The Journal of Laryngology and Otology
July 1993, Vol. **107**, pp. 636–638

Recurrent laryngeal papillomatosis: a case of florid papillomatosis following a remission of 30 years

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Abstract
Laryngeal papillomatosis is the commonest benign tumour affecting the larynx. Two forms are found i.e. juvenile onset and adult onset. Typically the juvenile onset form has a greater rate of recurrence and often remits with the onset of puberty (Corbitt *et al.*, 1988). The human papilloma virus (HPV) is the causative agent (Abramson *et al.*, 1987; Corbitt *et al.*, 1988), specifically types HPV6 and 11. Attempts have been made to correlate the clinical behaviour of these two modes with the viral serotype and other aetiological factors such as smoking and hormonal factors (Abramson *et al.*, 1987; Rimmel *et al.*, 1992). Studies, however have shown that there is considerable variation in behaviour (Steinberg *et al.*, 1983; Corbitt *et al.*, 1988; Crissman *et al.*, 1988). It is widely accepted that the disease 'burns' itself out, particularly with respect to the juvenile form. It is interesting and unusual therefore when the disease reappears after many years of remission. The following case report illustrates this point.

Key words: Papilloma; Laryngeal neoplasms; Recurrence

Case report

A 44-year-old female, heavy smoker, presented to the ENT department with a two-week history of gradually worsening dyspnoea. A provisional diagnosis of asthma had been made by her GP but despite treatment with inhaled bronchodilators and inhaled steroids she failed to improve. In the past she had had recurrent laryngeal papillomatosis requiring repeated surgery from 6 to 13 years of age. Since then she had no further problems and although her voice had always been hoarse this had deteriorated over the preceeding two to three weeks.

On examination she was noted to have marked inspiratory and expiratory stridor with dysphonia. Nasendoscopy revealed a large fungating white mass arising from the glottis. The remainder of her ENT examination was normal. General examination suggested reduced expansion in both lungs but there was no evidence of wheeze. She was treated with Heliox and antibiotics and the next day direct laryngoscopy and an elective tracheostomy were performed. A large fungating supraglottic mass was seen to arise on the right, obscuring the right true vocal fold. No abnormality of the left vocal fold was noted. Biopsies were taken and sent for histological and microbiological examination including fungal and TB studies.

The histological diagnosis was squamous cell papilloma with evidence of HPV infection. Interestingly sections also revealed the presence of fungus which was later confirmed as *Candida sp.* by culture. Systemic nystatin was commenced and further microlaryngoscopies were performed with laser treatment. The tracheostomy was allowed to close after four weeks and direct laryngoscopy thereafter revealed complete resolution of the papillomas.

Discussion

Although an infectious cause for recurrent papillomatosis was postulated as far back in 1923 by Ullman, it is only in the last ten years that identification of the human papilloma virus has been possible by the southern blot technique and more recently by *in situ* hybridization. The association of the same virus with genital condylomata and its implication in cervical cancer has prompted similar studies into the behaviour pattern of recurrent laryngeal papillomatosis (Abramson *et al.*, 1987; Corbitt *et al.*, 1988; Crissman *et al.*, 1988). Human papilloma viruses (HPV) 6 and 11 have been identified in laryngeal papillomas, type 11 being the most common (Abramson *et al.*, 1987). These virus types predominate in genital condylomata and it has been suggested that juvenile onset papillomatosis arises from perinatal maternal infection with genital condylomata (Quick *et al.*, 1978). However, HPV16, 18, 31, 33 and 35 are also found in the female genital tract but have never been identified in laryngeal papillomatosis. Virus types 16 and 30 have been identified in invasive carcinoma of the larynx (Kashima *et al.*, 1988). But unlike the pattern of disease associated with virus type in the female genital tract there is no similar association in the larynx.

In this case although the virus type has not been identified, the pathological features are classical of HPV infection and it is likely to be either type 6 or 11. We were fortunate to be able to obtain the original slides of the papillomas removed as a child and comparison with the present specimen confirms the close similarity between the two. It is possible that there had been reactivation of the HPV virus after a latent period of 31 years. The presence of HPV virus in normal tissue adjacent to papillomas has been demonstrated by Steinberg *et al.* (1983) and it is suggested that the activation of the virus in this normal tissue is responsible for the unpredictable pattern of disease. The factors important in reactivation of the virus are not clear. The juvenile form of the disease frequently regresses with the onset of puberty and it has been noted that pregnancy also influences the behaviour of the disease (Steinberg *et al.*, 1983; Corbitt *et al.*, 1988; Crissman *et al.*, 1988). This would suggest that hormonal factors have a part to play, although the precise association is unknown. Radiation, once used as a treatment for papillomatosis has been shown to result in malignant transformation (Brandsma *et al.*, 1989). Risk factors in laryngeal carcinoma including smoking

Accepted for publication: 10 April 1993.

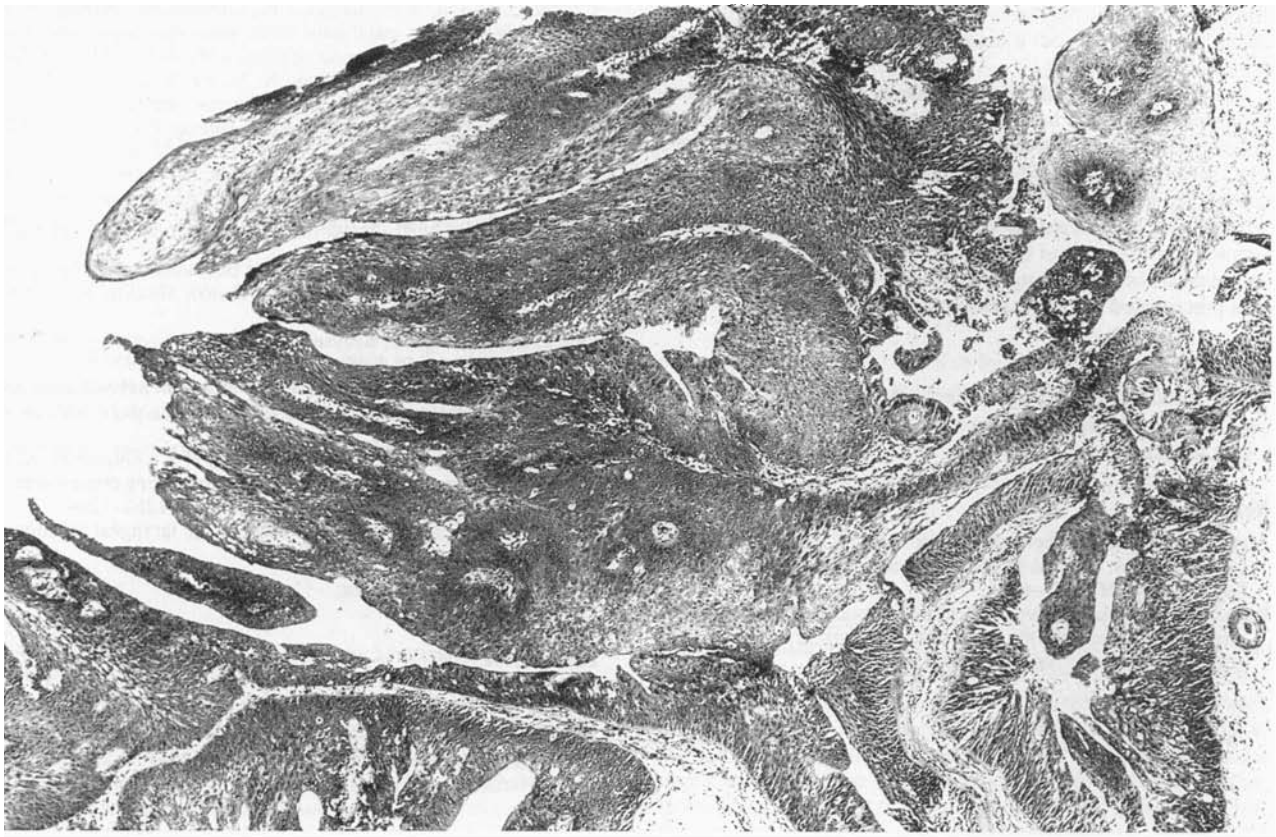

FIG. 1
The lesion showed a papillomatous appearance, with connective tissue covered by stratified squamous epithelium (H & E × 40).

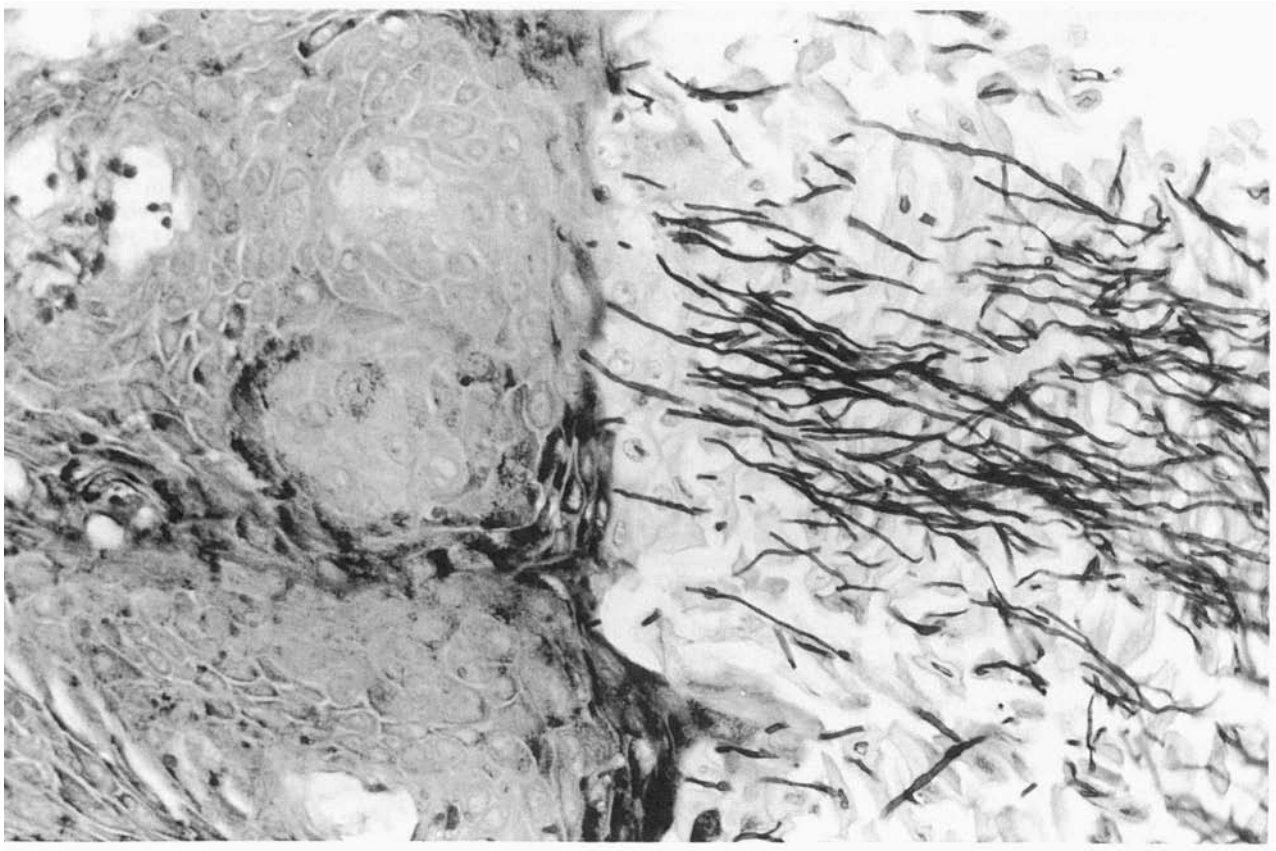

FIG. 2
Hyphae of *Candida spp.* are present superficially (H & E × 40).

https://doi.org/10.1017/S0022215100123941 Published online by Cambridge University Press

and alcohol intake may also play a part in the reactivation of latent papillomatosis but a direct link has yet to be established (Crissman *et al.*, 1988).

In the reported case there was a history of high cigarette consumption which may have been an influencing factor. Another feature of interest in this case was the association of inhaled steroid therapy and the rapid onset of stridor. Oropharyngeal candidiasis is a common finding in patients receiving inhaled steroids and is thought to be secondary to steroid immunosuppression (Milne and Crompton, 1974). It is possible that a combination of both laryngeal candidiasis and immunosuppression precipitated the acute symptoms in this case.

Acknowledgement

The authors gratefully acknowledge Mr S. Saunders, Consultant Otolaryngologist, St Georges Hospital, for allowing them to report this case.

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