Solitary Squamous Papilloma of the Bronchus Associated with Human Papilloma Virus Type 11


A 79-year-old female presented with persistent dry cough, and a chest radiograph showed a mass shadow in the right upper lung. Bronchoscopic examination revealed that the right main bronchus was severely obstructed by a polypoid tumor, which was diagnosed pathologically as squamous papilloma. After the failure of the attempted endobronchial snare to remove the tumor, right upper lobectomy was performed. The polymerase chain reaction (PCR) examination showed the presence of human papilloma virus type 11 DNA in the resected tumor, suggesting that this virus was the cause of this solitary squamous papilloma of the lung.

Key words: pathology, polymerase chain reaction, bronchoscopy

Introduction

Solitary squamous papilloma of the bronchus is a rare tumor. The incidence of this tumor is reported to be only five cases in 15,000 bronchoscopies (1). In Japan, only 16 cases have been reported (2), though these reports lacked an examination for human papilloma virus (HPV). The polymerase chain reaction (PCR) examination has been applied successfully in detection of HPV DNA in clinical samples; consensus primers of a broad spectrum of HPV genotypes have been developed, and the amplified HPV DNA can be typed by subsequent restriction mapping (3). This report documents an elderly female affected by a solitary squamous papilloma, in which the presence of human papilloma virus type 11 was confirmed by these examinations.

Case Report

A 79-year-old female suffered from a dry cough for about ten months; symptoms gradually worsened and dyspnea (Hugh-Jones II) started two months prior to admission. A general physician discovered an abnormal chest shadow, and she was referred to our hospital. She reported not having a history of appetite loss, weight loss or other diseases. The patient had no history of smoking and was not taking any medications.

Pulmonary examination revealed that the lungs were clear of auscultation, and results of the remaining physical examination were normal. Results of routine laboratory studies were unremarkable. Chest radiograph showed a mass shadow in the right upper lung. Bronchoscopic examination revealed that the right main bronchus was severely obstructed by a polypoid tumor. The tumor was arising from the right upper lobe and had a milky-white, smooth, cauliflower-like shape (Fig. 1). There were no tumorous lesions in the larynx or other bronchi. Pathologically, this tumor was determined to be a squamous papilloma. A repeated bronchoscopy was performed to remove the tumor by an endobronchial electrocautery using the snare technique. However, this approach failed because the tumor was so large that it was difficult to remove completely. The patient then underwent resection of the right upper lobe. The pathological findings showed that the papillomatous tumor measuring $3 \times 3 \times 4$ cm arose from the upper lobe bronchial mucosa and extending endobronchially. The tumor consisted of large numbers of papillomatous fronds, all lined by hyperplastic squamous epithelium showing mild parakeratosis. Koilocytosis was not seen in the squamous epithelium. Mitotic figures were rare and malignant degeneration was not found (Fig. 2). Therefore, the diagnosis of solitary squamous papilloma of the bronchus was established. A frozen tissue block was sent to a laboratory (SRL Company, Tokyo) for PCR examination with consensus primers to detect HPV DNA. In this study, HPV DNA was detected in the tumor, and the subsequent restriction mapping...
Discussion

Bronchial papillomas have three clinical presentations: multiple papillomas, inflammatory polyps, or solitary papillomas (4). Multiple papillomas are usually seen in children, and affect the larynx, trachea and bronchi. They are associated with the HPV. Inflammatory polyps arise in chronically inflamed bronchial mucosa. They should not be considered as neoplasms, and are not associated with the HPV. Solitary papillomas are the rarest type. They usually present as an endobronchial mass in the segmental bronchi and may go undetected for years. Their highest prevalence is reported to be in males in their 50s (5, 6). From the review of solitary squamous papilloma in 16 Japanese cases, five cases were asymptomatic and a high incidence was seen in patients in their 60s, with male cases being slightly more frequent (2). The present patient was 79-year-old and had symptoms of a recent dry cough. She did not have a chest radiograph for more than ten years, and may have had a papilloma when she was in her 60s without any symptoms.

The relationships between the type of HPV and the pathology of various diseases have been studied (7, 8). Since HPV protein E6 and E7 have a function which are able to bind the protein products of the tumor suppressor genes p53 and the retinoblastoma protein, HPV infection can induce cellular proliferation or dysplasia. Different HPV subtypes show different binding properties to these proteins; the E6 protein of HPV type 16 and 18 associates strongly with the wild type p53 protein in vitro, while that of HPV type 6 and 11 associates weakly or not at all (7). As a result, the degree of malignancy could be affected by the type of HPV. Actually, HPV type 16 and 18 are frequently associated with carcinomas of the uterine cervix and vulva, and are sometimes associated with lung cancer. On the other hand, HPV type 6 and 11 are considered to involve and result in benign multiple squamous papilloma of the larynx, trachea and bronchi. In the present case, the presence of HPV type 11 was demonstrated in resected material using a PCR examination, and our results indicated that HPV type 11 infection also might be a cause of solitary squamous papilloma of the lung. Flieder et al showed that HPV DNA was detected in 5...
of 7 solitary squamous cell papillomas (71%) using in situ hybridization (5). Katial et al speculated that the virus is acquired through aspiration of infected secretions of sexually active young males, which accounts for the late clinical presentation of solitary squamous papilloma in older males (9). However, the exact pathophysiology of solitary squamous papilloma has not been determined.

In the treatment of the present patient, endobronchial electrocautery was performed initially (10). Because of the failure to remove the tumor and to control the symptoms, upper lobectomy was conducted. Malignant change was not demonstrated in our case. However, a probable role for HPV type 11 in the process of malignant conversion in squamous papilloma has been reported (11), and curative resection may be recommended even in elderly patients. In small lesions, it is thought to be sufficient to cure only via bronchoscopic treatment such as electrocautery or photodynamic therapy or YAG laser (1).

In conclusion, a solitary squamous papilloma, which is a very rare lesion, was found in an elderly female patient. HPV type 11, detected by PCR methods, was considered to be associated with the pathological process of solitary squamous papilloma.

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References