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Assessment of early atherosclerotic findings in patients with nasal polyposis

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ABSTRACT

Objective: To investigate early markers of atherosclerosis in patients with nasal polyposis (NP) through measurements of carotid artery intima-media thickness (CIMT), flow-mediated vasodilatation (FMD) of the brachial artery and serum paraoxonase-1 (PON-1) activity.
Methods: Forty-five patients with NP were included in the study group and 45 healthy individuals in the control group. The diagnosis of patients with NP was predicated on anterior rhinoscopy, endoscopic nasal examination and coronal paranasal sinus computed tomography (CT). Measurements of CIMT and FMD of the brachial artery were performed by high-resolution ultrasonography. Serum PON-1 activity was evaluated by measuring the rate of paraoxon hydrolysis.
Results: Mean CIMT values were found to be increased in the NP group compared to the control group. However, mean FMD % values and serum PON-1 activity were significantly lower in the NP group compared to the control group. Moreover; the endoscopic polyps' scores and paranasal sinus CT scores were positively correlated with CIMT and negatively correlated with FMD % values and PON-1 activity. Disease duration also was positively correlated with CIMT and negatively correlated with FMD % values.
Conclusion: Impaired FMD, increased CIMT and decreased serum PON-1 activity may be considered to be risk factors for accelerated atherosclerosis in patients with NP who may have subclinical atherosclerosis and be at risk for cardiovascular events in the future.

1. Introduction

Nasal polyposis (NP) is a chronic inflammatory disease of the nasal and paranasal sinus mucosa. It frequently occurs bilaterally and causes chronic nasal obstruction, rhinorrhoae and anosmia [1]. Chronic nasal obstruction caused by NP may lead to increased upper respiratory tract resistance. This condition may result in cardiovascular complications. Systemic hypertension and increased pulmonary arterial pressure have been shown in patients with NP [2,3]. In cases with NP, cardiopulmonary symptoms are usually mild or absent. However, chronic changes without marker symptoms may gradually occur [2,4]. Atherosclerosis has an important role in this process. Numerous studies have demonstrated an association between obstructive sleep apnea syndrome (OSAS) and increased risk of atherosclerosis; however, the association between NP and atherosclerosis has not been investigated in detail [5–7].

Endothelial dysfunction as an early sign of atherosclerosis can be evaluated non-invasively as an impairment of flow-mediated vasodilatation (FMD) of the brachial artery in high-resolution ultrasonography [8]. FMD is defined as the percentage change in brachial artery diameter from baseline to reactive hyperemia (FMD %) [9,10]. An impairment of FMD is considered a sign of endothelial dysfunction and is a predictor of future cardiovascular events [11,12].

Another clinically useful method that may indicate subclinical atherosclerosis is the measurement of carotid artery intima-media thickness (CIMT) by high-resolution ultrasonography [13]. Increased CIMT is considered a marker of future cardiovascular and cerebrovascular events [14]. There is evidence of a correlation between CIMT and cardiovascular disease, especially coronary heart disease [15,16].

Paraoxonase-1 (PON-1) is synthesized in the liver and is a Ca^{2+}-dependent serum esterase [17]. It primarily complexes with high-density lipoprotein (HDL) and is responsible for the antioxidant activity of HDL [18]. PON-1 plays an important role in the protection

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of LDL and HDL from oxidation by hydrolyzing cell membrane lipids, an important step in atherosclerosis [19,20]. Also, previous studies have demonstrated that PON-1 activity is related to regulation of endothelial functions [21]. Interestingly, PON-1 activity is decreased in patients with hypercholesterolemia and type 2 diabetes mellitus, which are risk factors for atherosclerosis [22].

The purpose of this study was to investigate early markers of atherosclerosis in patients with NP by the measurement of CIMT, FMD of the brachial artery and serum PON-1 activity. In addition, we tried to find out whether early markers of atherosclerosis are related with extension of polyps and disease duration.

2. Materials and methods

2.1. Study population

The study group was composed of 45 patients with nasal polyposis and the control group was composed of 45 healthy subjects. Control subjects were recruited from the outpatient department of the Ear Nose Throat department in our hospital. Prior to subject enrollment, the study was approved by the ethics committee of the Erciyes University Medical School, and written informed consent was obtained from each participant.

The diagnosis of patients with NP was predicated on anterior rhinoscopy, endoscopic nasal examination and coronal paranasal sinus computed tomography (CT). The control group was also examined for evidence of any paranasal sinus disease by anterior rhinoscopy and endoscopic nasal examination. The Lund–Kennedy staging system was used to stage nasal polyps in both nasal cavities, based on the endoscopic appearances. Stage 0 for the absence of polyp, stage 1 for polyps not prolapsing beyond the middle turbinate, stage 2 for polyps extended below the middle turbinate, stage 3 for massive polyps occluding the entire nasal cavity and resulting in a maximum score of 3 per side [23]. The Lund–Mackay staging system was used in the assessment of paranasal sinus CT scans. This system relies on a score of 0–2 dependent on the absence, partial or complete opacification of each sinus system and of the vital osteomeatal complex resulting in a maximum score of 12 per side [24].

Exclusion criteria for all study participants included a history of using topical or systemic corticosteroids in the previous 4 weeks, smoking, alcohol abuse, hypertension, hypercholesterolemia, diabetes mellitus, coronary heart disease, history of myocardial infarction, liver or renal disease, active infectious disease, bronchial asthma, allergic rhinitis, major depression, neoplastic disease, history of cerebrovascular disease or auto-immune disease such as ankylosing spondylitis, systemic lupus erythematosus, rheumatoid arthritis, or Behcet disease. Subjects taking any drug vasodilation or vasoactive substances or anti-oxidants such as anti-oxidant vitamins, angiotensin-converting enzyme inhibitors, beta-blocking agents, diuretics or statins were also excluded from the study.

2.2. Blood sample collection

Following a fasting period of 12 h, all blood samples were collected in the morning from the antecubital vein. Blood samples were immediately centrifuged at 3000 rpm for 10 min. Serum samples were kept at −80 °C until analyses for measurement of serum concentrations of total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and serum paraoxonase-1 activity.

2.3. Measurement of serum paraoxonase-1 activity

Measurement of serum PON-1 activity was performed in the absence of basal activity. The rate of paraoxon hydrolysis (diethyl-p-nitrophenylphosphate) was measured by monitoring the increase of absorbance at 412 nm at 37 °C. The amount of generated p-nitrophenol was calculated from the molar absorptivity coefficient at pH 8, which was 17,000 M^{-1} cm^{-1} [25]. PON-1 activity was expressed as U/L serum.

2.4. Flow mediated dilatation (FMD) measurement

Endothelial dysfunction was evaluated using FMD. An ultrasound probe with high frequency was used to obtain longitudinal images of the brachial artery at a marked point 5–10 cm away from the antecubital fossa (Siemens Medical Sol. Mountain View, CA). All scans were done by the same examiner who was unaware of the subject's clinical status throughout the study. At baseline, two-dimensional images were gained to evaluate arterial diameter. For inducing ischemia, a blood pressure cuff was inflated to 50 mm Hg higher than systolic blood pressure for 5 min to occlude arterial flow, and arterial diameter measurements were made within 60 s of cuff deflation. Arterial diameter was measured from the close wall to the remote wall at the intima-media interface or to the clearest echocardiography line. Images were obtained in end diastole with electrocardiogram gating. Measurements were reported as % change in diameter.

2.5. Carotid artery intima-media thickness measurement

Carotid artery intima-media thickness (CIMT) measurements were made in the left lateral supine position while the neck was extended and the chin was turned away from the side being examined. The left and right common carotid arteries were imaged proximal to the bulb after obtaining the clearest visualization of the IMT of the far wall. The mean IMT measurement was performed by manual tracing of the intima-media in the far wall of the artery. The average of three end diastolic measurements was used for analysis. The mean value of the two sides (left and right) was taken.

2.6. Statistical analysis

All analyses were performed using SPSS 16.0 (SPSS for Windows 16.0, Chicago, IL, USA). Continuous variables were defined as mean ± standard deviation. One-sample Kolmogorov–Smirnov test was used for adequacy of all parameters to normal distribution. If the distribution was normal, independent samples t test was used for statistical comparison of data between the two groups. If the distribution was not normal, the Mann–Whitney U test was used. The Chi-square test was used to compare categorical variables between the two groups. The correlation between serum PON activity, mean CIMT values, brachial artery FMD values, disease duration, endoscopic polyps' scores and CT scan scores was assessed by Spearman correlation analysis. A p value of less than 0.05 was considered as statistically significant.

3. Results

The NP group comprised 29 men and 16 women with a mean age of 41.58 ± 10.7 years. The control group comprised 28 men and 17 women with a mean age of 39.84 ± 10.44 years. Age and sex distribution were similar between the groups. The variables triglycerides, total cholesterol, LDL-C and HDL-C were similar. However, serum PON-1 activity was significantly lower in the NP group when compared to the control group (59.28 ± 38.41 vs. 114.68 ± 58.41; $p < 0.001$) (Fig. 1). The demographic and clinical data of the study population are presented in Table 1.

Ultrasonographic results are presented in Table 2. The mean brachial artery diameter at baseline was 3.90 ± 0.51 mm in NP

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