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ORIGINAL ARTICLE

Herpes viruses and human papilloma virus in nasal polyposis and controls☆

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KEYWORDS
Sinusitis;
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Abstract
Introduction: Chronic rhinosinusitis with nasal polyps is a multifactorial disease entity with an unclear pathogenesis. Contradictory data exist in the literature on the potential implication of viral elements in adult patients with chronic rhinosinusitis.
Objective: To compare the prevalence of human herpes viruses (1–6) and Human Papilloma Virus in adult patients with chronic rhinosinusitis with nasal polyps and healthy controls.
Methods: Viral DNA presence was evaluated by real-time polymerase chain reaction application to nasal polyps specimens from 91 chronic rhinosinusitis with nasal polyps patients and nasal turbinate mucosa from 38 healthy controls.
Results: Epstein–Barr virus positivity was higher in nasal polyps (24/91; 26.4%) versus controls (4/38; 10.5%), but the difference did not reach significance ($p = 0.06$). Human herpes virus-6 positivity was lower in nasal polyps (13/91; 14.29%) versus controls (10/38; 26.32%, $p = 0.13$). In chronic rhinosinusitis with nasal polyps group, 1 sample was herpes simplex virus-1-positive (1/91; 1.1%), and another was cytomegalovirus-positive (1/91; 1.1%), versus none in controls. No sample was positive for herpes simplex virus-2, varicella-zoster virus, high-risk-human papilloma viruses (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59) and low-risk-human papilloma viruses (6, 11).
Conclusion: Differences in Epstein–Barr virus and human herpes virus-6 positivity among patients with chronic rhinosinusitis with nasal polyps and healthy controls are not statistically significant, weakening the likelihood of their implication in chronic rhinosinusitis with nasal polyps pathogenesis.

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PALAVRAS-CHAVE
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Herpesvírus e vírus do papiloma humano na polipose nasal e controles

Resumo
Introdução: A rinossinusite crônica com pólipos é uma doença multifatorial de etiopatogênese ainda não definida. Existem dados contraditórios na literatura sobre a implicação potencial de elementos virais na etiologia de pólipos nasossinusais.
Objetivo: Comparar a prevalência de herpes vírus humanos (1–6) e papiloma vírus humano em pacientes adultos com rinossinusite crônica com pólipos nasais (CRwNP) e controles saudáveis.
Método: A presença de DNA viral foi avaliada por PCR em tempo real, em amostras de pólipos nasais de 91 pacientes com CRwNP e na mucosa das conchas nasais de 38 controles saudáveis.
Resultados: A positividade do EBV foi maior nos pólipos nasais (24/91; 26,4%) do que nos controles (4/38; 10,5%), mas a diferença não foi significante (p = 0,06). O HHV-6 apresentou positividade menor nos pólipos nasais (13/91; 14,29%) do que os controles (10/38; 26,32%), (p = 0,13). No grupo CRwNP, uma amostra foi positiva para o vírus herpes simples (HSV-1) (1/91; 1,1%), e uma para citomegalovírus (CMV) (1/91; 1,1%); e nenhuma amostra foi positiva no grupo controle. Não houve amostra positiva para HSV-2, VZV, HR-HPV (16,18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59) e LR-HPV (6,11).
Conclusão: Diferenças de positividade do EBV e HHV-6 entre pacientes com CRwNP e controles saudáveis não são estatisticamente significantes, enfraquecendo a probabilidade de sua implicação na patogênese da CRwNP.

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a subdivision of idiopathic chronic rhinosinusitis (CRS).[1] It is a clinical syndrome characterized by persistent symptomatic inflammation of the nasal and paranasal sinuses mucosa.[1] The etiopathogenesis of CRSwNP is mainly attributed to a dysfunctional host–environment interaction.[2] Even though the identification of exogenous agents driving the secondary inflammatory mechanisms has been a field of extensive research, the potential involvement of viral infection is relatively unstudied.[1]

Herpes simplex virus-1 (HSV-1), herpes simplex virus-2 (HSV-2), varicella-zoster virus (VZV), cytomegalovirus (CMV), Epstein–Barr virus (EBV), and human herpes virus-6 (HHV-6), along with human papilloma viruses (HPV), are DNA viruses that have the capacity to incorporate into host DNA, to establish lifelong latent infections in the upper respiratory mucosa, and to reactivate in immunocompromised conditions.[3–6] Only a few studies[7–17] have investigated their potential role in CRSwNP, while their results are controversial. Furthermore, the highly sensitive quantitative real-time polymerase chain reaction (PCR) technique has been used for detection of these viruses in CRSwNP by only two studies so far.[11,17]

The aims of the present study were to evaluate and compare the prevalence of HHV, high-risk HPV types (HR-HPV; subtypes 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59), and low-risk HPV types (LR-HPV; subtypes 6, 11) in nasal tissue samples of patients with CRSwNP and healthy controls by employing the highly sensitive quantitative PCR technique, and to review the related literature.

Methods

This was a cross-sectional contemporary cohort study, which was conducted prospectively, from January of 2009 to January of 2013, on adult patients with CRSwNP undergoing functional endoscopic sinus surgery (FESS). CRSwNP diagnosis was made according to the criteria of the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS).[1] The control group consisted of healthy adult patients with nasal septal deviation undergoing septoplasty without CRS according to EPOS criteria.[1] Pediatric subjects, as well as patients with asthma, cystic fibrosis, primary ciliary dyskinesia, allergic fungal sinusitis, allergic rhinitis, inverted papilloma, and HIV seropositivity were excluded from the study. Subjects in both groups who had had an upper respiratory tract infection within two weeks before surgery, and those who had taken any nasal or systemic steroids within the last month prior to surgery were excluded from the study.

In CRSwNP patients, nasal polyp specimens were obtained from the paranasal sinuses during FESS, while in the control group tissue biopsies from the inferior turbinate mucosa were taken during septorhinoplasty. Nasal polyps and nasal tissues extracted during surgery were immediately transferred in sterile dry containers and shipped to the laboratory. By use of a surgical knife, the tissues were cut in half, and several pieces (2–4 mm) were taken from the deep tissue and divided into three parts: for conventional culture, for molecular techniques and for storage at −80 °C.

For each patient, the tissue pieces were inoculated on Sabouraud agar at 30 °C for 10 days and then on 5% sheep blood Columbia agar incubated in a 5% CO_2 atmosphere and an anaerobic atmosphere for 2 days. Gram staining