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Case Report

Sudden unexpected death due to hereditary angioedema — A case report

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ABSTRACT

Angioedema related to deficiency of the C1- esterase inhibitor protein (C1-inh) is characterized by lack of response to therapies, which include antihistamines, steroids and epinephrine. In case of laryngeal edema, mortality rate is an estimated mammoth 30 percent. The first case of such acquired form of angioedema related to the deficiency in C1- esterase inhibitor was published in 1972. In the present case, we entail details of one such case. [1,2]

1. Case Report

A 15-year-old Male child reported dead to the Casualty possibly during transit in the ambulance. Post Mortem was conducted and findings noted. External findings include a moderately nourished and moderately built male body with bluish discoloration of gums and nail beds of all the finger nails(Figures 1, 2 and 3).

Post mortem hypostasis fixed on the back with areas of contact pallor (Figure 4), cornea — hazy, pupils dilated and fixed

No external or internal injuries noted anywhere in the body.

Internal findings of the organs were noted.

The heart was normal in size, weighed 320 grams, with few sub epicardial petechial hemorrhages on both the surfaces of the heart; Cut section — All chambers contained fluid and clotted blood; Valves appeared normal, with patent Coronary Ostia; Coronaries and Great vessels appeared normal.

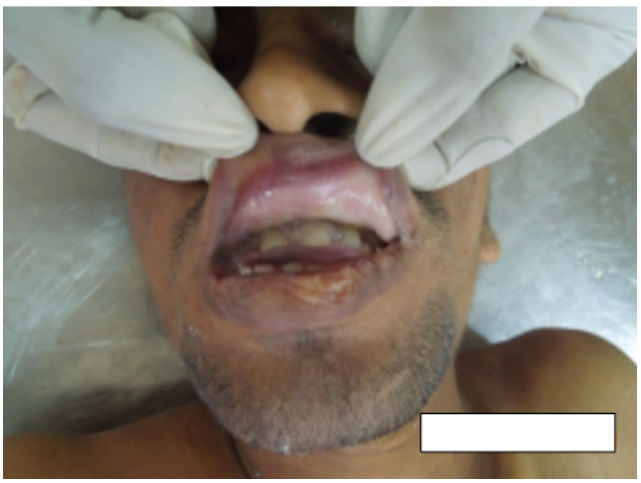

Fig. 1:

Lungs appeared normal in size; Right lung weighed 460 grams and Left lung weighed 390 grams. Few sub pleural petechial hemorrhages on the interlobar fissure of both the lungs were noted. Cut section of the lungs appeared

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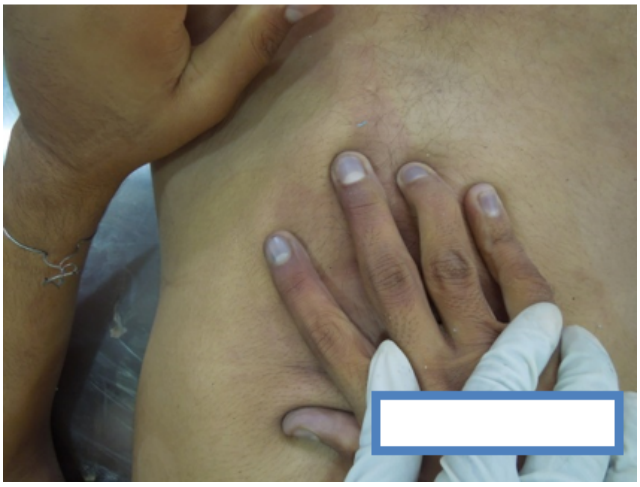

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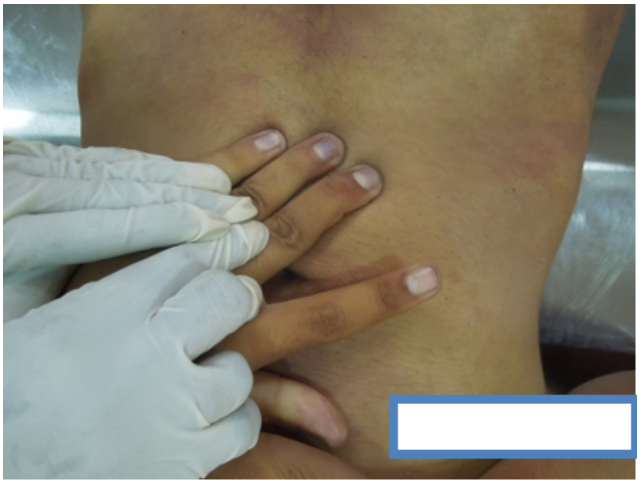

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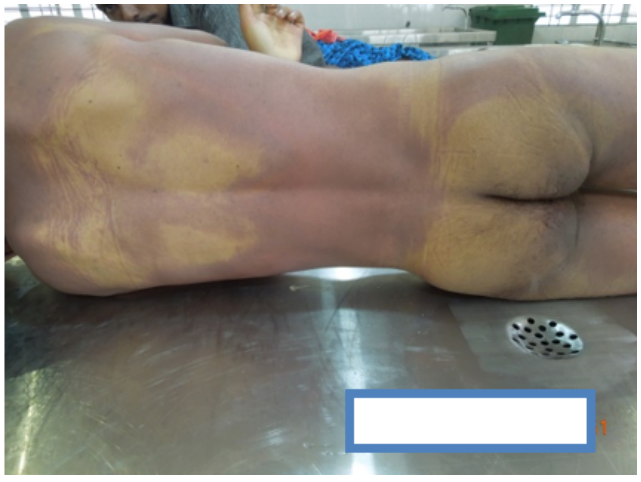
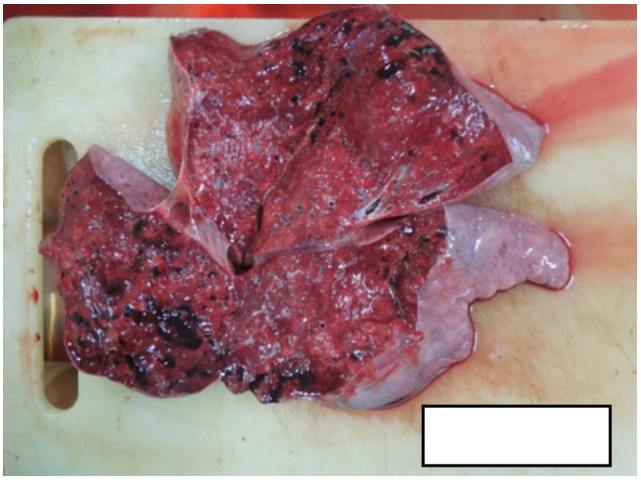


Fig. 4:

congested. (Figure 5 and Figure 6).



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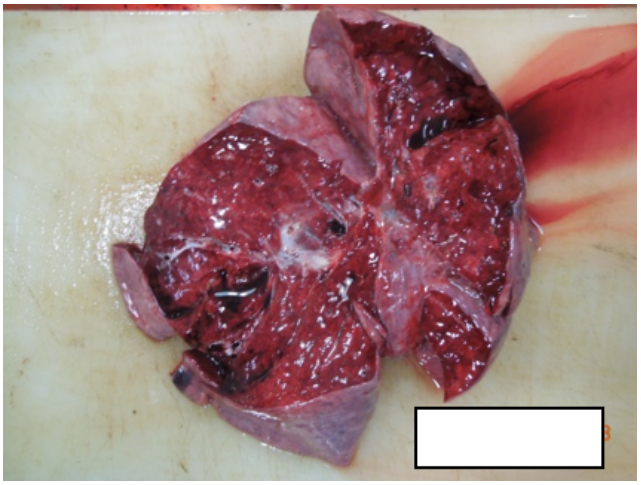


Fig. 6:

Pharynx, Larynx, Arytenoids, Vocal Cords and Trachea appeared empty and intact; Mucosa -edematous and occluding the lumen (Figures 7, 8, 9 and 10 and Figure 11). Hyoid bone and other laryngeal cartilages appeared intact.

Stomach contained 300 grams of partly digested food particles with no definite smell. Mucosa showed patchy areas of congestion (Figure 12). The liver, spleen and kidneys were normal in size and appeared congested on cut section (Figures 13 and 14 and Figure 15).

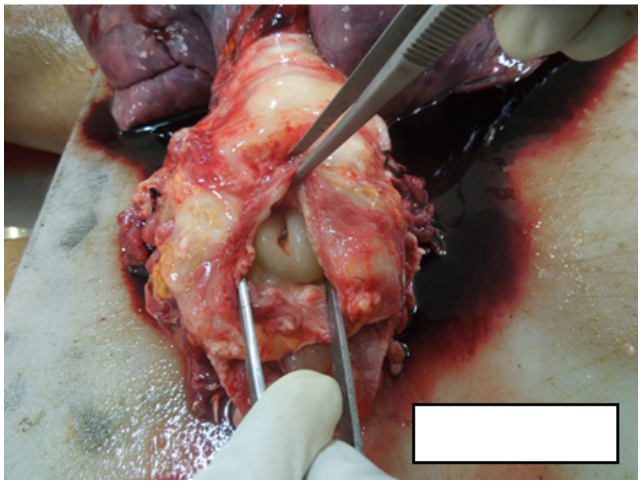
Bladder appeared empty and intact.

scalp, vault, duramater and Base of Skull were intact and the brain was normal (Figure 16).

Ribs, pelvis and spinal column were intact.

Viscera preserved and sent for chemical analysis, of which, the results showed no significant findings.

Tissue bits of larynx, brain and brainstem, Lung and Kidneys were preserved for histopathological examination.



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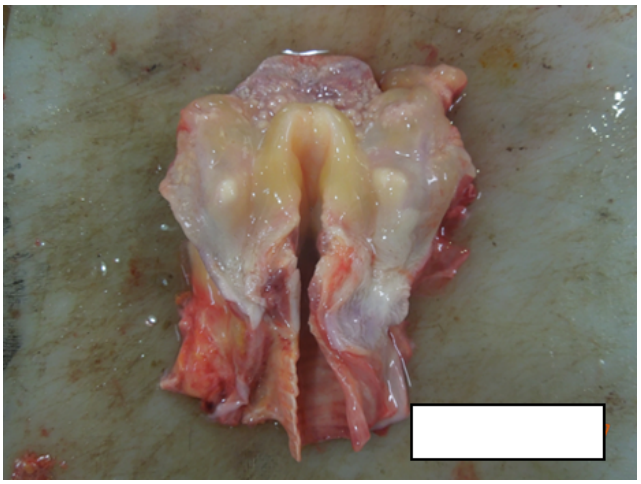

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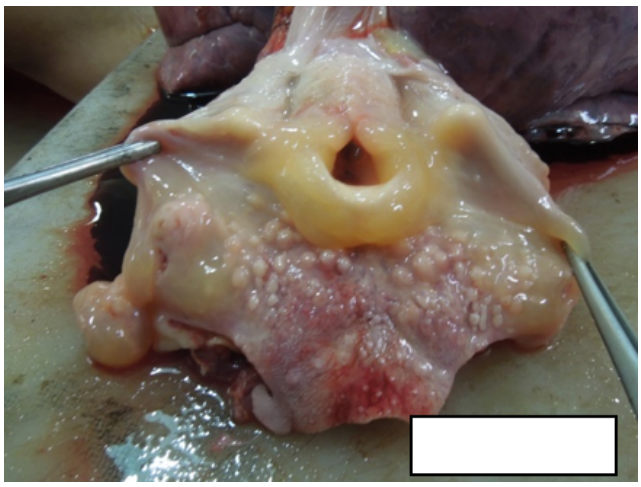

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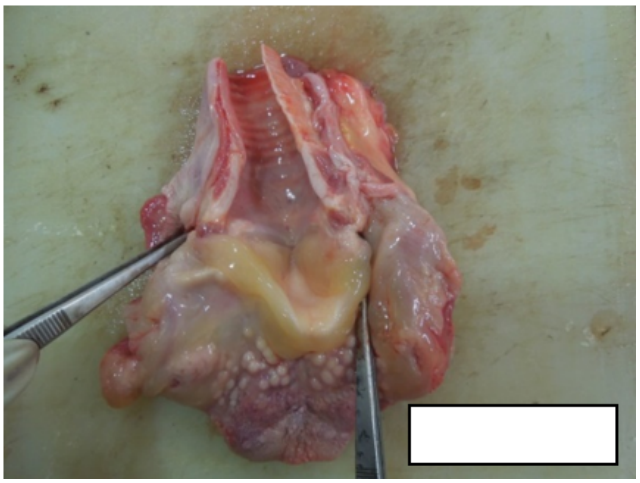

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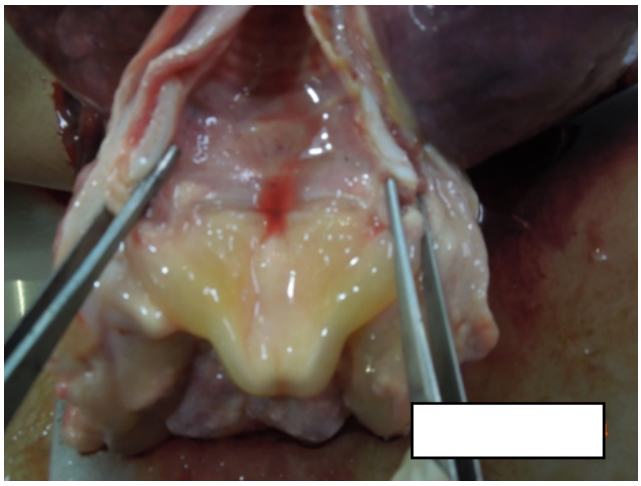

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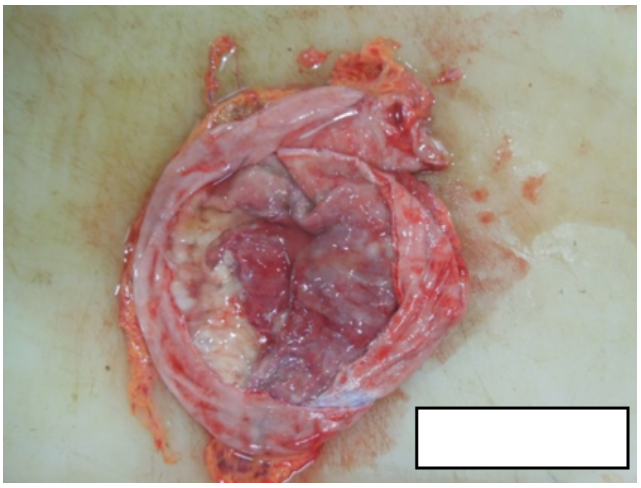

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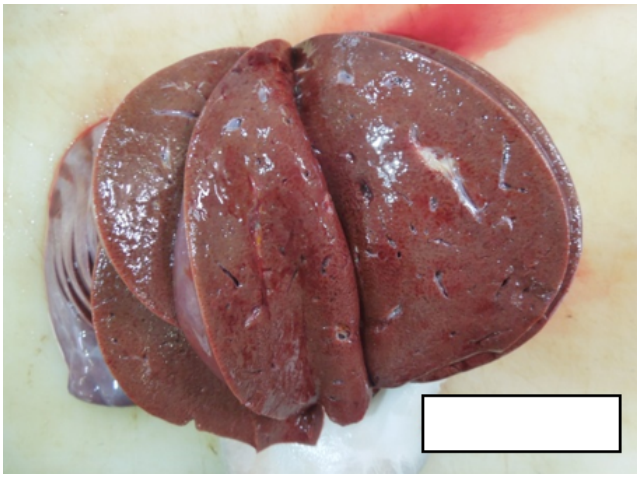

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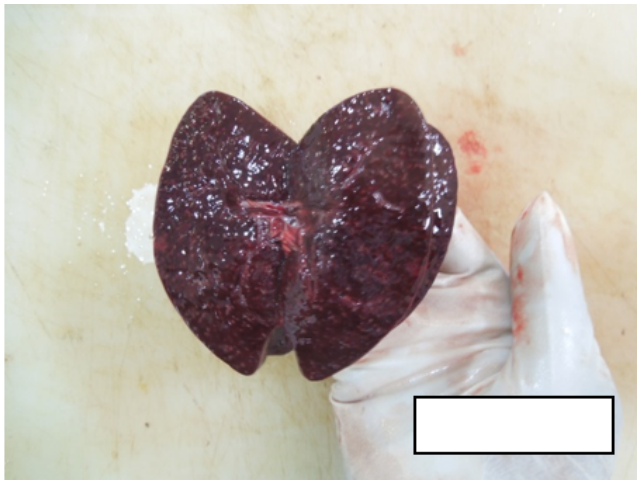

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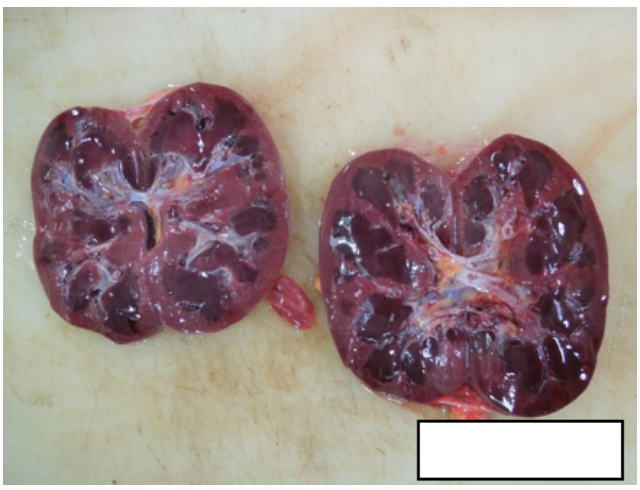

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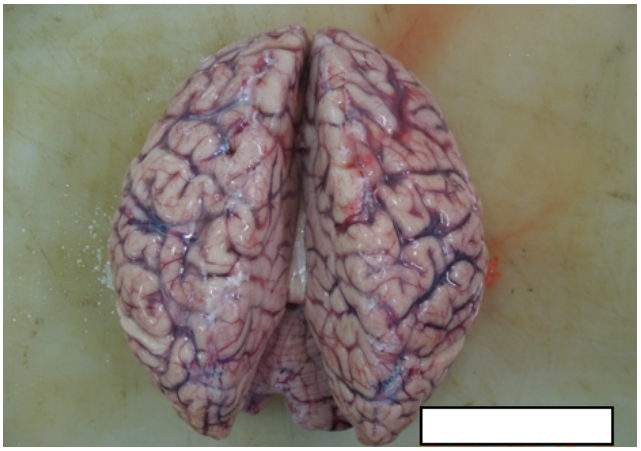


Fig. 16:

Opinion as inferred from the Post mortem report — Reserved pending the reports of chemical analysis of viscera and histopathological report.

Histopathological examination was done and inference recorded. Section from the larynx showed stratified squamous epithelium lining underlying stroma with eosinophilic proteinaceous material, mild lymphocytic infiltrate and scattered, dilated and congested blood vessels.

Sections studied form the epiglottis and right and left lateral laryngeal mucosa shows stratified squamous epithelial lining, underlying stroma shows eosinophilic proteinaceous material and mild to moderate lymphoplasmacytic infiltration and islands of cartilage.

Section studied from the strap muscle shows skeletal muscle bundles and interstitium shows congested blood vessels and areas of haemorrhage.

Features were suggestive of Laryngeal and Epiglottic edema.

- Arriving at an opinion it was inferred from the above findings that Asphyxia was the mode of death though the cause of Asphyxia could not be concluded. History elicited revealed that the case had been a known one of Hereditary Angioedema / C1 esterase inhibitor deficiency for the past 4 years (C3 — 112 mg/dl, C4 < 5.9 mg/dl, CRP — 0.817 mg/dl) (Figure 18) and had been on treatment (Danazol 400 mg OD) for the same, with occasional episodes of breathlessness (Treated with steroids for acute exacerbations).

Hence, it was concluded from the above that Hereditary angioedema (HAE) causing Asphyxia could be the most probable cause of death.

2. Discussion

Hereditary angioedema — It is a disorder usually characterized by recurrent episodes of severe swelling

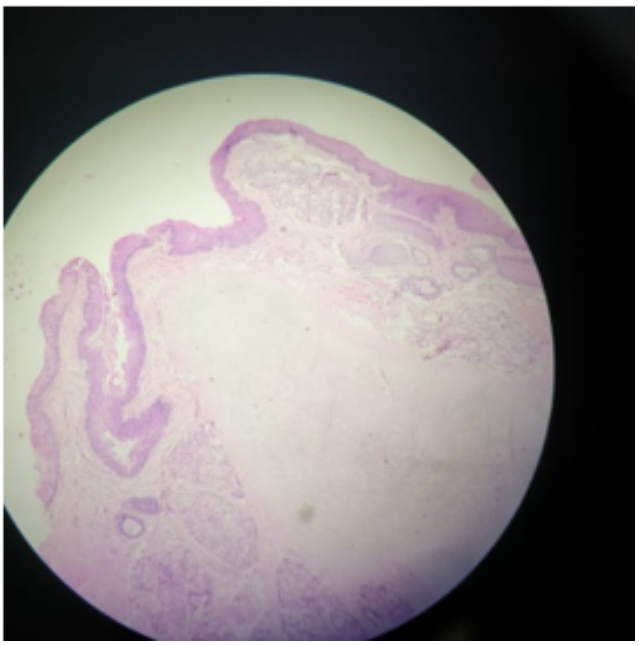
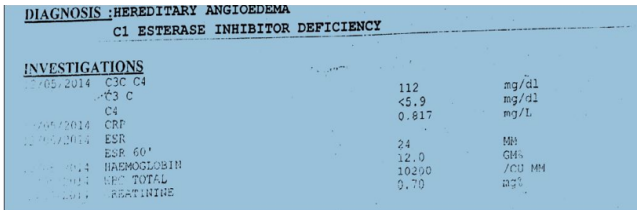


Fig. 17: HPE of vocal cord


DIAGNOSIS :HEREDITARY ANGIOEDEMA
C1 ESTERASE INHIBITOR DEFICIENCY

INVESTIGATIONS

05/2014	C3C C4		
	C3 C	112	mg/dl
	C4	<5.9	mg/dl
	CRP	0.817	mg/L
/2014	ESR		
	ESR 60'	24	MM
	HAEMOGLOBIN	12.0	GM%
	WBC TOTAL	10200	/CU MM
	CREATININE	0.70	mg%

Fig. 18: Lab report

(angioedema). Even though rare, HAE is associated with episodic attacks of oedema formation and that can lead to catastrophic consequences. Triggering factors include dental procedures, physical impact, psychological and physiological stress like menstruation and infections. Certain medications like OCP's and ACE inhibitors are also known to trigger HAE.[3]

During the acute phase, clinical manifestations may include diffused skin, peptic and respiratory mucosal oedema. Cerebral edema will occur, leading to migraine type pain, as well as cerebrovascular incidents.[3] Face edema may be seen in eyelids alone or will also involve the entire surface and the lips. Rarely it will also be seen in the oral cavity also.

Differential diagnosis of Melkersson-Rosenthal syndrome should also be kept in mind as the findings will be similar to that of HAE.[4] The key difference is that in the case of Melkersson-Rosenthal syndrome the lip swelling is stable and the other symptoms will not be present to diagnose of angioedema.

Extravasation of fluid in the peritoneal cavity in HAE will lead to ascites and fluid imbalance which causes hemodynamic shock. Aggressive fluid resuscitation will be necessary for prevention.

People on treatment with ACE inhibitors for hypertension and congestive cardiac failure will also have similar presentations as in HAE. Proper history taking and C1-INH level will be required for differentiating HAE and ACE-inhibitor induced angioedema.[3]

Usual presentation of HAE is seen mostly in the second decade of life but presentation during other stages of life is not uncommon. According to Bork et al.[6], the first ever HAE symptoms and signs were most commonly seen between 11 to 45 years of age, while the youngest known confirmed case at that time was a child of age.[3]

Interval between HAE crises differs for the same individual and from one person to another person. Factors influencing the frequency of episodes include triggering factors and medications.

Though oedema can affect any organ of the body, laryngeal oedema will be a worrisome and lethal symptom as it may lead to death by asphyxiation.[4,5] Initial presentation of HAE may be Life-threatening laryngeal oedema. It can be followed by edema of face and extremities. These symptoms could appear in all episodes of HAE in a single patient. Bork and Barnstedt[4] reported 4 fatal cases of laryngeal oedema in HAE patients where edema appeared 4 – 30 hours upon tooth extraction. On taking history, it was known that 3 of the 4 patients developed the symptom for the first time in their life. These patients have not been given C1-INH on therapeutic or prophylactic basis. This may be the reason for the poor clinical result.

According to Bork et al.[6], 61 out of 123 HAE patients (49.6%) had suffered more than one episode of laryngeal oedema. The ratio of incidence of laryngeal oedema: skin oedema: internal organ oedema was 1 : 70: 54. This states that laryngeal oedema is less common in HAE. The time taken from initial symptom to full blown laryngeal oedema was 8-12 hours (mean = 8.3 hours). Only one single case had full blown symptoms in less than 3 hours.

According to previous studies, factors which increases the incidence of laryngeal edema in HAE are:

1. Previous dental surgeries or during intubation
2. Age group between 11 and 45 yrs
3. Previous multiple, laryngeal oedema episodes
4. Previous encounter of facial edema

They have also discussed the following factors that reduce likelihood of laryngeal oedema in HAE:

1. Age less than 11 and above 45 years
2. 2. Absence of an episode of previous laryngeal edema (A patient could still suffer a fatal laryngeal episode that was their first ever episode)
3. Long-term prophylactic therapy

Administration of C1-INH factor as a prophylactic drug before surgeries and for acute episode of HAE has been proven effective.[5] Further it also states that failure to administer C1-INH on acute episodes of laryngeal oedema may be fatal to patients. Furthermore, HAE is not due to an allergic phenomenon; hence corticosteroids and antihistamines do not constitute effective therapy.[4]

3. Source of Funding

None.

4. Conflict of Interest

None.

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