

N.V. Babchenko, O.M. Grabovyi, Y.V. Diieva, S.E. Konovalov
O.O. Bogomolets National Medical University, Kyiv

HISTOLOGICAL PECULIARITIES OF NASAL CAVITY MUCOSA IN PATIENTS WITH DEVIATED NASAL SEPTUM AND POSTNASAL DRIP SYNDROME

e-mail: nazonex27@gmail.com

Nasal congestion is one of the most common complaints in otolaryngology. It is mostly caused by deviated nasal septum. Anatomic changes in the deviated nasal septum significantly deteriorate the function of the upper airways. The study group includes 45 patients with the deviated nasal septum, and with complaints about difficult nose breathing and feeling of postnasal drip. A control group of 29 people with deviated nasal septum, without postnasal drip. The studies revealed that the nasal mucosa of people in control group has standard anatomy characteristics, with slight variations. The respiratory epithelium with ciliary, goblet and intercalated cells in thin basal membrane was clearly distinguished. The lamina propria contained terminal mucosal glands parts and blood lacunae. The study results evidence that deviation of the nasal septum leads to specific histopathological changes in the nasal mucosa. These changes are significantly different on both sides of the nasal septum.

Key words: histology, postnasal drip syndrome, nasal septum deviation, nasal cavity, nasal mucus, mucociliary transport.

Н.В. Бабченко, О.М. Грабовий, Ю.В. Дієва, С.Е. Коновалов

ГІСТОЛОГІЧНІ ОСОБЛИВОСТІ СЛИЗОВОЇ ОБОЛОНКИ НОСОВОЇ ПОРОЖНИНИ У ПАЦІЄНТІВ З ВИКРИВЛЕННЯМ НОСОВОЇ ПЕРЕДІЛКИ ТА СИНДРОМОМ ПОСТНАЗАЛЬНОГО СТИКАННЯ

Закладеність носа є однією з найпоширеніших скарг, з якою стикається оториноларинголог. Однією з патологій, що спричинює виникнення даного стану є викривлення носової перегородки. При цьому стані відбувається компенсаторна перебудова всіх структур порожнини носа. Група дослідження включала 45 пацієнтів у віці від 18 до 55 років з діагнозом: викривлення носової перегородки, та відчуттям постназального стікання. До групи контролю увійшли 29 осіб що не мали скарг на порушення носового дихання. При проведенні досліджень ми спостерігалися атрофічні зміни респіраторного епітелію від незначного до виразного ступеня зі втратою специфічного клітинного складу епітелію. В окремих випадках спостерігалася виразна інфільтрація, ці ділянки виглядали як ерозивні дефекти, що загоїлися. Про це свідчила наявність тонкостінних кровоносних судин, підвищений вміст фібробластичних і лімфоїдних елементів. Власна пластинка містила мало кінцевих відділів залоз та кровоносних лагун. Наші результати свідчать про те, що викривлення носової перегородки призводить до специфічних гістопатологічних змін слизової. Ці зміни кардинально відрізняються по обидві сторони носової перегородки.

Ключові слова: гістологія, викривлення носової перегородки, постназальний синдром, носова порожнина, назальний секрет, мукоциліарний транспорт.

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Nasal congestion is one of the most common complaints in otolaryngology. It is mostly caused by deviated nasal septum [11]. According to various authors, anatomic changes in the deviated nasal septum significantly deteriorate the function of the upper airways, leading to snoring, vasomotor rhinitis, sinusitis, and postnasal drip syndrome.

The definition of postnasal drip syndrome (PNS) has been widely discussed by scientists. J. Frank described it as a common condition in the UK in the 19th century, defining it as a "pharyngeal type of chronic catarrh". The first to give the PNS a thorough analysis was Dobell in 1866, who defined it as a "postnasal catarrh", using the term which was previously used in reviews. The PNS most often characterizes a nosological condition that is associated with other disorders, like a pathological process in the nasal cavity, nasal sinuses, nasopharynx, where semifluid excretions flow down from the nasal cavity to the lower airways [1, 2].

Usually, the area of the nasal cavity is about 150 cm², and its volume – is about 15 ml. The specific anatomy of the nasal mucosa provides humidification, temperature regulation, and filtration of the inspired air, including filtration of the dust particles [5].

In a deviated septum all nasal structures undergo compensatory changes. These changes lead to such complaints as difficult nasal breathing, rhinorrhea, headache, nasal discomfort, mucosal dryness, nasal crusts, dry cough, and feeling of pharyngeal postnasal drip. The airflow dynamics directly depends on the degree, localization, and type of nasal septum deviation. According to Okuda M., Kanda T., due to changes in physiological dynamics of the airflow, compensatory nasal mucosa hypertrophy appears on the

incurvation side; also accompanied by abnormal anatomic changes of osteo-meatal complex and disordered mucus-ciliary clearance. Jang et al. studied increased inflammatory filtration and decreased gland acini in the mucosa on incurvation mucosa within the lower concha, compared with the control. They also dealt with the squamous metaplasia of the respiratory epithelium. According to Lakshit Kumar, lymphocyte filtration rate and squamous mucosal metaplasia on incurvation nasal septum were higher than on the convex one [8].

R.G. Mariappan in his study confirmed that patients with the deviated nasal septum, except for histological changes of the mucosa, have mucus-ciliary clearance changes [9].

The purpose of the study was to investigate nasal mucus histology in patients with deviated nasal septum and postnasal drip syndrome.

Materials and methods. The study was approved by the bioethical committee of the O. Bogomolets National Medical University, and it was held on the university clinical premises. A previous written consent from all patients was obtained.

The study group includes 45 patients (27 females and 18 males), aged 18-55 years old, diagnosed with the deviated nasal septum. The diagnosis was confirmed by endoscopy and CT, and the patients were admitted with complaints about difficult nose breathing and feeling of postnasal drip (Fig.1).

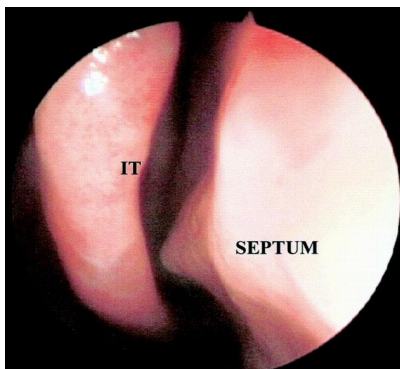


Fig.1. Patient with deviated septum in the middle, thorn-like deviation



Fig.2. Patient with deviated septum, opposite from the deviation side

A control group of 29 people included patients, diagnosed with deviated nasal septum, which was confirmed by endoscopy, without complaints about difficult nose breathing (Fig.2). The mucosa samples were obtained during surgeries of adjacent organs, which were performed via endoscopy (orbit injuries, orbit decompression, rhino-dacryocystostomy).

The histological study during septoplasty used samples of the lower nasal mucosa in the most deviated nasal part and those from the opposite side, sized ≤ 0.05 cm². The samples were treated in the 4% buffer formaldehyde (24 hours, 40C), after which they were embedded in paraplast [3]. The histological samples, 4 mm in width, were stained with hematoxylin and eosin, alcian blue under the pH 2.5, followed by the PAS- reaction.

The assessment of the mucosa was grounded on:

1. The semi-quantitative reaction of hyperplastic / atrophic changes of respiratory epithelium: where 0 – epithelium of relatively healthy people, 1 – affected homogenous property of an epithelial structure [4].

2. Semi-quantitative assessment of general respiratory epithelium infiltration, ratio: Lymphocytes /100 epitheliocytes in 5 positions of each sample.

3. Thickening of the respiratory epithelium basal membrane: presence/absence of characteristic (+/-).

4. Semi-quantitative assessment of general infiltration of the mucosal lamina propria: 0 – insignificant number of lymphocytes in relatively healthy people [4], 1 – twofold increase in the specific density of the inflammatory infiltration cells, 2 – increase in the specific density of the inflammatory infiltration cells by 2 – 5 times, 3 – increase in the specific density of the inflammatory infiltration cells by over 5 times.

5. Semi-quantitative assessment of mucosal swelling degree: 0 – absent swelling, 1 – slight swelling, 2 – moderate swelling, 3 – expressed swelling.

6. Semi-quantitative assessment of the mucosal lamina propria changes: 0 – absent bundles of collagen fiber, 1 – collagen fiber bundles in the mucosal lamina propria, 2 – dense bundles of collagen fibers, which occupy up to half of the mucosal incision, 3 – dense collagen fiber bundles occupying more than half of the cut mucosa area.

7. Area of terminal secretory mucosal gland parts in 1mm of its cut length (mm²/mm) (on digital images (x200, 12214x920 pixels), using software Imag J (Wayne Rasband (NIH), USA).

8. Area of mucosal blood lacunae in 1 mm of its cut length (mm²/mm) (see point 7).

9. Semi-quantitative assessment of glucosamine content in the goblet cells of respiratory epithelium: 0 – absent glucosamine, 1 – insignificant content, 2 – expressed content (appropriate to that in relatively healthy people), 3 – extensive content.

10. Semi-quantitative assessment of PAS+ in respiratory epithelium goblet cells: 0 – absent, 1 – insignificant content, 2 – expressed content (appropriate to that in relatively healthy people), 3 – extensive content.

11. Semi-quantitative content of the glucosamine on the mucosal secretory glandular cells: 0 – absent, 1 – insignificant content, 2 – expressed content (appropriate to that in relatively healthy people), 3 – extensive content.

12. Semi-quantitative assessment of PAS+ in the mucosal secretory glandular cells: 0 – absent, 1 – insignificant content, 2 – expressed content (appropriate to that in relatively healthy people), 3 – extensive content.

13. The obtained data were analyzed statistically, regarding the mean average, standard deviation, and standard error and mean error. Student T-test was used to assess the mean figure reliability, with a statistical significance threshold $p < 0.05$.

Results of the study and their discussion. The studies revealed that the nasal mucosa of people in control group has standard anatomy characteristics (Fig. 2A, Table 1), with slight variations. The respiratory epithelium with ciliary, goblet and intercalated calls in thin basal membrane was clearly distinguished (Fig. 2B). The epithelium contained single

lymphocytes and, sometimes observed, slight lymphocyte-plasmocytic infiltration. The mucosal lamina propria was formed by rough connective tissue with small content of fibroblasts, lymphocytes, and plasmocytes. It also contained macrophages and eosinophils. The lamina propria contained terminal mucosal glands parts and blood lacunae. The respiratory epithelium goblet cells and secretory gland parts included small content of glucosamines and proteoglycans Fig. 2C, 2D).

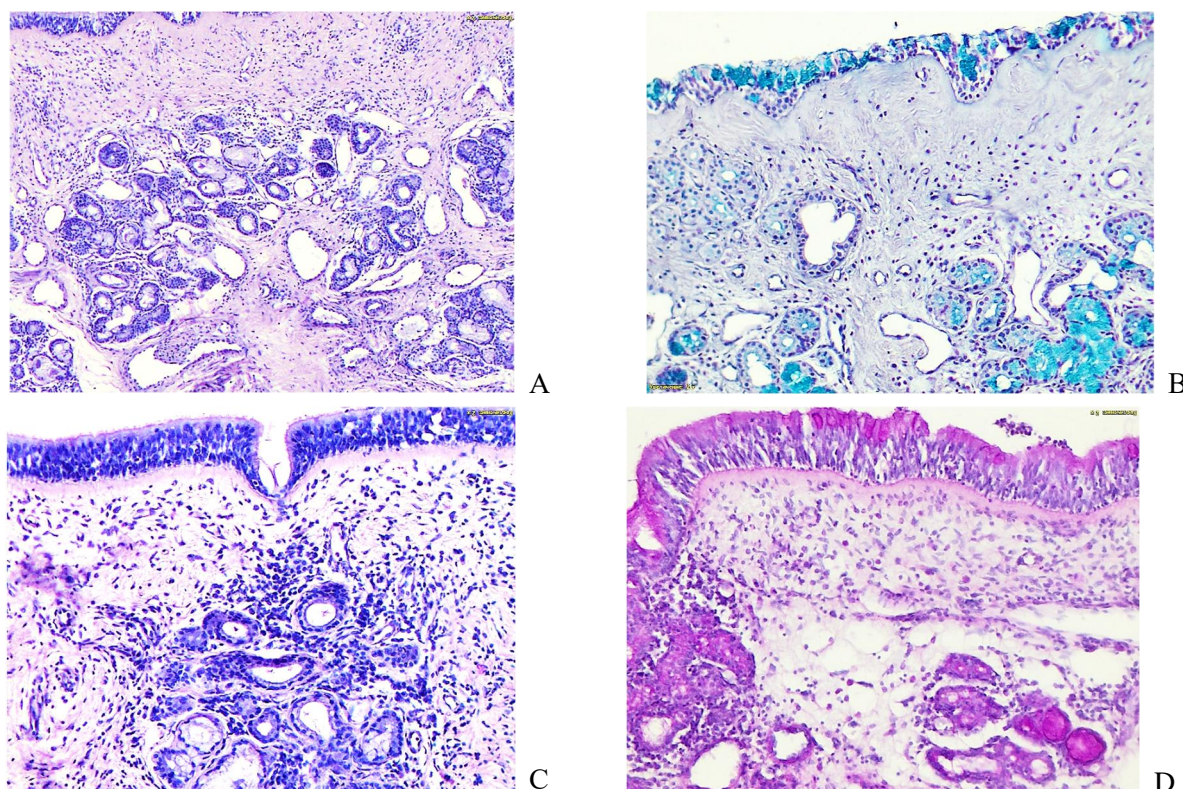


Fig. 2. Microscopic structure of the lower nasal concha cavity mucosa of a relatively healthy person. Microimage: A) Stained with hematoxylin and eosin, x100 B) Stained with hematoxylin and eosin, x200. C) Stained with alcian blue and hematoxylin, x200. D) Pas reaction, hematoxylin, x200.

The patients with deviated nasal septum develop several changes in the mucosa on the side of deviation: thickening of respiratory epithelium and its disorganization (Fig. 3A). In expressed fibrosis of the mucosal lamina propria its thickness changes, and the tissue resembles unilayer cubic epithelium where the cell types are not distinguished. In most cases, general infiltration of the mucosal lamina propria is observed, and it often spreads to the respiratory epithelium, which is accompanied by epithelial consolidation. If the last one is thickened, without expressed inflammatory infiltration, goblet cell content

risers, as well as the glucosamine and proteoglycan content. If it is infiltrated with lymphocytes, the content of the recalled substances drops.

Table 1

Characteristics of histological changes

Value	Control	In the concave nasal septum side	In the curved nasal septum side
Hyperplastic/atrophic respiratory epithelium changes (units)	0.103±0.057/ 0.207±0.085	1.667/0.111	0.133/1.911
Relation: lymphocytes.100 epitheliocytes in respiratory epithelium	9.276±0.387	18.1±0.472	10.83±0.342
Respiratory epithelium basal membrane thickening (% cases)	3.448	88.89	4.444
Semi-quantitative assessment of the mucosa lamina propria inflammatory infiltration	0.414±0.115	1.828±0.13	0.897±0.099
Mucosal swelling degree (units)	0.103±0.057	0.586±0.133	0.103±0.06
The mucosa lamina propria fibrous changes degree (units)	0.069±0.047	1.172±0.147	0.897±0.099
Area of terminal secretory areas of mucosal glands (mm ² /mm)	0.119±0.007	0.171±0.009	0.051±0.006
Area of blood lacunae of the mucosa (mm ² /mm)	0.064±0.004	0.153±0.012	0.028±0.002
Glucosamine content in the respiratory epithelium goblet cells (units)	1.966±0.077	2.448±0.115	0.621±0.091
PAS+ content in the respiratory epithelium goblet cells (units)	2.034±0.077	2.655±0.09	0.724±0.095
Glucosamine content in the mucosa gland secretory cells (units)	2.069±0.068	2.586±0.107	0.897±0.106
PAS+ content in the mucosa gland secretory cells (units)	1.966±0.077	2.655±0.09	1.103±0.091

In some cases, the described areas of the mucosa are characterized by expressed swelling. The number of the mucosal glands, under such conditions, totally increases, but with the fibrous changes it, and vice versa, falls. All this is also characterized by preglanular sclerosis. The same refers to glucosamine and PAS-positive substance content in the gland secretory cells.

The mucosal lamina propria of such patients usually has more fibroblasts than that one of healthy people. Quite often, rough collagen fiber bundles are observed, and these bundles may represent small, or sometimes, huge fibrosis foci. Usually, the blood sinuses area increases, and in some cases – drastically increases. Quite often, their walls undergo metamorphoses (Fig. 3B). Sometimes, thrombosis or fibrinous mass may be observed in the lumen.

Two patients had smooth cell respiratory epithelium metaplasia on the septum deviation side (Fig. 3C), and the other two patients had polyps in their mucosa (Fig. 3D). On the side, opposite to the septal deviation, most often, atrophic changes of respiratory epithelium were observed, ranging from insignificant to expressed ones, with the specific epithelial cellular content loss. Its inflammatory infiltration was not observed often, being slightly expressed.

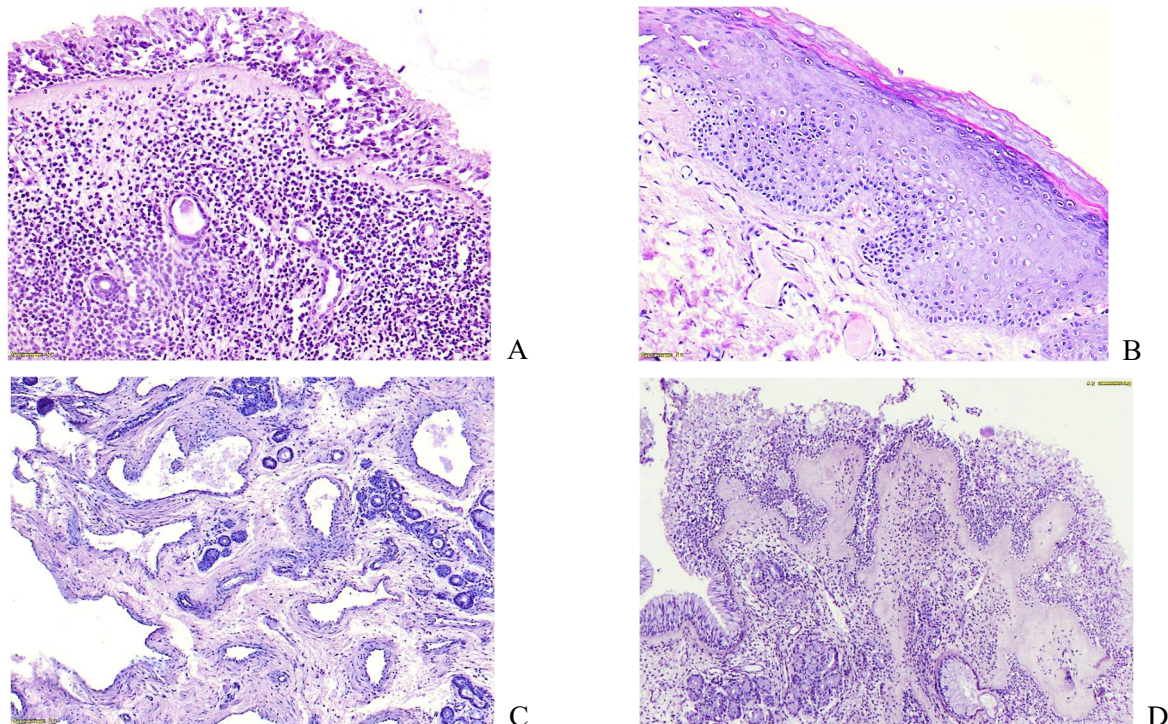


Fig.3. Microscopic structure of the lower nasal concha cavity mucosa on the deviation side. Stained with hematoxylin and eosin, microimage, x100.

The mucosal lamina propria was slightly infiltrated. In several cases, expressed infiltration was observed, the areas resembling erosive defects after healing. This was confirmed by thin-walled blood vessel presence, as well as increased content of fibroblastic and lymphoid elements (Fig. 4A).

The lamina propria contained a few terminal glandular departments and blood lacunae. In both cases, the mucosal lamina propria rough fibrous tissue transformation into the fatty tissue was observed (Fig. 4C).

Atrophic changes of the mucosa were accompanied by a decrease or disappearance of the glucosamines in the respiratory epithelium (Fig. 4D), and an increase of such substances in the gland secretory cells (Fig. 4E). The same refers to the PAS+ substances content changes (Fig. 4F).

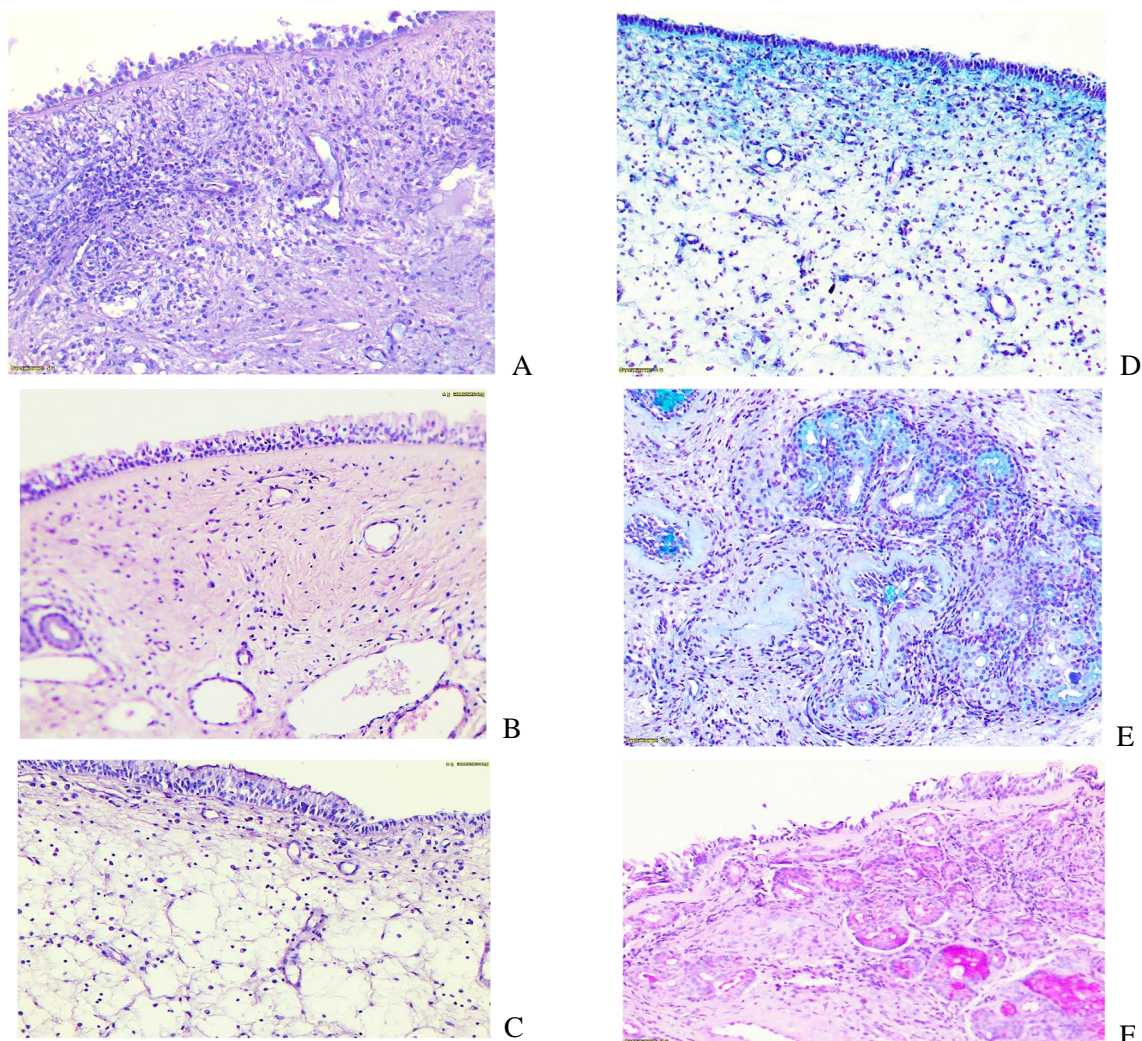


Fig. 4. Microscopic structure of the lower nasal concha cavity mucosa on the deviation side. A) Stained with hematoxylin and eosin ,x100. B) Stained with hematoxylin and eosin,x200. C) Stained with hematoxylin and eosin,x200. D) Stained with alcian blue and hematoxylin, x200. E) Stained with alcian blue and hematoxylin. X100. F) PAS reaction, hematoxylin,x100.

So, the conducted studies of the lower nasal concha cavity mucosa in patients with the deviated nasal septum and the postnasal drip syndrome showed its expressed changes, which were opposite on deviated and opposite side.

Generally, on the deviated (curved) side, these changes appear to be hyperplastic, with some peculiarities, which are not characteristic of hyperplasticity. This may be connected with changes in airflow due to distortion of normal architectonics of the nasal cavity, as well as that of mucociliary clearance, where it is increased.

As a consequence, compensatory thickening of epithelium and intensified production of the mucosa by goblet cells and mucosal cells are observed. Nonetheless, such compensatory reactions may be insufficient, or they may terminate with time, which will lead to mucosal lesions, which will result in mucosa inflammatory infiltration [10]. All this necessitates considering cellular cells of inflammatory infiltrate and lymphocyte content, including regulatory lymphocytes [14, 15]. Respectively, various types of the last ones may lead to opposite changes in the mucosa [3]. So, we could suppose, that the individual peculiarity of the patient's immune system may significantly affect changes in the mucosa.

In other cases, inflammatory infiltration may become a secondary alternative factor [7], which will lead to fibrous changes of the mucosa lamina propria and gland atrophy [2]. At the same time, a phenomenon of expressed hyperplasia of the blood sinuses and their wall fibrosis may be observed. This is probably related to individual reactive properties of the body, and, first of all, short-distance regulatory effects of the immunocompetent cells [6], as well as activation of other molecular pathogenetic fibrosis mechanisms [13].

Extreme manifestations of the mucosa chronic injury may be metaplasia of respiratory epithelium into multilayer smooth one [8], or development of mucosal polyps [10].

The changes of mucosa on the opposite nasal side, on the convex nasal cavity side may be characterized as atrophic-degenerative. Regarding the histological picture, it may be connected with poor blood supply, which is confirmed by a decreased number of blood microvessels [12]. This may cause atrophic changes in superficial epithelium and glands, as well as a decrease in their secretory function. Besides, poor blood supply may lead to mucosal erosions with their following healing, which was observed in the study. Under these conditions, a fatty transformation of the mucosa lamina propria connective tissue is not impossible. Although, preserved blood lacunae of the mucosa without changes in their walls, go contrary to such theory.

Conclusion

Deviation of the nasal septum is a cause of multiple morphological changes of the nasal cavity lateral walls mucosa, which with time may lead to disordered nasal respiration and result in new complications. The study results evidence that deviation of the nasal septum leads to specific histopathological changes in the nasal mucosa. These changes are significantly different on both sides of the nasal septum, though they are more expressed on the deviated (curved) side than on the convex. Deviation of the nasal septum predisposes to changes in the histological structure of the nasal cavity, hypertrophic changes in the curved side and atrophic in the convex, and, as a result, chronic inflammation and disbalance in mucociliary clearance, which, in its turn, may serve mechanisms of the postnasal drip syndrome.

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