



Distribution and density of CD1a+ and CD83+ dendritic cells in HPV-associated laryngeal papillomas

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Received 9 September 2008; accepted 21 October 2008

Available online 4 December 2008

KEYWORDS

Recurrent respiratory
papillomatosis;
Dendritic cells;
CD1a;
CD83

Summary

Background: Respiratory papillomatosis associated with human papilloma virus (HPV) infection is the most common benign laryngeal neoplasm. The age of patients at disease onset, HPV type, number of surgeries are well known prognostic factors of the disease course. The correlation between dendritic cell (DC) density in tumor tissue and clinical prognosis was established.

Aim: The aim of our study was to estimate the density of DC in laryngeal papillomas associated with HPV types 6/11 infection and to evaluate the relationship between the number of DC and the disease severity.

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Materials and methods: Our study included 40 randomly selected biopsy specimens from patients with HPV-positive laryngeal papillomatosis aged from 1.7 to 20 year. DC were immunohistochemically labelled with anti-CD1a antibodies and anti-CD83 antibodies. The density of DC was analysed in epithelial layer and lamina propria.

Results: In the epithelial layer of papillomas the number of CD1a+ and CD83+ DC was 86.2 (47.5–119.9) cells/mm² and 2.6 (0.6–7.9) cells/mm², respectively. In lamina propria – 15.3 (5.1–27.9) and 16.0 (6.7–33.2) cells/mm². For subgroups of patients with high number of operations (more than 3), early disease onset (children under 3 years of age) and lingering duration of disease (more than 1 year) we detected an increase of CD83+ DC in the epithelial layer. However, our data did not demonstrate a statistically significant difference in CD1a+ DC count neither in the epithelium nor in the lamina propria. Probably, the increase of CD83+ DC density in epithelial layer of patients with severe course of disease can be an evidence of impaired migration of matured DC.

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1. Introduction

Benign papillomas of the larynx are associated with human papilloma virus (HPV) types 6 and 11 [1,2]. Laryngeal papillomatosis is a rare disease, but papilloma is the most frequent benign laryngeal neoplasm, accounting for approximately 84% of benign tumors of the larynx [3–4].

While millions of people are exposed, relatively few develop clinical evidence of the disease. The clinical course is highly variable. Some patients spontaneously recover, while in others papilloma-virus infection induce recurrent respiratory papillomatosis (RRP), which is characterized by severe clinical manifestation, resulted in loss of patients' life quality. Children with RRP may require surgeries to prevent airway obstruction as often as 21 times per year [5]. Up to 3% of children with RRP will die of the disease [6]. The well-known negative prognostic factors of respiratory papillomatosis are early disease onset, high number of surgeries per year and HPV type 11 infection [5,7].

While the presence of HPV is necessary to develop RRP, it is not sufficient by itself. A growing body of evidence shows that the immune system plays a crucial role in determining the outcome of HPV infection. Thus, cellular immunity is responsible for eliminating the HPV-infected keratinocytes through the local or systemic immune response initiated by dendritic cells (DCs) [8].

According to a number of studies, DC density in the tumor tissue correlates with a prognosis in many human neoplasms [9–12]. A number of researchers consider that HPV reduces the number of DC in infected tissue, some investigators believe that HPV infection is associated with an increased DC count, while others have found no changes in this parameter [13–18]. Only a very limited number of studies have been published on DC density in the laryngeal mucosa, normal or involved in pathologic

processes. Up to now immunohistological studies of laryngeal papillomas have been carried out using antibodies against CD1a—common superficial marker of DC [19]. Actually the evaluation of matured DC density was not conducted. One of today's best-known surface markers for fully matured human DC is CD83, a member of the IgSF (immunoglobulin superfamily) of receptors. Although its functions in DC remain unclear, studies have indicated the role of CD83 in the modulation of antigen presentation [20,21].

The aim of our study was to estimate the density of immature and mature DC in laryngeal papillomas associated with HPV types 6/11 infection, using immunolabeling of DC with anti-CD1a and anti-CD83 antibodies and to evaluate the relationships between the severity of papillomatosis and DC number in laryngeal papillomas.

2. Materials and methods

2.1. Selection of patients

The retrospective study included 40 patients aged from 1.7 to 20 years old with laryngeal papillomas, observed in Saint Vladimir Moscow Children' Hospital, Snegiri Clinic, Regional Children's Clinical Hospital (Russia) and in University Clinic of Mainz. Informed consent was obtained from all patients. The clinical data were collected from medical records. The characteristics of patients are presented in Table 1.

2.2. Sample collection

Biopsy specimens of laryngeal papillomas obtained by microlaryngoscopy were fixed in 4% formaldehyde solution phosphate buffered at pH 7.4, processed according to the standard procedure and

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