MALIGNANT TRANSFORMATION OF RECURENT JUVENILE LARYNGEAL PAPILOMATOSIS

K. N. Subramaniam, N. Prepageran, M. A. Jalaludin, Gopala Krishnan
Dept. of Otorhinolaryngology, University of Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia

Introduction

Recurrent juvenile laryngeal papilloma, although usually confined to the larynx canoccasionally progress into nasopharynx, trachea and even into extensive bronchopulmunary disease. Most cases of recurrent laryngeal papilomatosis withbronchopulmunary involvement are cytologically benign and do not undergomalignant transformation. However, very rarely squamous cell carcinoma can arise in recurrent juvenile laryngeal papiloma in the absence of known risk factors such as radiation and smoking.

Case report

The patient was a 22-year-old lady with a history of symptomatic laryngeal papilomatosis since early childhood. Her first presentation to the Otorhinolaryngologist was at the age of 2 with history of stridor. A diagnosis of juvenile laryngeal papilomatosis was made then. A tracheostomy was perfonned in 1977 (at the age of 4 years) to maintain an open airway in view of her airway obstruction. Her condition necessitated multiple endoscopic removal of laryngeal papilomas and thus was referred to UMMC in 1986 for laser excision of the papilomas. Results of multiple biopsies were consistent with recurrent laryngeal papiloma and failed to demonstrate any evidence of malignancies. The patient was a nonsmoker, did not consume alcoholic beverages and did not receive any radiation. In 1993 (20 years of age), a routine chest x-ray revealed an opacity in the right upper zone. Biopsy of the lesion was concluded as benign and thus she was referred to the cardio thoracic unit where she underwent right upper lobectomy. During the operation, seedlings of the papilomas were noted in lower right lobe.

In view of the extensive and recurrent nature of the lesion with tracheobronchial involvement, the decision to start interferon was made. She was given an induction dose 3 miu daily (I.M.) for 28 days. This was followed by a maintenance dose of 3 miu (I.M) three times per week. Her progress was carefully monitored and serial CT scans were done to evaluate her progress. Despite the interferon therapy, the papilomas were noted to rapidly increase in size. The decision to use 5 cycles of 5-Fluro Uracil was then made. However in mid 1995 (22 years of age), she was noted to have changes in her routine CT scan compatible with malignant change and enlargement of right pre hilar lymph nodes was noted (Figure 1). Biopsy of the lung lesion was reported as Squamous cell Carcinoma. Patient was again referred to the Cardio thoracic unit and right pnuemonectomy was done. Intraoperatively, tissues were removed from chest wall and these were also noted to be invaded by carcinoma. The decision was made for chemotherapy followed by radiotherapy. She underwent one cycle of Mitramycin, Ifosomide and Cisplatin, however she expired after the first month of chemotherapy.

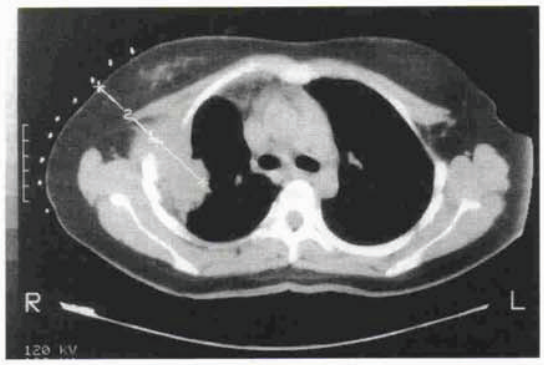

Figure 1. CT scan of lung showing carcinoma and rib erosion

Discussion

Juvenile laryngeal papilomatosis are the most commonest benign neoplasms of the respiratory tract of children. The exact etiology still remains unknown although viral cause is widely believed. These lesions are multiple, recurrent and often involve bronchi and bronchioles, even extending into alveolar region. These lesions rarely undergo malignant transformation unless previously radiated. Adult laryngeal papilomas on the other hand are less frequently seen and are usually solitary. They also have a much higher incidence of

Corresponding address:
Dr. K. N. Subramaniam
Dept. of Otorhinolaryngology
University of Malaya Medical Centre
50603 Kuala Lumpur, Malaysia

malignant transformation.

Juvenile laryngeal papilomatosis often starts in the upper airway and progresses to involve distally. Several hypotheses have been suggested for this behavior, including posttraumatic transplantation following intubation, multiple biopsies, tracheostomy and also viral dissemination. Such recurrence and spread is not seen in the adult variety. It has been suggested that multiple lesions, deeply attached lesions, severe basal cell hyperplasia, high nuclear cytoplasm ratio and large nuclei are more prone to recurrence (I). Distal spread to bronchiole tree and alveoli is also associated with higher risk of neoplasm than papilomas confined to the laryngeal region. This is also associated with higher morbidity with higher incidence of pneumonia, brochiectasis and abscesses.

There have been several reports of malignant transformation in juvenile laryngeal papiloma in the western world. Toso reported a patient who was a heavy smoker with a late age of onsef (2); Shapiro *et al* described a patient who was a heavy smoker and an alcoholic (3). In situ and invasive malignant neoplasm was noted in the laryngeal papilomas. Brach *et al* and Russel and Kessler reported young patients who were non-smokers with lung involvement and malignant transformation was noted in the lung lesions. 2 cases were reported in the German literature; Kaiser and Justus each described malignant change in long-standing, recurrent juvenile papilomas without radiotherapy (4). Chandra Bewtra described a similar case in 1982. The first 2 reports suggested that heavy smoking and alcohol consumption might have contributed to the malignant change. The other reports have many similarities to our patient. In all of these cases, including ours, extensive papilomatosis involving pulmonary airways with malignant transformation involving pulmonary regions, for which, no demonstrable cause is found.

Use of radiotherapy is contraindicated in the treatment of recurrent juvenile laryngeal papilomatosis, as is it associated with an increased incidence in malignant change (1). The incidence of stricture, cartilage necrosis and abnormal maturation of larynx has also been noted. Laser has been effectively used in many centers as the main modality of treatment of surgical excision of papilomas and till date, there has been no evidence to link it to any malignant transformation. 5 Floro Uracil was used in this patient due to the rapid involvement of the pulmonary tree and has not been shown to cause any malignant change either. Rady in 1998 showed that malignant transformation of recurrent laryngeal papilomatosis is associated with integrated human papillomavirus type 11 DNA and mutation of P53(5). In conclusion, incidence of malignant change is higher in long standing, severe, diffuse papilomatosis of the tracheo bronchial tree and this may arise as a result of radiotherapy, smoking and alcohol consumption and very rarely spontaneously.

References

1. Chandra Bewtra, R. Krishnan, S.L. L Malignant change in non-irradiated JRPPARCH-OTO 1982; 8; 114-116.
2. Toso G: Benign or Malignant? Laryngoscope 197: 81: 1524-1521.
3. Shapiro. Malignant degeneratlon ofnon-irradiated JKRP Ann Utol 1976; 85: 10-110.
4. Justus: HNO 1970; 18: 349-3354.
5. Rady, Schndigm Weiss, Hughes, Tyring, Laryngoscope 1998, 735-740.