were used to compute means and Standard Deviations (SD). Fisher's exact, multivariate logistic regression and Student t-tests were included in the study. Group comparisons were evaluated using ANOVA and Levene's test. Chi-square analysis and Mann-Whitney rank tests were performed where appropriate. All p-values less than 0.05 were considered statistically significant.

Results

There were a total of 199 patients identified and included in the study. 120 patients (60.3%) were female. The majority of patients (134 patients, 67.3%) were discharged, with the remaining patients (65, 32.7%) requiring inpatient admission. The mean age of the admitted patients was 60.9 years (SD 21.0) and of the discharged patients was 51.4 years (SD 21.2) (p=0.0032). Forty-two (64.6%) of the admitted patients were female, compared to 58.2% of the discharged patients (p=0.48). Of the 65 admitted patients, 3.1% had a past medical history of angioedema, compared to 0.7% of the discharged patients (p=0.25).

Initial vital signs were a mean of 148 mm Hg (SD 24) systolic blood pressure in the admitted patients and a mean of 144 mm Hg (SD 25) for those discharged (p=0.63). The mean respiratory rate was 19/min (SD 3.8) in the admitted group, and 18/min (SD 2.3) in the discharged group (p=0.16). A mean pulse oximetry of 97.8% (SD 2%) was noted in the admitted patients and a mean of 98% (SD 1.6%) was noted for the discharged patients (p=0.77). Similar to these vital signs, other vital signs were not significantly different between the two groups, including diastolic blood pressure (p=0.63), heart rate (p=0.48), and temperature (p=0.57).

In most cases, the possible inciting factor was unknown (44.7%). Medications such as Lisinopril (28.1%) and other ACE inhibitors (5.5%), as well as bactrim (6.2%), were recorded as possible triggers for the reaction.

Physical exam data of the patients was divided into four categories based on the location of edema: Group 1- external (lips and face); Group 2 - internal (oropharynx, uvula, or tongue); Group 3 - both internal and external; and Group 4 - absence of swelling. Data was obtained from the physical exam section of the provider note. As shown in (Figure 1), external swelling was most evident in 58 of the discharged patients (82.9%) and evident in 12 of the admitted patients (17.1%). The majority of admitted patients experienced either internal or both external and internal swelling (68% or 44 of 65 admitted patients).

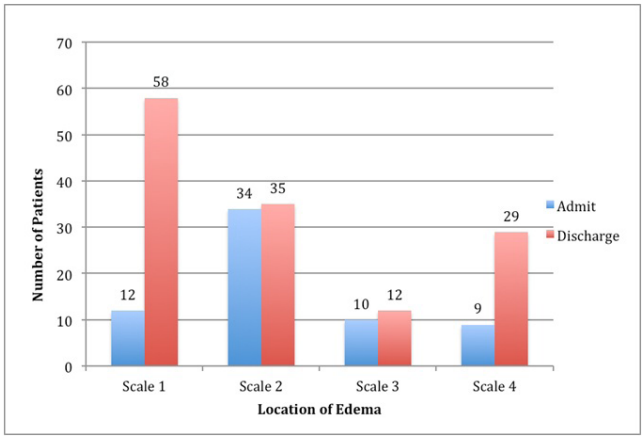

Figure 1: Disposition of patients who presented to Emergency Department with Angioedema.

Variables/Predictors	Odds Ratio (95% Confidence Interval)	p-value
Age	1.02 (1.002-1.035)	.027
Group 1: external (lips and face)	reference	--
Group 2: internal (tongue, oropharynx, uvula)	4.27 (1.93-9.41)	.0003
Group 3: both (internal and external)	3.62 (1.26-10.5)	.0172
Group 4: absence of swelling	1.64 (0.61-4.41)	.33

Table 1: Multivariate associations of age and location of swelling as related to hospital admission.

Odds ratio for Scale = 2, 3 and 4 are with respect to Scale = 1 and all were adjusted for AGE

Table 1 shows a multivariate analysis for the location of swelling and hospital admission. For each one year increase in age, there was a 2% increase in odds of admission (odds ratio, 1.02; 95% confidence interval). The patients who experienced group 2 internal swelling (P=.0003) or group 3 internal and external swelling (P=.0172) were most likely to be admitted to the hospital when compared those who experienced group 1 external swelling alone. Group 2 and 3 patients were also associated with a four-fold increase in odds of admission compared to group 1 patients (odds ratio, 4.27; 95% confidence interval). Of the five patients intubated upon admission, four of them experienced group 2 internal swelling.

Of the 134 discharged patients, 24 patients experienced recurrence of angioedema or allergic reaction. Of the patients who suffered another episode, 16 patients experienced it within 48 hours, 1 of whom who experienced this within 24 hours. The remaining 8 patients experienced recurrence over 48 hours following ED discharge. Of the discharged patients who were identified to have experienced a recurrence, only four patients returned to the ED. A logistic regression test for the recurrence of angioedema within 48 hours and location of swelling revealed that scale 3 patients, with both external and internal swelling, had a higher odds of recurrence when compared to the other scales (odds ratio, 4.81; P=.029). Twenty of the discharged patients could not be reached to gather follow-up data regarding recurrence.

The majority of patients (134, or 67.3%) were discharged, and 65 (32.7%) were admitted to the hospital. The admitted patients were divided into four bed classifications: observation (4.6%), medical floor (46.2%), progressive care (43.1%), and critical care (6.2%). (Figure 2) illustrates admission by bed type.

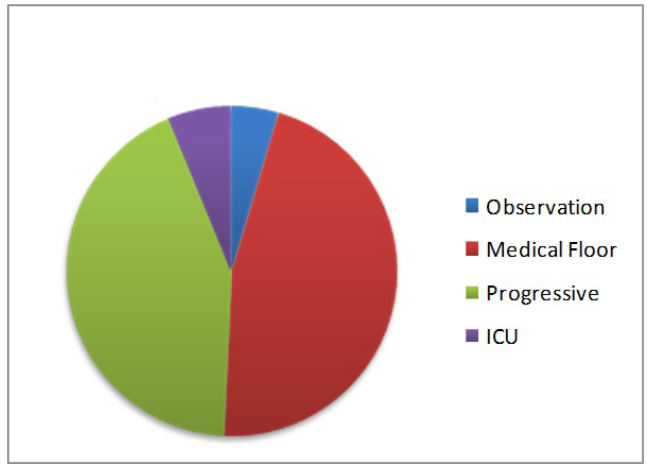

Figure 2: Admission Bed Type

Five patients in the admitted cohort required intubation. Four patients were intubated by anesthesia in the Emergency Department. Fiberoptic intubation was used in three patients and glidescope assistance was used for the fourth patient. Sedation was utilized but not traditional Rapid Sequence Intubation (RSI) medications. The final case was taken from the Emergency Department to the Operating Room. This patient was intubated using fiberoptic assistance with an Ear-Nose-Throat specialist at the bedside in case of emergent tracheostomy. No patient in the study required cricothyrotomy. Treatment in the ED with epinephrine for admitted patients, either subcutaneous or intramuscular administration, was 24.6% compared to 6.0% of discharged (P=0.0004). Discharged patients were more likely than admitted patients to receive oral treatments in the ED (26.1%, P=.0043).

Discussion

The study found that the majority of patients presenting to the ED for angioedema were discharged home (67.3%). This finding is consistent with previous studies which published values of 58% to 95.4%, far exceeding the percentages of inpatient admission [3,6-8]. Our study discovered a strong correlation between the location of swelling for angioedema patients and admission to the hospital. Patients experiencing a combination of external and internal or internal swelling alone were more likely to be admitted to the hospital. Three other studies that categorized the swelling on a scale similar to this study, also found that patients experiencing swelling from group 1 were discharged more frequently than group 2 or 3 [6,9,10]. Those patients who only experienced external swelling or no swelling at all were considered stable to be discharged home.

Previous studies have also reported that that not only were group 1 patients more likely to be discharged, but this was also the most common type of swelling when compared to other types of edema [9]. However, in the present study, there was not a significant difference between the prevalence of group 1 (35%) and group 2 (34%) swelling.

In this study, there were five patients (7.7%) who required intubation. This is consistent with the findings by other studies in which 10-11% of patients were incubated [6,9,11]. Several studies also found that patients experiencing edema in the mouth or the base of the tongue were at a high risk for airway compromise [3,9,12]. The study by Chiu et al., [9] discovered that half of the intubated patients were categorized as group 2 internal edema. Interestingly, we found that in the five patients ventilated, four suffered from prominent group 2 swelling. This finding further illustrates that evidence of swelling in the uvula, tongue, and/or oropharynx can cause serious upper airway obstruction and is a factor that physicians consider when determining appropriate disposition.

Among the discharged patients, 24 experienced a second episode of symptoms relating to angioedema. Although a substantial number of patients had recurrence, only four returned to the hospital for additional care. Of the four, two patients were admitted to the hospital in the progressive care unit while the other two patients were treated and discharged home. All patients with recurrence that returned to the hospital had either group 2 or 3 swelling. The data suggests that any degree of internal swelling may be a prognostic finding potentially warranting admission or close follow-up for higher recurrence potential. We were unable to gather information about the recurrence rate from 20 patients.

Limitations

There were some limitations to the present study. The etiology of angioedema was not always clear and the cause may influence disposition. We attempted to find causal agents such as drugs but information was often missing or unclear in this retrospective review. The retrospective medical chart review limits the information that can be obtained from the records and application to other fields. Specifically, it is possible that physical exam documentation of the oropharynx was inaccurate or incomplete. We were also unable to contact a portion of the patients who were discharged to follow-up on any possible recurrence introducing selection bias.

Conclusion

Angioedema can be life threatening if not managed properly by patients and physicians, but there is a significant spectrum of this diagnosis. Although airway compromise is a major consideration, disposition can include safe discharge home or admission to a non-ICU bed. Many factors, specifically the location of edema, are all considered when deciding to admit the patient to the hospital. Patients with internal swelling, involving the mouth or oropharynx are more likely to require admission compared to patients with external swelling alone. Although a substantial number of patients had a secondary recurrence after initial discharge, very few individuals required further treatment in the hospital setting. Elderly patients with a prevalence of internal swelling were more likely to require admission. Further prospective research is necessary to fully understand and validate these concepts.

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