



Angioedema: A Life Threatening Airway Emergency: A Case Report

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Summary: Angioedema is a rare event (Incidence: 100 to 3000/100,000 persons) which can lead to a life threatening airway emergency in a very short time and this necessitates urgent intervention. We present a case of potentially life-threatening postoperative swelling of the tongue, oro-pharynx and submandibular area that developed in a patient after giving second dose of antibiotic (Cefotaxime). With the treatment, the patient had an uneventful outcome. The principal treatment of angioedema is the discontinuation of the precipitating agent and airway management. Patients with swelling limited to face and oral cavity may require monitoring only. However, those with swelling in the floor of mouth, tongue and supraglottic or glottic areas should have their airway secured by fibre-optic guided tracheal intubation.

Keywords: Angioedema, post-operative care, fibre-optic bronchoscope, adrenaline

Antibiotics are generally administered in orthopaedic surgeries before incision and again on completion of surgery. Though skin testing should be done prior to administration of antibiotics, a negative test does not rule out the possibility of angioedema, which is a complement mediated reaction, and can occur on the second or third administration of the antibiotic. We are sharing one such case of angioedema that developed on administration of second dose of antibiotic, which led to a rapidly increasing facial and oro-pharyngeal oedema, subsequently leading to stridor and desaturation. The management of angioedema is discussed.

Case Report: An eight year old male child, ASA I, with a history of fall few hours back was scheduled for open reduction and internal fixation (k-wiring) of inter-condylar fracture humerus (because of involvement of epiphyseal region). The case was planned under general anaesthesia. He had no positive history or history of any in hospital treatment prior to this episode of injury. No history of



allergies was given by the patient/guardian. There was no history of prior surgery or anaesthesia exposure.

On general and systemic examination, there were no abnormal findings. As per protocols for general anaesthesia in an asymptomatic child, the patient is investigated for haemoglobin only, which was 11.5mg/dl. The child's weight was 24 kg.

Sensitivity testing for antibiotic administration was done prior to surgery by intradermal skin testing, which was negative. After 6 hours fasting, the patient was taken to the operation theatre and monitors were attached. The vitals were: pulse: 94/min, BP: 110/70 mm of Hg, SpO₂ on room air was 98%. A 22g intravenous cannula was secured in left upper limb; the patient was then given midazolam (0.7mg) and Pentazocin (12mg) and Ringer's lactate was started at the rate of 350 ml/hr for first hour. After adequate pre-oxygenation, tracheal intubation was done using thiopentone 125 mg and vecuronium 2 mg (0.08 mg/kg). Anaesthesia was maintained with halothane and nitrous oxide in oxygen using Bain's circuit for controlled ventilation. Intraoperatively, he remained in a supine position and additional (maintenance) dose of vecuronium was given once. He also received intravenous paracetamol 250 mg for post operative analgesia and ondansetron 4 mg IV as prophylaxis for post operative nausea and vomiting. At the end of procedure, residual neuromuscular blockade was reversed with neostigmine 1.25 mg and glycopyrrolate 0.2 mg. The patient was extubated after return of protective reflexes and spontaneous respiration. At this time, the patient received antibiotic (Cefotaxime) at orthopedician's request. The intraoperative course, lasting for about an hour, was uneventful. Plan was to shift the patient to recovery room.

Before shifting, just a few minutes after extubation we noticed some tongue and facial swelling in submandibular and parotid area. The patient was awake and alert with stable vital signs. With the suspicion of angioedema, injection Dexamethasone 4 mg, Chlorpheniramine 12.5 mg and Ranitidine 25 mg were given. Despite treatment, the patient's tongue and facial swelling continued to increase in a symmetrical fashion. We did not have access to fibre-optic bronchoscope, so possibility of fibre-optic bronchoscope guided intubation was ruled out. A call was sent to the E.N.T surgeon for emergency tracheostomy. In the mean while, the patient was able to maintain a patent airway with the use of triple manoeuvre and oro-pharyngeal airway and was maintaining oxygen saturation above 90% on 100% humidified oxygen, but with increasing stridor. At that time, adrenalin 0.1 mg IV (1 ml of 1/10000 solution of adrenalin) was administered and adrenalin nebulisation was also started. Slowly the swelling started regressing. The patient was monitored inside operation theatre with adrenalin nebulisation repeated twice and IV adrenalin repeated once. His tongue size and sub-mandibular swelling had significantly decreased and simultaneously, the stridor was also relieved, SpO₂ also came up to 95% on O₂ by venti-mask. The patient was then shifted to ICU for further management and monitoring. The tongue swelling was completely resolved in 3-4 hrs. The patient was now maintaining SpO₂ without O₂.

In the ICU, the patient continued to receive levo-cetirizine, ranitidine and dexamethasone for 2 days.



Discussion: The differential diagnosis of postoperative tongue swelling includes angioedema, allergic reaction and anaphylaxis, hematoma formation, and tongue congestion secondary to traumatic or prolonged compression during surgery. Our patient's presentation was devoid of systemic symptoms, hypotension, or dermatologic manifestations seen during an allergic or anaphylactic reaction. A discrete, hard, discoloured mass was not present to suspect a hematoma. Tissue congestion caused by the surgical instruments or procedure was ruled out because the surgical instruments did not directly disturb these areas. Our patient did demonstrate a symmetric, soft, non pitting oedema that is characteristic of angioedema. He had a presentation that makes angioedema a reasonable diagnosis.

It is estimated that up to 25% of the united states population experience an episode of urticaria or angioedema during their life time.^{1,2} Urticaria\angioedema can be immune mediated, non immune mediated, complement mediated and autoimmune mediated³. All these mechanisms cause degranulation of mast cells and release of histamine, prostaglandins, leukotrienes and PAF.^{2,3,4} These mediators ultimately lead to endothelial activation, vasodilation and increased vascular permeability.

Angioedema commonly presents as an abrupt onset of non-pitting, non-pruritic swelling of dermis, subcutaneous and submucosal layers.^{4,5,6} However, angioedema has been associated with certain medication, allergens, physical trauma, and hereditary or acquired autoimmune abnormalities in the complement system. Hereditary and acquired forms of C1 esterase inhibitor deficiency/dysfunction exist, and these patients are susceptible to developing acute swelling after dental or surgical manipulation. Our patient did not have any oral/dental manipulation. Medications that have been implicated include antibiotics (penicillin, cephalosporins, sulphonamides, vancomycin), opioids, nonsteroidal anti-inflammatory drugs, ACE inhibitors, and angiotensin II receptor antagonists.⁷⁻¹¹ Accounting for 38% to 68% of all cases, ACE inhibitor- associated angioedema is the most common cause of angioedema.¹²⁻¹⁵ The incidence of ACE inhibitor-associated angioedema is one to two in 1000. The development of angioedema in a patient taking ACE inhibitors can occur early (weeks) or late (years) in the course of therapy¹⁶. Associated mortality is currently high at 11%. The mechanism of angioedema in patients taking ACE inhibitors is not fully understood. It is thought to be secondary to an increase in kinins.

Various antibiotics (penicillin, cephalosporins, sulphonamides, vancomycin) are also known to induce angioedema and anaphylaxis.¹⁷ Cephalosporins share the beta lactam nucleus with penicillins, yet are less likely to cause anaphylaxis. There is either cross reactivity or independent sensitization such that penicillin allergic patients react to cephalosporins with greater frequency than patients who are not allergic to penicillin. Risk of an immediate reaction with first generation cephalosporin in patients allergic to penicillin has been reported to be from 5% to 16.5% whereas with second generation cephalosporin it is 4%^{18,19} for the 3rd and 4th generation cephalosporin the reaction rate is 1% to 3%.^{17,18,19} A negative skin test does not rule out reactivity to cephalosporins. A study done by Blanca et al revealed that patient may respond normally to the first dose of cephalosporin but may be allergic to the second dose²⁰. Our patient had received 1st dose at the time of induction which he tolerated well but developed angioedema with 2nd dose of cephalosporin.



The principal treatment of angioedema is the discontinuation of the precipitating agent and airway management. Patient with stridor, accessory muscle use, tongue oedema and oedema of the floor of mouth require immediate intubation.^{12,13,21} Angioedema is usually self-limiting, and the swelling usually resolves spontaneously in 2 to 3 days. Early identification of angioedema and early intervention could reduce mortality and unnecessary surgical airways. Chiu et al presented an algorithm for airway management based on classifying the symptoms of angioedema into 3 types. It has been recommended that a patient with severe type 2 or type 3 angioedema may require tracheal intubation.¹²

Classification of angioedema as described by Chiu et al:

Type	Presentation	Management
I	Swelling is limited to face and oral cavity and excludes the floor of the mouth	May be observed in the ward.
II	Swelling extends to the floor of the mouth, tongue, soft palate, and / or uvula	Close observation in the intensive care unit. If severe, proceed to fiber-optic intubation.
III	Swelling extends to supra-glottic and glottic structures	Close observation in the intensive care unit. If severe, proceed to fiber-optic intubation.

In the series of Chiu et al, 21% of type II and 33% of type III angioedema patients required intubation. Our patient had characteristics of type II (or type III since we could not view the supraglottis and glottis because of lack of availability of fiberoptic bronchoscope in our institution) angioedema. As the patient was maintaining saturation above 90% with O₂ face mask and the facial oedema started regressing over 10-15 minutes. So intubation was not done and the patient was kept under close observation.

In treating angioedema of all aetiologies, steroids, antihistamines, epinephrine, and humidified oxygen are widely used. However, they have not been shown convincingly to provide any benefit. In cases of hereditary angioedema, androgens that increase the serum concentration of C1 esterase inhibitor concentrate is successful. Though Fresh frozen plasma contains C1 esterase inhibitor, its use is not recommended in angioedema because it also contains C4, which could lead to the continuing activation of the complement system.²²

We conclude that though the patient may tolerate the first dose of cephalosporin well, angioedema can also occur with the second dose. So we should always keep a high index of suspicion for angioedema in a patient with tongue swelling in the immediate postoperative period even if the patient was not allergic to first dose of antibiotic. Early assessment of the airway and



appropriate intervention may prevent mortality and morbidity associated with late recognition of airway compromise.

References:

1. Mathews, K.P., Urticaria and angioedema. *J Allergy Clin Immunol*, 1983. 72 (1): p.1-14.
2. Dibbern, D.A., Jr. and S.C. Dreskin, Urticaria and angioedema: an overview. *Immunol Allergy Clin North Am*, 2004. 24 (2): p. 141-62,v.
3. Henderson, R.L., Jr., A.B. Fleischer, Jr., and S.R. Feldman, Allergists and dermatologists have far more expertise in caring for patients with urticaria than other specialists. *J Am Acad Dermatol*, 2000. 43 (6): p. 1084-91.
4. Kaplan; A.P. and M.W. Greaves, Angioedema. *J Am Acad Dermatol*, 2005. 53 (3): p. 373-88; quiz 389-92.
5. Champion, R.H., et al., Urticaria and angio-oedema. A review of 554 patients. *Br J Dermatol*, 1969. 81 (8): p. 588-97.
6. Varadarajulu, S., urticaria and angioedema. Controlling acute episodes, coping with chronic cases. *Postgrad Med*, 2005. 117 (5): p. 25-31.
7. Krishnaswamy, G. and G. Youngberg, Acute and chronic urticaria. Challenges and considerations for primary care physicians. *Postgrad Med*, 2001. 109 (2): p. 107-8, 111-4, 119-23.
8. Bhalla, M. and G.P. Thami, Delayed diagnosis of angiotensin- converting enzyme (ACE) inhibitor induced angioedema and urticaria. *Clin Exp Dermatol*, 2003. 28(3): p. 333-4.
9. Grattan, C.E., The urticaria spectrum: recognition of clinical patterns can help management. *Clin Exp Dermatol*, 2004. 29 (3): p.217-21.
10. Howard, P.J. and M.R. Lee, Beware beta-adrenergic blockers in patients with severe urticaria! *Scott Med J*, 1988. 33 (5): p. 344-5.
11. Sanchez-Borges, M., A. Capriles – Hulett, and F. Caballero- Fonseca, Cutaneous reactions to aspirin and nonsteroidal anti-inflammatory drugs. *Clin Rev Allergy Immunol*, 2003. 24 (2): p.125-36.
12. Grattan, C., S. Powell, and F. Humphreys, Management and diagnostic guidelines for urticaria and angio- oedema. *Br J Dermatol*, 2001. 144 (4): p.708-14.
13. Chiu, A.G., et al., Angiotensin-converting enzyme inhibitor-induced angioedema: a multicenter review and an algorithm for airway management. *Ann Otol Rhinol Laryngol*, 2001. 110 (9): p. 834-40.
14. Gunkel, A.R., et al., Angioneurotic edema as a reaction to angiotensin-converting enzyme inhibitors. *Am J Otolaryngol*, 1996. 17 (2): p.87-91.
15. Megerian, C.A., J.E. Arnold, and M. Berger, Angioedema: 5 years' experience, with a review of the disorder's presentation and treatment. *Laryngoscope*, 1992. 102 (3): p. 256-60.
16. Sondhi, D., M. Lippmann, and G. Murali, Airway compromise due to angiotensin-converting enzyme inhibitor- induced angioedema: clinical experience at a large community teaching hospital. *Chest*, 2004. 126 (2): p. 400-4.



16. Brown, N.J., et al., Black Americans have an increased rate of angiotensin converting enzyme inhibitor- associated angioedema. Clin Pharmacol Ther, 1996. 60 (1): p.8-13.
17. Kelkar P.S., Li J.T.-C.: Cephalosporin allergy. N Engl J Med 345. (11): 804-809.2001; Citation
18. Greenberger P.A.: Drug allergy. J Allergy Clin Immunol 117. (2): S464- S470.2006; Full Text.
19. Grammer L.C., Greenberger P.A.: Drug allergy and protocols for management of drug allergies. 3rd edition Oceanside PubsProvidence (RI)2003. p. 1-42
20. Blanca M., Fernandez J., Miranda A., et al: Cross-reactivity between penicillins and cephalosporins: clinical and immunologic studies. J Allergy Clin Immunol 83. (2): 381-385. 1989; Abstract
21. Vleeming.W.et al., ACE inhibitor-induced angioedema. Incidence, prevention and management. Drug Saf, 1998. 18 (3): p. 171-88.
22. Lorijean K Reed, Jin Meng, Girish P. Joshi. Tongue swelling in the recovery room: a case report and discussion of postoperative angioedema. J Clinical Anaesthesia: May 2006: Vol.18, Issue 3, pages 226-229.