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Tracheobronchial involvement of laryngeal papillomatosis at onset

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Abstract
A case of adult onset laryngeal papillomas with tracheal and bronchial involvement present at onset is presented. The presence of human papilloma virus (HPV) DNA type 6/11 is demonstrated by *in situ* hybridization.

Key words: Papilloma; Larynx; Trachea; Bronchi; Papilloma viruses

Introduction

It has been reported that tracheal and bronchial extension eventually will appear in two per cent of patients with laryngeal papillomas (Batsakis *et al.*, 1983). However, the simultaneous presence of laryngeal, tracheal and bronchial squamous cell papillomas at first presentation has never been published before.

Case report

A 46-year-old male, without any history of laryngeal or pulmonic diseases, complained of hoarseness of two-months duration. He had had no previous hospitalization or intubation. At clinical examination several laryngeal tumours were visualized by indirect laryngoscopy. Under general anaesthesia and direct laryngoscopy the tumours were removed by surgical excision from the laryngeal surface of the epiglottis, vocal folds, subglottic area, trachea, and the left main bronchus (Figure 1).

Histopathology

Histological examination of the specimens revealed numerous squamous cell papillomas with little or no surface keratinization. Basal cell hyperplasia was seen in several areas, and koilocytic cells were prominent. However, dysplasia did not occur in any specimen. The histological picture and the degree of koilocytosis appeared constant in all the papillomas examined.

DNA hybridization

Sections were cut from six paraffin blocks and placed on poly-L-lysin slides. The sections were deparaffinized in xylene and rehydrated through graded ethanol, and treated with pronase (0.01 mg/ml) for five minutes. Hybridization was performed against human papilloma virus (HPV) type 6/11, 16/18 and 31/33/35 using a commercial kit (Enzo pathogen identification kit), according to the manufacturer's recommendations for hybridization, washes and development of the positive signals. The sections were counter-stained with Mayers haematoxylin, mounted with aquamount and coverslipped.

In four out of six sections a positive signal was seen for HPV type 6/11. The signals were most clearly seen in the upper parts of the epithelium, and predominantly in the nuclei of koilocytic cells (Figure 2).

The patient revealed recurring papillomas two, three, five and 14 months after the first operation. The recurring papillomas were all located in the larynx at the vocal folds, and subglottic region. There were no recurrences in the trachea or main bronchus.

Discussion

Laryngeal papillomatosis is a rare disease with an incidence in Denmark of 3.84×10^{-6} per year (Lindeberg and Elbroend, 1990). The incidence rate is approximately the same in juvenile and adult onset papillomas.

Juvenile onset papillomas are defined as non-keratinized papillomas arising in patients younger than 20 years at onset, and adult ones in patients older than 20 years at time of diagnosis. In the juvenile group solitary papillomas are rare. According to Lindeberg and Elbroend (1990) only six out of 51 cases were

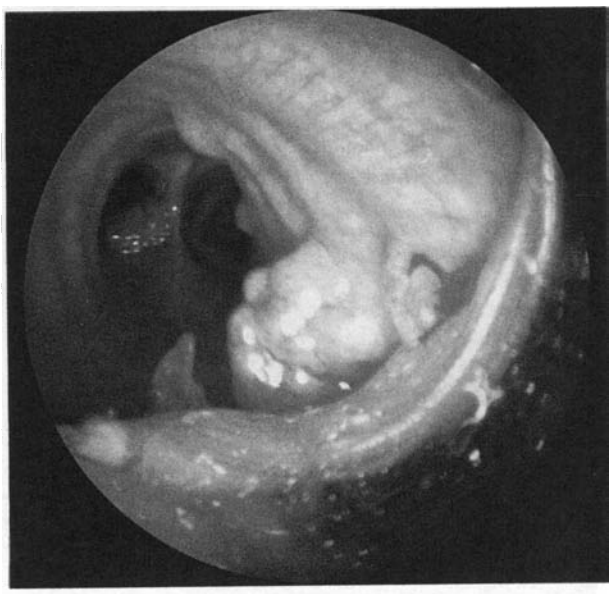

FIG. 1
Photograph taken during bronchoscopy showing papillomas in both trachea and left main bronchus.

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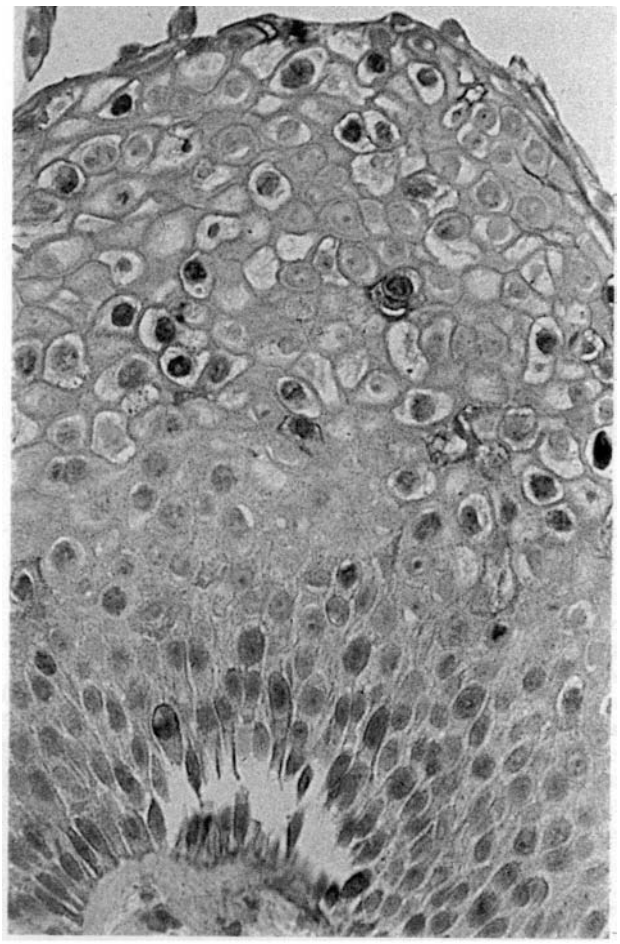

FIG. 2

Histological picture of one of the papillomas showing positive reaction with *in situ* hybridization. (Counterstained with H&E; ×320).

solitary papillomas. In the adult group of onset papillomas most cases are solitary. Lindeberg and Elbroend (1990) found 33 out of 130 cases where the papillomas were multiple.

According to Batsakis *et al.* (1983) two per cent of all patients with laryngeal papillomatosis will eventually develop bronchial involvement. This typically occurs in children with juvenile papillomas, in whom a tracheotomy has been performed. The bronchial involvement in adult onset papillomas has been described a few times before, but never with an initial involvement of the bronchial region.

In recent studies of laryngeal papillomas, *in situ* hybridization has revealed HPV 6/11 in a very high percentage of the cases (Lindeberg and Johansen, 1990; Dickens *et al.*, 1991). The positive reaction was seen in cells in the upper part of the epithelium and often in koilocytic cells.

The occurrence of HPV 16, in laryngeal papillomas, has only been described once (Dickens *et al.*, 1991). In a series of 27 benign laryngeal papillomas (juvenile as well as adult onset, both multiple and solitary) Dickens *et al.* (1991) demonstrated HPV 11 in 48 per cent of the papillomas. Three papillomas were positive for both HIV 6, 11 and 16. This unexpected finding was confirmed by polymerase chain reaction.

For many years the pathogenesis of laryngeal papillomas has been discussed. Recent studies of juvenile papillomas suggest that HPV, like other viruses (herpes and cytomegalovirus) (Smith *et al.*, 1991) may be transmitted during birth by aspiration of vaginal secretions, or the virus may even be transmitted before birth (Lindeberg and Elbroend, 1989).

The pathogenesis of adult onset papillomas is more uncertain although a link has been suggested between the adult onset papillomas and oral–genital contact by sexual partners with genital warts. This patient had no previous history of HPV infections at other sites and no information about sexual partners was obtained.

It has been assumed previously that the spread of the papillomas from the larynx to trachea and bronchi was due to iatrogenic spread during laryngoscopy and bronchoscopy. Our case with primary spread to the trachea and left main bronchus shows, that the spread is not always, iatrogenic.

Acknowledgement

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References

Batsakis, J. G., Raymond, A. K., Rice, D. H. (1983) The pathology of head and neck tumors: papillomas of the upper aerodigestive tract. Part 18. *Head and Neck Surgery* **5:** 322–344.

Dickens, P., Srivasteva, G., Leong, S., Larking, S. (1991) Human papilloma virus 6, 11 and 16 in laryngeal papillomas. *Journal of Pathology* **165:** 243–246.

Lindeberg, H., Elbroend, O. (1989) Laryngeal papillomas: clinical aspects in a series of 231 patients. *Clinical Otolaryngology* **14:** 333–342.

Lindeberg, H., Elbroend, O. (1990) Laryngeal papillomas: the epidemiology in a Danish subpopulation 1965–84. *Clinical Otolaryngology* **15:** 125–131.

Lindeberg, H., Johansen, L. (1990) The presence of human papilloma virus (HPV) in solitary adult laryngeal papillomas demonstrated by *in situ* DNA hybridization with sulphonated probes. *Clinical Otolaryngology* **15:** 367–371.

Smith, E., Johnson, S., Pignatari, S., Cripe, P., Turek, L. (1991) Perinatal vertical transmission of human papilloma virus and subsequent development of respiratory tract papillomatosis. *Annals of Otology, Rhinology and Laryngology* **100:** 479–483.

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