A Deeper View in the Pathogenesis of Vasomotor Rhinitis

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Abstract: Introduction: Vasomotor rhinitis cause nasal symptoms that occur in response to environmental conditions, such as changes in temperature or relative humidity, odours (e.g., perfumes or cleaning materials), passive tobacco smoke, alcohol, sexual arousal, and emotional factors. Such hyper-reactivity to nonallergic triggers is not mediated by increased neural efferent traffic to the blood vessels supplying the nasal mucosa. It can also occur in allergic rhinitis, when the term mixed rhinitis is applied. Objectives: The present study aimed to study the pathogenesis of VMR by electron microscopy to see if there is another cause for this disease. **Material and Methods**: It was a prospective randomised study which was held at Benha Faculty of Medicine, in the period from January 2009 to November 2011. It was conducted on 45 patients divided into two groups. The study was carried out in a group of 39 patients (21 males, 18 females; age range 25- 38 years) with VMR and 6 control patients (4 males, 2 females; age range 22- 34 years). Study Group The patients were affected by typical symptoms of VMR, consisting of nasal obstruction and profuse watery rhinorrhoea. Based on the personal history of the patients, these symptoms had been present for a period of at least 2 years (range 2-6 years). At anterior rhinoscopy, the turbinate were hypertrophied causing significant obstruction of the nasal cavities .Control Group Six patients who were doing other ENT operations with no nasal complaints nor diseases. Methodology: Electron microscopy was done for them. Specimens were fixed in cacodylate buffered formaldehyde glutraraldehyde-R. Post fixed in buffered 1%osomium tetraoxide, dehydrated and embedded in spurris resin. Ultrathin section were double stained by 10 % Reynolds lead citrate. Examination was done by TEM (philipo400). **Results**: The electron microscopic sections of patients with VMR showed loss of intercellular junction with separated cells, cilia are shorter, sparce and deformed, apoptic cells in the epithelial layer, the epithelial cells are full of vesicles and goblet cells. Another type of secretory glands are also seen, loss of the smooth surface of endothelial cells and the basal lamina is thickened. **Conclusion**: The pathology of the vasomotor rhinitis starts first in the submucosal vessels with angiopathy similar to the diabetic angiopathy then the epithelial changes take place. Surgical or Medical treatment directed to the sympathetic system may or may not improve the case depending mainly on how much the submucosal blood vessels are affected.Presence of another type of secretory granules in the submucosal glands need more histochemical studies.
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Key words; VMR, electron microscopy & pathogenesis.

1. Introduction

VMR (nonallergic rhinitis) without eosinophilia sometimes termed idiopathic rhinitis. Symptoms are nasal obstruction, increased secretions, or both, however sneezing and pruritus being less common. This clinical presentation is likely caused by a heterogeneous group of disorders with a pathogenesis that is incompletely understood. ([1])

Vasomotor rhinitis can more specifically cause nasal symptoms that occur in response to environmental conditions, such as changes in temperature or relative humidity, odors (e.g., perfumes or cleaning materials), passive tobacco smoke, alcohol, sexual arousal, and emotional factors. Such hyper-reactivity to nonallergic triggers is not mediated by increased neural efferent traffic to the blood vessels supplying the nasal mucosa and can also occur in allergic rhinitis, when the term mixed rhinitis is applied . [(1)]

Patients with vasomotor rhinitis are include two subgroups: "runners," who demonstrate "wet" rhinorrhoea; and "dry" patients, who exhibit nasal obstruction and airflow resistance with minimal rhinorrhoea. [(2)]

Nonallergic rhinitis is a common disease that probably affects as many as 17 million Americans. Approximately 22 million people suffer a combination of nonallergic rhinitis and allergic diseases (mixed rhinitis). Both nonallergic and mixed rhinitis occur more frequently in adults than in children, commoner in females than in males, and are more likely to be perennial than seasonal. [(3)]

It is well known that allergic rhinitis is induced by the reaction of antigen and IgE antibody. On the other hand, vasomotor rhinitis is a nonallergic and non-infectious rhinitis, and its aetiology is believed to be an imbalance of autonomic nervous system. [4]

Because the subjective symptoms of these 2 types of rhinitis are similar, it is difficult to distinguish between them. However, because effective therapy is different for each, rapid and definite diagnosis is important. [5]

The pathophysiology of idiopathic rhinitis is unknown but the disease is classified as being non-allergic on the basis of negative serum IgE radioallergosorbent assay (RAST) and skin prick tests. In contrast, allergic rhinitis has inflammatory pathology mediated by IgE and mast cells, with more infiltration of plasma cells and IgE+ cells. It was observed that surgical procedure, which stops both the sympathetic and parasympathetic fibres from reaching the nasal respiratory mucosa, does not result in improvement of nasal congestion. This seems to contradict the hypothesis of increased parasympathetic activity playing a role in the genesis of the vascular disorders found in VMR. It-has been speculated that the mechanism of nasal congestion could consist of a decrease in the sympathetic influences, rather than over activity of the parasympathetic fibres. [5]

VMR is characterized by the presence of chronic symptoms for 9 or more months each year. It can be differentiated from allergic rhinitis (AR) by the relative later age of onset, frequent lack of atopic comorbidities as AR may be co-exist with allergic asthma and allergic conjunctivitis. [6] Nature of triggering factors, and type of symptoms. Precipitants include climate changes, and nonspecific olfactory irritants, such as perfumes and tobacco smoke. Nasal obstruction and rhinorrhoea are hallmark features of VMR and are more commonly seen than sneezing or itching. Patients with VMR were more likely than patients with AR to report headaches, nasal pressure, and posterior rhinorrhoea and less likely to be affected by sneezing, nasal pruritis, and conjunctival symptoms. [6]

Aim of the work

As treatment of VMR either surgical or medical is not satisfactory till now in improving symptoms or in duration of relief, pathophysiology of VMR had to be revised to see if there is another cause for this disease.

2.Material and methods

It was a prospective randomised study which was held at Benha Medical School a tertiary teaching hospital, in the period from January 2009 to November 2011. It was conducted on 45 patients divided into two groups. The study was carried out in a group of 39 patients (21 males, 18 females; age range 25- 38 years) with VMR and 6 control patients (4 males, 2 females; age range 22- 34 years).

Study Group

The patients were affected by typical symptoms of VMR, consisting of nasal obstruction and profuse watery rhinorrhoea. Based on the personal history of the patients, these symptoms had been present for a period of at least 2 years (range 2-6 years).At anterior rhinoscopy, the inferior turbinate were hypertrophied causing significant obstruction of the nasal cavities. IgE assessed for each patient with exclusion of patients with increased IgE from the study.

Control Group

Six patients who were doing other ENT operations with no nasal complaints nor nasal diseases.

Methodology

1-The ethics committee of Benha Medical School approved the study and informed consents were signed by all patients. The specimens were taken from the inferior turbinates.

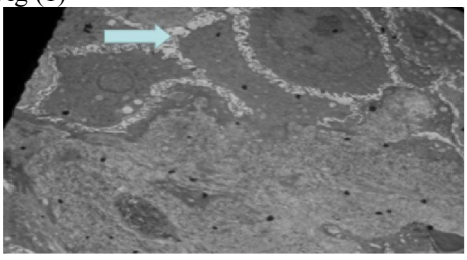
2- Electron microscopy was done for them. Specimens were fixed in cacodylate buffered formaldehyde glutraraldehyde-R. Post fixed in buffered 1%osomium tetraoxide, dehydrated and embedded in spurris resin.

Ultrathin section were double stained by 10 % Reynolds lead citrate. Examination was done by TEM (philipo4001)

3.Results

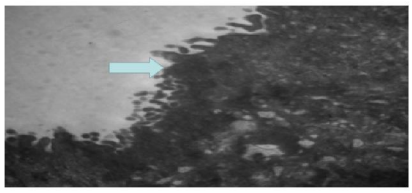
These electron microscopic sections highlight the main points for demonstrating our work

Fig (1)



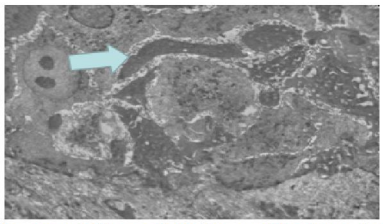
Lost of intercellular junction with separated cells

Fig (2)



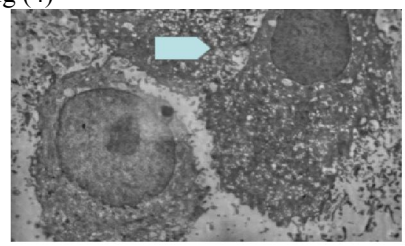
Cilia are shorter, sparse and deformed

Fig (3)



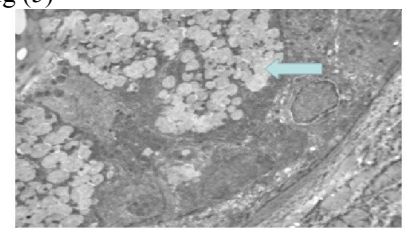
With apoptotic cell in the epithelium layer

Fig (4)



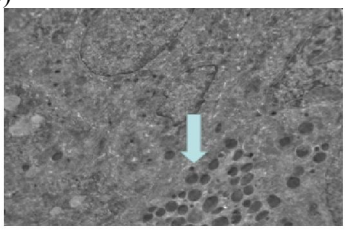
- The epithelium cells are full of vesicles

Fig (5)



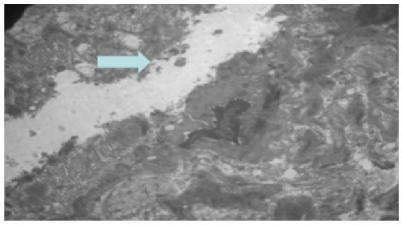
- Goblet cells are full of abundant vesicles some are mucous glands other are serous glands

Fig (6)



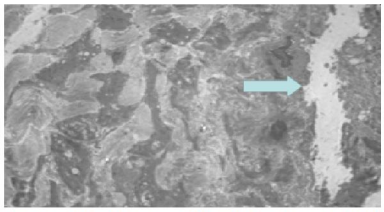
- Another third type of secretory glands is also seen

Fig (7)



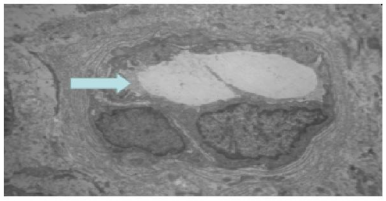
- Los of the smooth surface and cytoplasmic degeneration of endothelial cells

Fig (8)



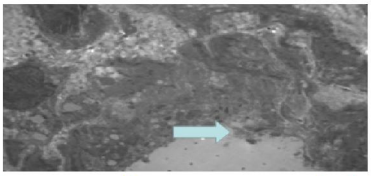
- Due to repeated injury of the blood vessels the basal lamina become multilayer instead of thin layer

Fig (9)



- the basal lamina is thickened and lysozymes in the endothelial cells

Fig (10)



Degeneration represented by dilated endoplasmic reticuluilar pirinucliolar hallows

4. Discussion

Reduction in epithelial thickness and disappearance of cilia were found. The ultrastructural study confirmed the findings obtained by light microscopy. Indeed, complete ciliary loss, absence of intercellular junctions and marked distension of the intercellular spaces were observed in the damaged epithelium. Goblet cells and epithelial cells were recognizable and full of vesicles.

Why the response of vasomotor rhinitis to medical treatment vary a lot from one patient to another and in the same patient in different occasions. The postganglionic fibres form the deep petrosal

nerve, which joins the greater superficial petrosal nerve to form the vidian nerve. Notably, the vidian nerve includes both parasympathetic and sympathetic fibres, although the relative composition might vary widely based on species and even based on individuals. [7]

Endoscopic vidian neurectomy, which interrupts both sympathetic and parasympathetic fibres bound to nasal respiratory mucosa, was effective in dealing with the rhinorrhoea associated with vasomotor rhinitis but resulted in little improvement of the nasal congestion [8].

It was observed that this surgical procedure, which stops both the sympathetic and parasympathetic fibres from reaching the nasal respiratory mucosa, does not result in improvement of nasal congestion. This seems to contradict the hypothesis of increased parasympathetic activity playing a role in the genesis of the vascular disorders found in VMR. It-has been speculated that the mechanism of nasal congestion could consist of a decrease in the sympathetic influences, rather than over activity of the parasympathetic fibres. [9]

So we assume there is another mechanism that causes the pathogenesis of this disease.

Reviewing our results with others we found that some of the authors had assumed a number of mechanisms for the vasomotor rhinitis pathogenesis.

In an earlier study, Braat *et al.,* [4] did not find differences between subjects with nonallergic rhinitis and control subjects in terms of vascular or secretory nasal responsiveness to histamine; however, these investigators identified that nasal provocation with cold dry air could clearly distinguish the 2 groups. The mechanism through which cold air causes nasal reactions is complex.

Sanico *et al.,* [10] found Nerve Growth Factor (NGF)highly expressed in the glandular and respiratory epithelium; in addition to some inflammatory cells, primarily eosinophils, express and release this neurotrophin. Nasal secretions contain NGF, more so in individuals with allergic rhinitis compared with healthy control subjects, and allergen challenge of subjects with allergic rhinitis leads to acute release of NGF in nasal fluids.

Therefore, a link between allergic rhinitis and NGF clearly exists, and the hypothec that NGF might be responsible for sensorineural Hyperresponsiveness, at least in allergic rhinitis, has drawn some support. [11]

Cold air causes nasal reactions through complex mechanisms. [4]The severe damage to the nasal respiratory epithelium that occurs in VMR probably allows airway irritants and other environmental agents to easily affect the subepithelial structures, causing increased reactivity of the afferent trigeminal fibres and recruitment of visceral reflexes.

The results of this research and previous evidence indicate that different pathophysiological mechanisms probably occur in VMR. The cytotoxic and cytostatic effects of excessive NO production and the oxidative stress following peroxynitrite formation probably play a significant role in the epithelial disruption. The expression of iNOS in the smooth muscle cells of the cavernous sinuses is not accompanied by peroxynitrite formation. This probably favours the nasal congestion found in VMR. [12]

Finally, accumulation of secretions in the nose may not exclusively be due to hypersecretion; a reduced mucociliary clearance rate will also result in accumulation of secretions in the nose. Viscous secretions, drained as postnasal drip', is usually produced in the paranasal sinuses, which have many goblet cells (pure mucous secretion) and very few glands (seromucinous secretions). [13]

In our study we concentrated on the submucosal structures as a possible aetiology for vasomotor rhinitis.

We found that whatever the neurological cause either sympathetic inhibition or parasympathetic predominance or imbalance between them the end organelles effect is on the blood vessels and epithelial and submucosal glands.

Hyperscretions from both goblet cells and submucosal glands that contains serous and mucous secretory glands in additional to other third type of secretory glands found in 60%of our study group patients.

The submucosal blood vessels are dilated with loss of the smooth surface and cytoplasmic degeneration of endothelial cells.

Due to repeated injury of the blood vessels the basal lamina becomes multilayer instead of thin layer a change similar to diabetic angiopathy.

The basal lamina is still thickened and lysozymes in the endothelial cells.

Degeneration represented by dilated endoplasmic reticuluilar perinucliolar hallows.

Conclusion

We concluded that

1-reviewing the facts in our study we found that the pathology of the vasomotor rhinitis starts first in the submucosal vessels with angiopathy similar to the diabetic angiopathy then the epithelial changes take place. Surgical or Medical treatment directed to the sympathetic system may or may not improve the case. This depends mainly on how much the submucosal blood vessels are affected.

2-Presence of another type of secretory glands in the submucosal glands need more histochemical studies to know its nature.

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