Squamous papilloma of the larynx

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Papilloma is a benign exophytic neoplasm of epithelium on a connective tissue core. In the larynx the stratified squamous variety is the commonest form of papilloma. They are found in both adults and children, but, in the latter, because of the much narrower diameter of the airway, the symptoms are more serious and treatment is more urgent and difficult. It is thus customary to divide the condition on the basis of the age of the patient into juvenile and adult types. In some juvenile cases the papillomas persist into adult life.

Infection of the cells of squamous papillomas of the larynx by human papillomavirus is frequent (see below), and has been closely correlated with the presence of koilocytosis. In a few cases of papillomatosis some of the material shows a papillary transformation not only of squamous cell epithelium, but also of respiratory epithelium. The latter comprises nonmalignant respiratory epithelium featuring both ciliated cells and goblet cells, the appearances being reminiscent of those of the entity of cylindric cell papilloma of the nose and paranasal sinuses. Papillomas showing respiratory epithelial hyperplasia have a decided tendency to recur. Difficulty may be experienced in distinguishing two other types of neoplastic lesion, which occur particularly often on the vocal cords, from squamous papilloma: i) keratotic plaque with dysplasia; and ii) carcinoma of both verrucous squamous and regular types.

Raised plaques composed of thickened squamous epithelium with a keratinized surface are seen quite frequently in biopsy. They show a mild to severe degree of dysplasia of the deeper layers of their squamous cells. It is important to separate these lesions from squamous papillomas because the former have a malignant potential which is not possessed by the latter. A careful examination of the whole biopsy for evidence of cylinders of papilloma formation and the branching that is associated with them will usually suffice to distinguish this lesion. The degree of dysplasia exhibited by the plaque is often more severe than would be expected in a papilloma.

Squamous carcinoma may exhibit papilloma formation and should not be mistaken for benign squamous papilloma. The pattern is not, however, as symmetrical as in papillomas and branching of papillae is unusual. Verrucous squamous carcinoma may display very long papillae, usually without branching. The rete ridges are irregular and the basement membrane is rarely hyalinized, a feature which is frequent in papillomas. Squamous cells of the intermediate layer in verrucous carcinomas and some papillar areas of regular squamous carcinoma are larger than those of the corresponding layer in squamous papillomas, showing a mean area of more than 300 æm2 on image analysis.
Squamous papillomas arising in childhood, although similar in morphology and etiology to those arising in adults, are distinct in some important respects. Their incidence has a female preponderance, unlike those occurring in adults, which have a male preponderance (see below). They may arise at any age of childhood and have been described as early as 18 months. Treatment in juvenile onset cases is more difficult and more prolonged than the adult onset papillomas and children, having smaller airways, require tracheostomy more frequently than do adults. After tracheostomy the tendency of papillomas to spread down the trachea to the main bronchi is greater in children than in adults. After many episodes of surgical removal followed by recurrence, the florid papillomas may eventually cease to recur. Malignant alteration of juvenile papillomatosis has been described. A few cases are on record in which malignancy took place many years after treatment of juvenile papillomatosis by radiotherapy. In these cases, it must be presumed that the carcinoma was the result of the radiation.

Most adult papillomas arise de novo in adult life with an age incidence which is maximum in the fourth decade. About 20% of adult papillomas have arisen in childhood. Males are affected twice as often as females. The maximum incidence of onset is in the fourth decade. The tendency to recurrence, and hence the number of operations required for removal of adult papillomas, is related to the form which the papillomas take at the onset. If the papillomas form a solitary mass in the larynx there is little tendency to recurrence and a single endoscopic operation to remove the papilloma is required. Two or more distinct laryngeal lesions, separated by clinically normal epithelium, require many more endoscopic operations. A third group which may be designated as florid papillomatosis, where there is involvement of every part of the larynx, necessitates frequent removals, eventually tracheostomy and even laryngectomy.

A viral basis for squamous papillomas of the larynx has been under consideration for many years. Viruses leading to neoplasia may be classified as either RNA viruses, such as the virus which produces the Friend virus lymphoma in mice, or DNA viruses, such as that producing the Shope papilloma of rabbit skin and the Papova virus. The human papillomavirus (HPV) is a member of this latter group which is known to give rise to the lesions of verruca vulgaris and condyloma acuminatum. It seems likely that squamous papillomas of the larynx are also caused by this virus. The HPV has not been propagated in culture. Electron microscopic observations have for the most part been unsuccessful in the search for virus particles in laryngeal papillomas. Virus-like structures have been found in the nuclei of laryngeal squamous papilloma cells. After an extensive search, however, the localization of HPV antigen using the immunoperoxidase method in paraffin sections of squamous papillomas has yielded more encouraging results. The antibody detects HPV antigen in nuclei of squamous cells of the papillomas, near the surface of the tumor. Greater sensitivity in the detection of HPV and its types has become available with the use of molecular biological techniques, in particular that of in situ hybridization which has enabled the demonstration of HPV type 6 and the related type 11 in the cells of benign papillomas. The hybridization signal, like that of immunocytochemical positivity, is always confined to the nuclei of the superficial stratified squamous epithelium. Both viral types are usually found together. About 66% of both adult and juvenile cases are positive for HPV types 6 and 11. The proportion of cases giving positive signals for HPV is, however, much higher in cases with multiple confluent lesions than in those with single isolated lesions. It seems possible that the detection of HPV 6 and 11 in biopsy specimens at initial endoscopy might be a useful prognostic indicator, because those patients whose biopsy tissue shows many nuclei positive for HPV types 6 and 11, especially on more than one occasion, are more likely to have a worse eventual outcome. The presence of HPV 6 and 11 may also be used to monitor interferon treatment. The presence of signal for virus is closely correlated with that of koilocytosis in routinely stained sections.

References