CASE REPORT

Edema of the Uvula: Etiology, Risk Factors, Diagnosis, and Treatment

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Abstract

Edema of the uvula (EU) is a rare occurrence sometimes associated with angioedema, urticaria, and anaphylaxis. We analyze the causes, predisposing factors, and characteristics of EU in a group of 58 patients with a mean (SD) age of 48.2 (15.2) years over the course of a year.
Of the 58 patients studied, 49 (84.5%) were male and 44 (75.9%) presented isolated EU. Thirty-two patients (55.1%) with no clear etiology were classed as idiopathic. Snoring and a high body mass index were more prevalent in these patients. A variety of probable causes were identified in 26 patients (44.9%). In this group, EU was usually accompanied by urticaria, angioedema, and anaphylaxis and there was also a greater prevalence of atopy.
We found that EU was idiopathic in just over half of the patients studied and that the predisposing factors were being overweight and having a tendency to snore. Patients with EU should be tested for allergies to drugs, airborne allergens, and food.

Key words: Allergy. Idiopathic. Obesity. Edema of the uvula. Snoring.

Resumen

El edema de úvula (EU) aislado en el adulto es una entidad poco frecuente. En ocasiones va asociado a angioedema, urticaria y anafilaxia. Analizamos las causas, características y factores predisponentes del EU, así como su evolución.
Estudio finalizado en 58 pacientes, 49 (84,5%) hombres, edad media de 48,2 (DE= 15,2) años. En 44 el EU se presentó aislado. En 32 (55,1%) no se identificó una clara etiología, los catalogamos como idiopáticos. En ellos fue más prevalente la incidencia de roncopatía y un índice de masa corporal más elevado. En 26 (44.9%) la causa del EU fue por diversas etiologías. En este grupo el EU se presentó aislado en pocas ocasiones y solía ir acompañado de urticaria, angioedema y anafilaxia.
El EU es frecuentemente idiopático. Observamos como factores predisponentes el sobrepeso y ser roncador. Es necesario descartar la alergia a fármacos, neumoalergenos y alimentos.

Palabras clave: Alergia. Idiopático. Obesidad. Edema de úvula. Roncador.

Introduction

Edema of the uvula (EU) usually manifests as fullness of the oropharynx and difficulty in talking. It can be accompanied by difficulty in breathing and, since it affects the vocal cords, dysphonia [1]. Constitutional and mechanical anatomical defects (such as a long uvula) have been reported as predisposing factors [2]. There have been few studies of this medical condition. Most of the reports of EU in the literature are isolated clinical cases describing a variety of etiologies including allergy and consumption of nonsteroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor antagonists (ARA II) [3]. The condition has also been associated with the consumption of cannabis and cocaine [4,5] and the topical application of *Ecballium elaterium* [6-9], a plant belonging to the Cucurbitaceae family with anti-inflammatory properties and used in the treatment of sinusitis and rhinitis. Other causes of EU are infection of the upper respiratory tract, trauma (caused by endoscopy, orotracheal intubation, or oropharyngeal

aspiration), vascular alterations such as superior vein cava syndrome, ligature of the internal jugular vein, decrease in plasma osmotic pressure (occurring in renal insufficiency), obstruction of lymphatic flow after ligature of the thoracic duct, and increase in capillary permeability to proteins, occurring in diabetes or lupus. Differential diagnosis should be conducted for epiglottitis, myxedematous infiltration in hypothyroidism, and granulomatous infiltration in sarcoidosis and Merkelson-Rosenthal syndrome.

The aim of the present study was to analyze the etiology, predisposing factors, and characteristics of EU in patients treated at our hospital and followed for a year.

Case Description

A prospective study was conducted between September 2005 and April 2007 using a protocol jointly drawn up by the allergy unit and the ear, nose, and throat (ENT) service at Hospital Universitari Joan XXIII in Tarragona, Spain. The protocol was applied to patients with EU who visited the emergency department or were referred by their general practitioner to the allergy unit or ENT service. After an initial visit, patients were assessed approximately every 3 months for a year.

The protocol involved confirmation of EU by direct visual observation of the oropharynx, followed by nasofibroscopy. During history taking, special emphasis was placed on investigating personal and family histories of atopy and angioedema. A record was also made of patients' body mass index (BMI), regular medication, and illnesses occuring at the same time as EU. When a probable association was found with a causal agent, the latency period and subsequent consumption, where relevant, were assessed. Other data recorded were the frequency of episodes and the time of occurrence.

All patients underwent blood tests and biochemical analysis with measurement of erythrocyte sedimentation rate, hepatic enzymes, calcium and phosphorus levels, thyroid profile, antinuclear antibodies, anti-DNA, antithyroid antibodies, protein profile, complement levels (C3, C4, C1 inhibitor and C1q), as well as serum tryptase and total and specific immunoglobulin (Ig) E levels depending on skin test results.

Other examinations included skin prick tests to test for sensitization to common food and airborne allergens, stool tests for parasites, a chest X-ray to rule out pulmonary disease or tumors, a sinus X-ray, and spirometry with examination of both the inspiratory curve to check for extrathoracic obstruction and the expiratory curve.

Quantitative variables were described with means (SD) and categorical variables with absolute and relative frequencies. Groups were compared using the nonparametric Kruskal-Wallis test for continuous variables and the χ^2 test for categorical variables. Multiple logistic regression analysis was used to evaluate the association between snoring and idiopathic etiology adjusted for BMI and sex. Results were presented as odds ratios (OR) with their respective 95% confidence intervals (CIs). The level of statistical significance was set at $P \leq .05$. Data were analysed using the SPSS 12.0 statistical program (SPSS Inc., Chicago, Illinois, USA).

Our study comprised 58 patients, 49 (84.5%) of whom were men, with a mean (SD) age of 48.24 (15.2) years. EU was not concomitant with other complaints in 44 (75.9%) of the cases.

The patients were divided into 2 groups according to the etiology of EU. Group 1 consisted of patients in whom no clear cause was detectable (n=32, 55.1%) and group 2 of patients in whom a probable cause was detected (n=26, 44.9%). Snoring was significantly more prevalent in group 1 than in group 2 ($P<.0001$) and logistic regression adjusted for BMI and sex revealed a significant independent association between idiopathic EU and snoring (OR=14.45, 95% CI, 3-67.4). Group 1 also had a significantly higher BMI ($P<.005$) and frequency of episode recurrence ($P<.001$) than group 2.

In group 2, the suspect causal agents were airborne allergens in 8 patients, all of whom had symptoms of allergic rhinitis when the EU had occurred; food allergens in 4 patients (seafood [n=2], hazelnuts [n=1], and walnuts [1]); *Anisakis simplex* in 1 patient; hypersensitivity to NSAIDs in 3 patients (2 of whom had more than 1 episode with the same NSAID and good tolerance of other NSAIDs); glucosamine

Table 1. Comparative Statistical Analysis Between Patients with Idiopathic Edema of the Uvula (EU) and Those With EU With a Probable Cause[a]

	Idiopathic Group (n=32)	Group With Probable Cause (n=26)
Age, y	50.81	47.28
Male/female	30/2	19/7
Associated clinical manifestations		
Urticaria	1	8[b]
Angioedema	2	10[b]
Anaphylaxis	0	3[b]
Single episode/various episodes	3/29[c]	12/14
Atopy	7	16[d]
Early morning occurrence	19	11
Gastroesophageal reflux	10	5
Long uvula	14	9
Body mass index, kg/cm^2	28.81[e]	26.93
Snoring	28[f]	8
Primary treatment		
Medical	29	24
Immunotherapy	0	0
Surgery	3	1

[a]Data are presented as number of patients unless otherwise specified.
[b]$P<.001$.
[c]$P<.001$.
[d]$P<.0001$.
[e]$P<.05$.
[f]$P<.0001$.

sulphate in 1 patient (2 separate episodes, hence no further tests); and ipratropium bromide in 1 patient (negative skin test; inhalation challenge test not performed because the patient was 85-years-old). Eight patients were found to have secondary causes, including consumption of cannabis (1 patient), ACE inhibitors (non-allergic) 2 patients), recent orotracheal intubation (1 patient), and pharyngotonsillar infection (4 patients). In comparison with the idiopathic group, EU in this group was more frequently accompanied by other clinical manifestations such as urticaria, angioedema, and anaphylaxis in the case of food allergies ($P<.0001$). Atopy was also more prevalent ($P<.0001$). There were no differences in the smoking habits of the 2 groups.

Table 2. Etiologies of Edema in the Uvula in Study Group (n=58)

Etiology	No. of patients
Unknown	32
Airborne allergens	8
Food allergy	4
Anisakis simplex	1
NSAIDS	3
Glucosamine sulphate	1
Ipatropium bromide	1
Cannabis	1
ACE inhibitors (no allergy)	2
Orotracheal intubation	1
Pharyngotonsillar infection	4

Abbreviations: ACE, angiotensin-converting enzyme; NSAIDs, nonsteroidal anti-inflammatory drugs.

Only 15 patients (25.9%) presented a single episode, while 43 patients (74.1%) presented repeated episodes. Twenty-three patients had a longer uvula than normal. In 30 patients, the episodes always occurred in the early morning. In 15 patients, gastroesophageal reflux that had never been treated or had been treated only occasionally was reported. Nasofibroscopy was normal in 50 patients. In 2 patients, hyperemia of the arytenoids, an indirect indication of gastroesophageal reflux, was observed. In another 2 patients, band hyperemia was observed (one of the patients was a habitual smoker and the other had poor phonation in the workplace). In 2 more patients, edema of the vocal cords was observed. This edema was the beginning of an autoimmune hypothyroidism in 1 of the patients (later diagnosed with allergic rhinitis due to sensitivity to house dust mites and *Parietaria judaica* pollen). The other was caused by poor phonation. In 1 patient, papillomatous lesions were observed in the uvula and larynx, with biopsy findings compatible with papilloma virus infection. In another patient recently diagnosed with acute cerebellar ataxia, hypokinesia of the vocal cords was observed and a tracheostomy performed.

The patients were treated with antihistamines and corticosteroids. One was given immunotherapy for monosensitization to *Parietaria judaica* pollen. Excision of the uvula was considered in patients with recurring episodes, patients with an acute episode resistant to medical treatment, and patients whose symptoms progressed rapidly.

EU-related symptoms were fully controlled in 26 of the 58 patients. These patients included those with food allergy (n=4), *Anisakis simplex* sensitization (n=1), EU secondary to orotracheal intubation (n=1), pharyngotonsillar infection (n=3), those who had taken NSAIDs, ACE inhibitors, glucosamine sulphate, and ipratropium bromide, 9 patients from the idiopathic group, and 1 patient sensitized to airborne allergens who underwent surgery because of repeated episodes.

Discussion

Few reports in the literature have analyzed the causes and predisposing factors of EU [2,10]. In our study, EU was idiopathic in most cases (55.1%), a finding that coincides with the results of other series. In the idiopathic group, EU with no other symptoms (urticaria, angioedema, or anaphylaxis) was predominant, while in the other group, EU was usually accompanied by other clinical manifestations such as urticaria, angioedema, and anaphylaxis, with atopy also being more prevalent. There were also differences between the 2 groups in terms of recurrence, with episodes being more common in the idiopathic group. It is not possible to compare these results with those of other studies because only isolated cases have been reported in the literature. Snoring was more also prevalent in the idiopathic group, a finding that was also observed by Daschner et al [10]. Logistic regression analysis of this group revealed an independent association between EU and snoring following adjustment for sex and BMI. Being a snorer would therefore seem to indicate a variable degree of upper airway obstruction, without a necessarily high BMI [11].

We found no differences between the 2 groups in terms of early morning occurrence, gastroesophageal reflux, or longer uvula.

In conclusion, EU was idiopathic in just over half of the cases studied and most common in middle-aged men. Certain factors, such as being overweight and snoring, were predisposing factors. Patients with idiopathic EU were more likely to have recurring episodes than those with a known cause. Patients with EU should be tested for allergies to drugs, airborne allergens, and food, especially when the condition is associated with other clinical manifestations.

References

1. Evans TC, Roberge RJ. Quincke's disease of the uvula. Am J Emerg Med. 1987; 5: 211-16.
2. McNamara RM. Clinical characteristics of acute uvulitis. Am J Emerg Med. 1994; 12: 51-2.
3. Rodríguez A, Matilla B, Gozalo F. Angioedema por Ibersartán. Rev Esp Cardiol. 2001; 54: 532-3.
4. Boyce SH, Quigley MA. Uvulitis and partial upper airway obstruction following cannabis inhalation. Emerg Med. 2002; 14: 106-8.
5. Hidalgo JJ, Jiménez E, Sempere E, Feliu M. Angioedema

de úvula tras consumo de cocaína por vía intranasal. Med Clín. 2002; 119: 438-9.
6. Satar S, Gokel Y, Toprak N, Sebe A. Life-threatening uvular angioedema caused by Ecballium elaterium. Eur J Emerg Med. 2001; 8: 337-9.
7. Raikhlin-Eisenkraft B. Ecbalium elaterium remedy or poison. J Toxicol Clin Toxicol. 2000; 38: 305-8.
8. Kloutsos G. Upper airway edema resulting from use of Ecballium elaterium. Laryngoscope. 2001; 111: 1652-5.
9. Gianella A, Cabrera D, Mardónez J.M, Saldias F. Hierbas medicinales y graves efectos adversos: Angioedema de úvula causado por uso de Ecballium elaterium. Rev Méd Chile. 2002; 130: 1407-10.
10. Daschner A, Vega F. Uvular angioedema: clinical and etiologic aspects in a series of 17 patients. XXII EAACI Congress. 2004 June 12-16; Madrid Spain. Amsterdam: Springer; 2004. p. 57-8.
11. Miller RJ, Gerhardt MA. Uvular edema secondary to snoring under sleep sedation. Anesth Prog. 2006; 53:13-6.

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