RESEARCH ARTICLE

Structural Changes in the Nasal Mucosa in the Hypertensive Patients Suffering from Recurrent Epistaxes

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ABSTRACT

Introduction: Epistaxis is a common symptom in hypertensive patients. However, the relationship between hypertension and epistaxis is controversial and poorly understood.

Objective: The present work was to study the histopathological changes underlying recurrent nasal bleedings in the patients with arterial hypertension (AH).

Materials and methods: We have undertaken a prospective study based on the university clinic of Rostov-on-Don. Twenty-two hypertensive patients aged between 51 and 63 with recurrent epistaxis underwent surgical interventions due to severely deviated nasal septum hampering the search for the source of bleeding. Simultaneously nasal mucosae biopsies were taken in the bleeding point area. Tissue specimens were subjected to histological and ultrastructural investigations.

Results: Histological and ultrastructural investigations of the biopsy samples revealed erythrocytic, hyaline, and fibrin thrombi in the vessels of the microcirculatory system, deendothelization, and destruction of the basement membrane alongside vascular subendothelium exposure. The above-mentioned changes in the nasal cavity mucosa lead to necrosis foci, which are the bleeding points.

Conclusion: The cause of the nasal bleeding associated with AH is not a mechanical rupture of blood vessels but thrombosis and necrosis in the nasal mucosa.

Clinical significance: Drug hemostatic treatment of hypertensive patients suffering from recurrent epistaxes is counterindicative due to possible serious thromboembolic complications (myocardial infarction, apoplexy, etc.). In case of a severely deviated septum hampering the search for the bleeding vessel, the treatment guidelines should include septoplasty.

Keywords: Arterial hypertension, Epistaxis, Microcirculatory disturbance, Nasal mucosa, Prospective study.


INTRODUCTION

Epistaxis is among the most common reasons why patients resort to primary health centers.¹

Arterial hypertension (AH) is often complicated with epistaxis. However, the pathogenesis of AH epistaxis is unclear.²,³ Knopfholz et al.⁵ evaluated the incidence of epistaxis in hypertensive patients according to the stages of hypertension and compared blood pressure data in these episodes to the routine data. They concluded that the epistaxis incidence in hypertensive patients is not associated with hypertension severity.

Epistaxis occurrence rate does not correlate with the hypertrophy stage of the left ventricle that reflects the hypertension severity.⁶ Many authors have questioned the pathogenic association between epistaxis and AH.⁶,⁷ Thus, Viehweg et al.⁸ concluded that AH may only prolong the already existent epistaxis without being its immediate cause.

The objective of the present study was to detect the pathomorphological changes in the nasal mucosa vessels in the patients suffering from AH, and these changes are the risk factors for recurrent epistaxes.

MATERIALS AND METHODS

This was a prospective study carried out over a period of 3 years from January 2016 till December 2018, involving 22 male and female patients aged between 51 years and 63 years admitted in the university clinic of Rostov-on-Don due to recurrent epistaxis.

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Inclusion Criteria

Previous diagnosis, i.e., AH, second stage, precedent examination by the otorhinolaryngologist, excluding vascular malformations in the nasal cavity, admission within 12 hours since the start of hemorrhage, severely deviated nasal septum narrowing the bleeding nasal half.

Exclusion Criteria

Intake of anticoagulants 4 weeks prior to visiting the hospital, posterior nasal bleeding, allergic or vasomotor rhinitis, acute infectious diseases, blood disorders, and serious somatic diseases at the decompensation stage.

All the cases were evaluated for brief history, physical examination, diagnostic nasal endoscopy, hematological, and biochemical profile.

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During admission, all the patients showed high arterial pressure: systolic up to 164 ± 17 mm Hg and diastolic up to 102 ± 16 mm Hg, which exceeded their typical indices. The laboratory examination of all the patients demonstrated some signs of hypercoagulation (hyperfibrinogenemia, enhanced level of soluble monomeric fibrin complexes in the blood, and normal platelet levels, prothrombin, and thrombin time).

Nasal cavity endoscopy revealed a severely deviated nasal septum expressed as a quadrangular cartilage dislocation toward the bleeding side and large bone ridges on the same side, which prevented detection of the bleeding vessel in spite of nasal cavity anesthesia and using an aspirator.

Epistaxis was initially stopped by a conventional anterior nasal packing and then the patients underwent antihypertensive therapy. After the packing was removed, epistaxis recurred in all the patients for two or three times in spite of the fact that arterial pressure went down to the value typical for the patient or even went lower. Due to recurrent epistaxes, all patients underwent septoplasty, with the aim of creating access to the bleeding vessel and coagulation of the same. Surgery was done under general anesthesia. The bleeding vessel was located in the septum middle areas behind the deviated part (14 patients), in the septum frontal lower areas (6 patients), and in the nasal cavity bottom area (2 patients). All the bleeding points were coagulated with bipolar electrocoagulation. During the surgery, mucosa biopsy samples were taken near the bleeding point, making the size of the samples 1–1.5 mm, and then the samples were histologically and ultrastructurally examined. The patients were informed on the nature, aims, and volume of the surgical intervention and obtained their agreement in writing. The control set for the pathomorphological study was postmortem nasal mucosa biopsy samples of 10 patients who, while alive, had suffered from AH, second stage.

For histological examination, 4-μm sections of formalin-fixed, paraffin-embedded tissues were stained with hematoxylin–eosin, based on Van Guison and Mallory methods.

To perform electron microscopy, the samples were drained in a drop of fixer (2.5% glutaric dialdehyde solution), additionally fixed in 0.1 M phosphate buffer (pH 7.4) for 1 hour at a temperature of 4°C, and then fixed in 1% osmium tetroxide solution in the same buffer for 1 hour at a temperature of 4°C. After its dewatering in the growing concentration spirits, the material was placed in EPON 812. The sections obtained in the ultramicrotome LKB Bromma 8800 (Sweden) were contrasted with uranyl acetate and plumbum citrate and inspected in the electron microscope JEM-100B manufactured by JEOL (Japan).

**Results**

The histological inspection of biopsy sample showed that the mucosal epithelium was preserved in the majority of those suffering from epistaxis; yet in six cases, there were microerosions, and four cases revealed necrotic areas on the nasal mucosa. These data characterize patchiness of the affected mucosa because in epistaxis mucosa is defected in 100% of cases, while biopsy samples may not show any defects.

Erosions and necrosis were caused by expressed microcirculatory disturbance in the nasal mucosa vessels. The subepithelial plexus vessels revealed erythrocyte aggregation and plasma separation, sludged blood, various thrombi, often hyaline, rarely erythrocytic, or fibrin in the form of a thin net, partly lysed as a result of fibrinolysis (Fig. 1). Occasionally subepithelial plexus vessel thrombosis resulted in mucosa necrosis (Fig. 2A).

The lamina propria vessels also showed dystrophic changes in endothelium, its focal desquamation with exposure of basement membrane and adhesion of erythrocytes at these points, thrombocytes or fibrin thin net with positive staining ac. to Mallory. Isolated fibrin or mixed thrombi were also seen here (Figs 2B to D). Larger arterial vessels showed plasmorrhagia and vessel wall hyalinosis, while some arteries demonstrated middle coat hypertrophia with a moderate reduction in its lumen, and such changes are peculiar to AH.

Histological examination of the lamina propria arteries in the control set revealed plasmorrhagia, vessel wall hyalinosis, and tunica media hypertrophy, which are typical of those with AH. The mucosa did not show any signs of thrombosis or necrosis.

Electron microscopy revealed changes in the nasal mucosa capillary endothelium. There were destructed tight junctions combining the lateral areas of the neighboring endotheliocytes or their cytoplasmic apophyses, which leads to fragmented solid endothelial layer and exfoliated endotheliocytes, resulting in the formation of large breaches enabling emission of plasma and formed elements outside the bloodstream.

Endotheliocyte desquamation is often coupled with massive deendothelialization and basement membrane deterioration alongside subendothelium exposure (Fig. 3), which provokes inclusion of proaggregant factors (fibronectin, I, III, IV, and V collagens, Willebrand factor, etc.). The rheological impairments were expressed as rouleaux, sludge of erythrocytes, and fine fibrin fibers, which are especially demonstrative in the adjacent thrombi.

Nasal mucosa erosions and necrotic patches make a morphological substrate for epistaxis development. Multiplicity of such necrotic patches and erosions justifies difficulties in the search of bleeding point often faced by clinicians.

**Discussion**

The question of cause-and-effect links between epistaxis and AH is still unsolved. Most researchers analyze correlations between epistaxis and AH levels. However, the presence of high arterial blood pressure during the actual episode of nasal bleeding cannot establish a causative relationship with epistaxis because of confounding stress and possible white coat phenomenon.

Our study shows that epistaxis is not caused by a mechanical rupture of the vessel during high arterial pressure but caused by nasal mucosa vessel thrombosis and necrosis, which become sources of bleeding.

The factors predisposing nasal mucosa vessel thrombosis in those suffering from AH are the tendency to hypercoagulation in such patients, impaired neurohumoral regulation of the vascular tone in this group of patients, and damaged endothelium of the microcirculatory bloodstream vessels, which were shown by our ultrastructural investigation and noted by other authors.

In a normal condition, the endothelial cells provide thromboresistance when in contact with circulating blood. Damaged endothelium loses its athrombogenic properties. What is more; the vascular endothelial apoptotic cells show high procoagulative activity as a result of increased phosphatidylserine expression and loss of membrane anticoagulant characteristics. Dys trophy and desquamation of the vascular endothelium in the nasal mucosa revealed by ultrastructural studies trigger a cascade of biochemical changes leading to thrombi formation. Our data agree with the opinion of Lubianca Neto et al.
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stating that long-lasting AH raises the nose bleed risk mainly due to the vasopathic effect.

Hypercoagulation and erythrocytosis which are an integral part of AH pathogenesis form preconditions for nasal mucosa thromboses. For some period of time, the blood coagulation and anticoagulation systems in this group of patients are in a state of a delicate balance, which may be upset by some minimum stimulus (blood loss, medical manipulation, stress, physical activity,
admission of some medications). If, in addition to this one or several local “permitting” factors (impaired endothelium, dilatation of pathologically changed vessels, slow flow or microcirculatory way stasis, disclosure of arteriovenous shunts, blood viscosity increase) may lead to the development of vascular thrombosis with vessel wall necrosis and nasal bleeding.

Our study had definite limitations since it involved only those patients who were recommended for operative treatment; however, our data obtained through up-to-date pathomorphological methods quite persuasively characterize the morphological substrate of epistaxis in hypertensive patients.

Another important item that has to be taken into account while treating epistaxis patients is the necessity to follow the treatment guidelines not only in terms of the bleeding cause but also with regard to the patients’ personality traits.16 Severe nasal septum deviation hampering the investigation of the nasal cavity is to be surgically removed to enable electric coagulation of the bleeding vessel or to perform full-value packing.

**Conclusion**

Although epistaxis in AH patients is usually observed during increase in blood pressure, the immediate cause of such bleedings is not due to the rupture of mechanical vessels but due to impaired vessel endothelium, disordered blood microcirculation, and coagulation leading to nasal mucosa thrombosis and necrosis.

**Clinical Significance**

In view of the obtained data on thrombi formation in the nasal cavity mucosa in AH patients, such patients with recurrent nose bleeds cannot be treated using traditional hemostatic drugs due to the risk of further stimulation of thrombosis. This group of patients is characterized by a relative lack of plasma blood-coagulating factors, which is conditioned by high cytosis (in other words, a lack of coagulating factors per a cell volume unit). This results in the formation of crumbly erythrocytic thrombi, which easily tear away while tampons are removed from the nasal cavity. In case of strong recurrent epistaxis, it is reasonable to prescribe transfusions of fresh frozen donor plasma and cryoprecipitate to correct the relative deficit of blood coagulating factors.

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**References**


