International Journal of Pediatric Otorhinolaryngology (2006) 70, 2061—2066

ELSEVIER

International Journal of Pediatric Otorhinolaryngology

www.elsevier.com/locate/ijporl

Children and partners of patients with recurrent respiratory papillomatosis have no evidence of the disease during long-term observation

Valentin Gerein [a,b,*], Iouri L. Soldatski [c,d,1], Natalia Babkina [a], Elena K. Onufrieva [d,2], Nadzeya Barysik [a], Herbert Pfister [e,3]

[a] *Department of Pediatric Pathology, Institute of Pathology, Johannes Gutenberg University of Mainz, Langenbeckstrasse 1; 55101 Mainz, Germany*
[b] *Pediatric Clinic of Johann Wolfgang Goethe University, Frankfurt am Main, Germany*
[c] *Department of Otorhinolaringology, I.M.Sechenov's Moscow Medical Academy, Moscow, Russia*
[d] *Department of Otorhinolaringology, St.Vladimir Moscow Children's Hospital, Rubtsovsko-Dvorcovaya str., 1/3, Moscow 107014, Russia*
[e] *Institute of Virology, University of Cologne, Fürst-Pückler-Straße 56 50935, Cologne, Germany*

Received 5 May 2006; received in revised form 18 July 2006; accepted 19 July 2006

KEYWORDS
Recurrent respiratory papillomatosis;
HPV transmission;
Parents;
Partners;
Pregnancy;
Children

Summary

Objective: Recurrent respiratory papillomatosis (RRP) is the most common benign neoplasm affecting the larynx and upper respiratory tract. The aim of our study was to investigate whether children and partners of patients with RRP develop the same disease and to determine whether there is an impact of pregnancy on the course of RRP.

Patients and methods: Thirty-eight of 42 patients with RRP were accepted for a multicenter prospective study in Germany in 21.06.83—12.03.90. Mean follow-up duration was 15.3 ± 1.8 years. The data of partners of patients with RRP was collected during the period of observation and then updated via interviews in January 2006. Twenty-nine children and four grandchildren were born to 14 patients with RRP. Fifteen of 448 cases of patients with RRP were treated in Saint Vladimir Moscow Children's Hospital in Russia in 1988—2003 and analyzed retrospectively. Sixteen children and one grandchild were born to 15 patients with RRP from Russia. In both studies, the virus type of patients with RRP was identified by nested PCR or Southern

* Corresponding author. Tel.: +49 6131174551; fax: +49 6131173546.
E-mail addresses: v.gerein@web.de (V. Gerein), ysoldatsky@aport.ru (I.L. Soldatski), solnatasha@mail.ru (N. Babkina), kompas@mail333.com (N. Barysik), herbert.pfister@medizin.uni-koeln.de (H. Pfister).
[1] Tel.: +7 495 2688326.
[2] Tel.: +7 495 2688376.
[3] Tel.: +49 221 4783901; fax: +49 221 478 3902.

0165-5876/$ — see front matter
doi:10.1016/j.ijporl.2006.07.018

blot hybridization. Statistical analysis was perfomed using Fisher's exact test (probability value set at $p < 0.05$).
Results: All children born to patients with RRP were healthy. RRP was not diagnosed in any of them on the basis of clinical or histological examination. Four of 45 children developed dysphonia, two of them had vocal cord nodules. None of the sexual partners of patients has developed RRP during the follow-up period. Pregnancy was accompanied by excessive growth of papillomas in all women (100%) with RRP associated with HPV type 11, and only in 16.7% of women with RRP associated with HPV type 6 ($p = 0.001$).
Conclusions: Patients with RRP are able to have healthy children regardless of the stage of the disease. Partners of RRP patients do not develop RRP during an observation period of 15 years. Pregnancy has a negative impact on the course of RRP and local laryngeal status in patients; it is more significant in HPV type 11 associated cases as it is manifested by more rapid papillomas growth and more frequent recurrence.

1. Introduction

Recurrent respiratory papillomatosis (RRP) is considered to be the most common benign neoplasm of the larynx in children. Despite its benign histology, sometimes RRP leads to morbid consequences. High recurrence rate and tendency to spread throughout the respiratory tract make it difficult to treat, especially in cases associated with a long course of the disease and a malignant transformation [1,2]. The viral etiology of RRP [3] and the role of HPV type 6 and HPV type 11 in the course and prognosis of RRP are ultimately determined [4,5]. However, over the last years, an increase in the lifetime of patients even with severe forms of RRP, has been observed. Their social adaptation is compromised by a lack of knowledge about their disease and modes of transmission. Modes of HPV transmission remain arguable. Some authors distinguish a direct non-sexual transmission, from one person to another; maternal transmission, during delivery or caesarean section [6]; transmission in utero, through semen [7], as an ascending infection [8], transplacentally and through sexual abuse [9]. To the date, there is no indication of a risk of transmission from parents with RRP to their children. In this context, a number of questions, such as risk level of RRP for children and sexual partners, an impact of pregnancy on the RRP course and prognosis become particularly important. In order to answer these questions, research was conducted as prospective study in Germany and retrospective study in Russia.

2. Patients and methods

Fourty-two patients with active histologically confirmed papillomas in the airway passages were enrolled in a multicenter prospective study between 21.06.83 and 12.08.90 in Germany. They were operated on and subsequently treated with alfa-interferon till the achievement of macroscopic remission or till the discontinuation of therapy because of an insufficient response to treatment. The mean therapy duration was 32.4 ± 21.6 months. Four patients were excluded because they moved away during the first 3–6 months of therapy. Thirty-eight patients with RRP were followed up till 31.01.2006 (the mean follow-up duration was 15.3 ± 1.8 years after the end of alfa-interferon therapy). The data of partners of patients with RRP was collected via interview in January 2006. Twenty-nine children and four grandchildren were born to 14 parents with RRP. The basic characteristics of patients are presented in the Table 1.

The records of 448 patients with RRP treated in Saint Vladimir Moscow Children's Hospital in Russia in 1988–2003 were reviewed [10]. Fifteen patients matched our criteria as they had histologically confirmed papillomas, gave birth to children and their complete anamnesis was available. The cases were analyzed retrospectively in January 2006. The data of partners of patients with RRP was collected via interviews in January 2006. Sixteen children and one grandchild were born to RRP patients from Russia.

In both studies, the virus type was identified by nested PCR or Southern blot hybridization according to the generally accepted principles. Mean age of patients at the end of the observation period in both studies was 33.7 ± 14.3 (range from 17.8 to 66.8). Among patients of the two cohorts, pregnancy occurred in 22 patients with RRP at different stages of the disease and in eight female partners of patients with RRP. Twenty-one patients gave birth to children and one patient terminated her pregnancies because of the start of the fast growth of papillomas. In 45 cases, pregnancy ended in term by delivery of a healthy mature infant. Mean age of children at the