International Journal of Pediatric Otorhinolaryngology 79 (2015) 262–266

Contents lists available at ScienceDirect

International Journal of Pediatric Otorhinolaryngology

journal homepage: www.elsevier.com/locate/ijporl

Case Report

Recurrent laryngeal papillomatosis with oesophageal involvement in a 2 year old boy: Successful treatment with the quadrivalent human papillomatosis vaccine

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ARTICLE INFO

Article history:
Received 10 September 2014
Received in revised form 16 November 2014
Accepted 18 November 2014
Available online 25 November 2014

Keywords:
Children
Recurrent respiratory papillomatosis
Recurrent oesophageal papillomatosis
Quadrivalent human papilloma vaccine

ABSTRACT

Authors present a case report of a 2-year-old boy with recurrent laryngeal papillomatosis with oesophageal involvement due to human papilloma virus types 6 and 11, who needed surgical treatment every 4–6 weeks, altogether 11 times. After detailed immunological evaluation of basic immunological parameters, and *in vitro* detection of good responses to routine childhood immunization, a therapeutic vaccination has been decided with a 4-valent HPV vaccine. Following the third vaccine dose both laryngeal and oesophageal lesions disappeared completely, and for 2 years follow-up no papillomas could be detected. Vaccination could be a promising method in the treatment of RRP in children.

1. Introduction

Recurrent respiratory papillomatosis (RRP) is a relentless, relatively rare disease of viral origin in which squamous papillomas frequently obstruct the respiratory tract of children and young adults, necessitating emergency interventions. Although many therapeutic modalities have been administered, so far no therapy has been proved to be curative for this process. Our case report proposes a completely novel therapeutic approach: immunization. The basic idea of this method is, that HPV infection itself can cause a local disease in the mucous epithelium and not evoke a general immune response. On the contrary, immunization with good host capability produces effective humoral and cellular response against the causative agents.

2. Case report

2.1. Clinical history prior to immunization with the quadrivalent HPV vaccine

Our patient, a 2 and a half year old, otherwise healthy boy (born 1st June 2010) was first admitted to the Intensive Care Unit of the a Regional Tertiary Care Hospital at the age of 3.5 months, because of aphonia and severe inspiratory stridor. According to his parents there was no history consistent with upper respiratory infection, trauma, or foreign body aspiration. Direct laryngoscopy was performed and it revealed laryngeal papillomatosis, so he was sent to Heim Pal Children's Hospital in Budapest for surgery. On the 20th September 2010 a cold knife microlaryngoscopic surgery was performed and large amount of papilloma tissue was removed from the whole supraglottic and glottic area. Microscopic examination also revealed papillomas in the hypopharynx, and therefore flexible oesophagoscopy was performed. This examination showed papillomas along the whole length of the oesophagus in islands with a size of 1–4 mm (Figs. 1 and 2). Removal of these tissues was not attempted because of the high risk of bleeding and

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http://dx.doi.org/10.1016/j.ijporl.2014.11.022
0165-5876/

Fig. 1. Laryngoscopy prior to HPV4 immunization.

Fig. 2. Oesophagoscopy prior to HPV4 immunization.

perforation. The child was discharged from the hospital next day in good physical condition. However due to rather frequent recidivism, he had to be readmitted thereafter on average every 3–5 weeks for surgery, including LASER surgery.

The repeated surgery occasions in time are shown in Fig. 3.

From the removed papillomas HPV types 6 and 11 could be isolated by molecular biological methods. As both HPV 6 and HPV 11 antigens are represented in the quadrivalent HPV vaccine (Silgard, MSD), the idea of immunization occurred to us, considering the exceptionally high number of emergency surgical procedures due to critical airway obstructions (11 times) and the consecutive anxiety, suffering of the child as well as the whole family. Ethical considerations of immunizing a 2-year-old boy against HPV were discussed and the approval of the local Ethical Committee was obtained.

Prior to HPV immunization the child's capacity to mount neutralizing antibodies as well as some humoral and cellular immune response parameters and evidence of various age related immunization responses (e.g. MMR) were tested to rule out immunodeficiency.

2.2. Methods

2.2.1. Detection of the patient's humoral immune response

Blood samples were collected before the first vaccination to evaluate immune response to mumps, rubella, measles and influenza viruses, as the patient received MMR vaccine (Priorix, GSK) at the age of 15 months, according to the National Immunization Plan in Hungary. Specific antibody levels against the three viruses were detected by immnofluorescent assay (EUROIMMUNE). Anti-influenza antibodies were tested against the three different influenza prototype strains (A/California/7/2009 (H1N1); A/Perth/16/2009 (H3N2); B/Brisbane/60/2008) with haemagglutination inhibition assay based on the CDC protocol.

2.2.2. Evaluation of the patient's cellular immune response

Blood samples for peripherial blood mononuclear cell (PBMC) separation were obtained in sterile heparinised vacutainer tubes (4 ml) before the first and after the third HPV vaccine dose. PBMCs were isolated by Ficoll-Plaque PLUS (GE Healthcare) density centrifugation at 950 × *g* for 20 min. The PBMCs were washed twice with AIM-V medium (Invitrogen, Carlsbad, CA, USA). The PBMCs were diluted at the concentration of 1.8×10^6 cells/300 μl AIM-V.

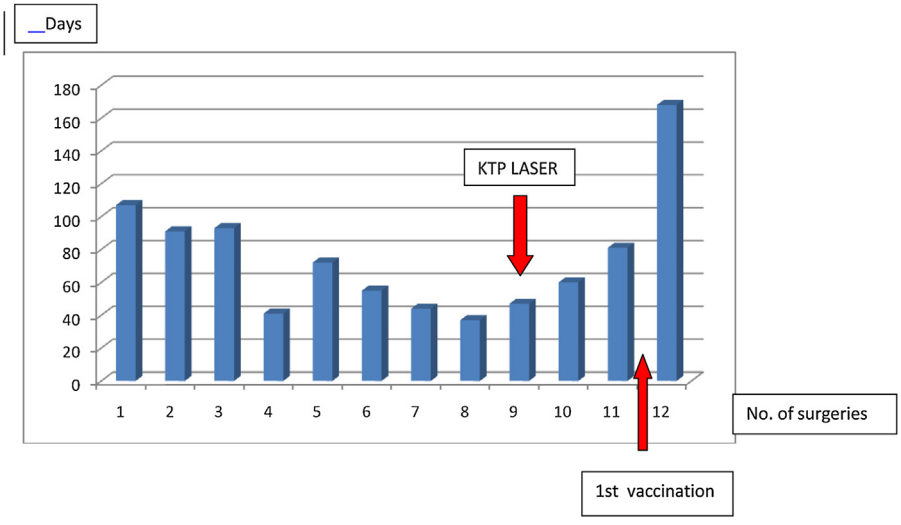

Fig. 3. Time intervals in days between surgeries.